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Establishment and validation of a prediction model for death during hospitalization in elderly patients with sepsis combined with acute kidney injury

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Abstract: Objective To initially establish a prediction model for death during hospitalization in elderly patients with sepsis combined with acute kidney injury (AKI) and validate it. **Methods** Clinical data of 378 elderly patients with sepsis combined with AKI treated in the First Affiliated Hospital of Harbin Medical University from January 2019 to December 2023 were retrospectively included. The clinical data of 378 elderly patients with sepsis combined with AKI treated in The First Affiliated Hospital of Harbin Medical University from January 2019 to December 2023 were retrospectively included. Based on the outcome during hospitalization, they were divided into death group (122 cases, 32.28%) and survival group (256 cases, 67.72%). Multivariate logistic regression was used to screen the independent risk factors for hospitalized death in septic AKI patients, and a prediction model was established accordingly. The model was evaluated using receiver operating characteristic (ROC) curves. **Results** The results of multivariate logistic regression showed that age>70 years (*OR*=1.387, *95%CI*:1.083-1.776), AKI stage III (*OR*=2.006, 95 *CI*: 1.388-2.899), Sequential Organ Failure Assessment (SOFA) score>10 (*OR*=1.791, *95%CI*:1.266-2.536), procalcitonin (PCT)>3.67 ng/mL (*OR*=1.553, *95%CI*: 1.166-2.068), and activated partial thromboplastin time (APTT)>40 s (*OR*=1.290, 95%CI:1.090, 95%CI: 1.090, 95%CI: 1.090, 95%CI: 1.090, *95%CI*: 1.090). *95%CI*:1.040-1.602) were independent risk factors for all-cause mortality during hospitalization in elderly patients with sepsis combined with AKI (*P*<0.05). Based on the results of multivariate analysis, an equation for the risk of in-hospital death (C-index) in patients with sepsis combined with AKI was established, C-index = -1.722 + 0.327 × (age) + 0.696 × (AKI stage) + 0.583 × (SOFA) + 0.440 × (PCT) + 0.255 × (APTT). The ROC curves showed that the C-index predicted all-cause mortality in elderly patients with sepsis combined with AKI. The index predicted in-hospital death in elderly patients with sepsis combined with AKI with an AUC of 0.876 (95% *CI:* 0.837-0.915), an accuracy of 81.22%, a sensitivity of 78.69% and a specificity of 82.42%. **Conclusion** The prediction model based on age, SOFA score, PCT, AKI staging, and APTT can help to identify the high-risk group of elderly patients with sepsis combined with AKI at an early stage of death during hospitalization, and then intervene and adjust the treatment strategy at an early stage, which can help to improve the prognosis of patients.

Keywords: Elderly; Sepsis; Acute kidney injury; Activated partial thromboplastin time; Sequential Organ Failure Assessment
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Sepsis, a systemic syndrome due to dysregulated infection, is a common critical condition in intensive care medicine, which can cause multi-system injury and high risk of short-term mortality, and is one of the major challenges in global public health. Acute kidney injury (AKI) is the most common peripheral organ injury in sepsis, which manifests itself as an acute decline in renal function, and sepsis-associated AKI accounts for about 50% of all types of AKIs. Even with early intervention, renal function is difficult to fully recover in a short period of time in the majority of cases, and adversely affects the patient's prognosis, and is an important cause of ICU death [1-2]. Currently, there are major difficulties in the prevention of AKI, and common molecular markers for early diagnosis of AKI also have the limitation of insufficient sensitivity, so early identification of AKI is also difficult. Early intervention to reduce deaths in patients with sepsis-associated AKI is a key clinical concern [3]. To date, studies related to sepsis-associated AKI have focused on the clinical characterization of the patients and the diagnostic aspects of AKI, with a lack of in-depth analysis of prognosis [4-6]. The establishment of a prediction model that can predict the death of AKI patients with sepsis is of great clinical significance, as it can help to identify the high-risk group for death at an early stage and then provide targeted interventions according to the risk factors, which can not only improve the efficiency of diagnosis and treatment, but also help to optimize the medical resources. This study established a preliminary prediction model of death during hospitalization in elderly patients with sepsis combined with AKI and evaluated it, aiming to provide reference for clinical decision-making.

1 Material and methodology

1.1 Study subjects

The clinical data of 378 elderly patients with sepsis combined with AKI who were hospitalized from January 2019 to December 2023 in the First Hospital of Harbin Medical University were retrospectively included.

Inclusion criteria: (1) meeting the diagnostic criteria related to AKI due to sepsis [7-8] ; (2) elderly population, aged ≥60 years; (3) hospitalization with clear clinical regression during hospitalization.

Exclusion criteria: (1) the presence of previous renal diseases; (2) the combination of other critical diseases, such as acute pancreatitis, severe pneumonia; (3) the presence of immune dysfunction, hematologic diseases and chronic infectious diseases; (4) hospitalization time of less than 24 hours.

1.2 Methodology

1.2.1 Data collection

Baseline clinical data of patients were collected through online medical records, which mainly included demographic characteristics, comorbidities, severity of sepsis, hematological indexes at admission and AKI stage. Among them, demographic characteristics included gender, age, smoking, and alcohol consumption. Comorbidities included diabetes mellitus and hypertension. The severity of sepsis was primarily assessed using the APACHE II score and the Sequential Organ Failure Assessment (SOFA) score. Hematological indicators included complete blood count (leukocytes, platelets), liver function [albumin, alanine aminotransferase (ALT), aspartate transferase (AST), lactate], renal function (uric acid), inflammatory factors [C-reactive protein (CRP), procalcitoninogen (PCT), interleukin 17 (IL-17)], and coagulation function [fibrinogen, D-dimer, prothrombin time (PT), activated partial thromboplastin time (APTT)].

1.2.2 Study grouping

Based on the regression during hospitalization, patients with sepsis AKI were divided into 122 cases (32.28%) in the death group and 256 cases (67.72%) in the survival group.

1.3 Statistical methods

Statistical analysis was performed using the R software. Continuous variables were described by $\bar{x}\pm s$, and independent sample *t* test was used for comparison between groups. Categorical variables were described by cases (%), and χ^2 test was performed for comparison between groups. Multivariate logistic regression was used to screen the independent risk factors for in-hospital death in septic AKI patients, and a prediction model was established accordingly. The model was evaluated using the ROC curve. $P<0.05$ was considered as statistically significant difference.

2 Results

2.1 Univariate analysis of death in patients with sepsis combined with AKI

Compared with the survival group, the death group accounted for a significantly higher proportion of advanced age (>70 years), coronary heart disease, AKI stage III, high SOFA score, elevated lactate levels, increased PCT, IL-17, fibrinogen, APTT levels, and decreased albumin levels, and the difference was statistically significant ($P<0.05$). The difference between the two groups in terms of gender and underlying coexisting diseases was not statistically significant ($P>0.05$). **[Table 1]**

Tab.1 Comparison of clinical data between the death group and the survival group

Item	Death group (*n*=122)	Survival group (*n*=256)	t/χ^2 value	*P* value
Sex [cases (%)]			1.131	0.288
male	78 (63.93)	149 (58.20)		
female	44 (36.07)	107 (41.80)		
Age [cases (%)]			5.648	0.018
≤ 70 years	32 (26.23)	99 (38.67)		
>70 years old	90 (73.78)	157 (61.33)		
Diabetes mellitus [cases (%)]	43 (35.25)	77 (30.08)	1.018	0.312
Hypertension [cases (%)]	50 (40.98)	81 (31.64)	3.185	0.074
Coronary heart disease [cases (%)]	23 (18.85)	26 (10.16)	6.154	0.013
Smoking [cases (%)]	48 (39.34)	91 (35.54)	0.512	0.474
Alcohol consumption [cases (%)]	49 (40.16)	112 (43.75)	0.435	0.510
AKI staging [cases (%)]			36.008	<0.001
I	24 (19.67)	115 (44.92)		
II	36 (29.51)	84 (32.81)		
III	62 (50.82)	57 (22.27)		
APACHE II ($\bar{x}\pm s$)	27.35±5.84	26.13±5.37	1.952	0.052
SOFA ($\bar{x}\pm s$)	10.53±2.76	9.11±2.32	5.091	0.000
Platelets ($\times10^9$/L, $\bar{x}\pm s$)	116.33±27.91	122.15±30.06	1.746	0.082
Albumin (g/L, $\bar{x}\pm s$)	28.89±5.17	30.12±4.94	2.167	0.031
Leukocytes ($\times10^9$/L, $\bar{x}\pm s$)	14.98±3.56	14.21±3.69	1.862	0.064
ALT (U/L, $\bar{x}\pm s$)	36.17±7.62	34.92±8.15	1.380	0.168
AST (U/L, $\bar{x}\pm s$)	43.78±12.39	41.80±10.11	1.610	0.108
Uric acid (μmol/L, $\bar{x}\pm s$)	323.59±68.13	308.77±72.16	1.843	0.066
Lactate (mmol/L, $\bar{x}\pm s$)	2.60±0.51	2.48±0.49	2.135	0.033
CRP (mg/L, $\bar{x}\pm s$)	49.38±12.17	47.56±10.91	1.421	0.156
PCT (ng/mL, $\bar{x}\pm s$)	3.82±1.13	3.29±0.84	4.990	<0.001
IL-17 (ng/L, $\bar{x}\pm s$)	32.12±7.91	30.40±6.58	2.166	0.031
Fibrinogen (g/L, $\bar{x}\pm s$)	4.80±1.22	4.29±1.43	3.287	0.001
D-dimer (mg/L, $\bar{x}\pm s$)	4.21±0.95	4.10±0.92	1.045	0.297
PT (s, $\bar{x}\pm s$)	21.59±5.83	20.37±5.56	1.908	0.057
APTT (s, $\bar{x}\pm s$)	41.32±6.76	38.67±5.49	3.962	<0.001

2.2 Multivariate analysis of death in patients with sepsis combined with AKI

Indicators with $P<0.05$ in the univariate analysis were further screened for factors influencing in-hospital

death in patients with sepsis combined with AKI using multivariate logistic regression. The variable assignments are shown in **Table 2**. The results showed that age >70 years, SOFA score >10, PCT >3.67 ng/mL, AKI stage III, and APTT >40 s were independent risk factors for all-cause mortality during hospitalization in elderly patients with sepsis-combined AKI (P<0.05). **[Table 3]**

Tab. 2 Multivariate analysis variables for mortality in sepsis patients with AKI

Variables	Description of the assignment
Y (dependent variable)	Death during hospitalization = 1, survival = 0
Independent variable	
X1 (age)	>70 years = 1, ≤70 years = 0
X2 (coronary heart disease)	Yes = 1, No = 0
X3 (AKI staging)	Phase III = 1, I-II = 0
X4 (SOFA)	>10 points = 1, ≤10 points = 0
X5 (Albumin)	>30 g/L=1, ≤30 g/L=0
X6 (lactate)	>2.56 mmol/L=1, ≤2.56 mmol/L=0
X7 (PCT)	>3.67 ng/mL=1, ≤3.67 ng/mL=0
X8 (IL-17)	＞32 ng/L=1, ≤32 ng/L=0
X9 (fibrinogen)	＞4.50 g/L=1, ≤4.50 g/L=0
X10 (APTT)	＞40 s=1, ≤40 s=0

Tab. 3 Multivariate logistic regression analysis of mortality in sepsis patients with AKI

Variables	*β*	*SE*	*Wald*	*OR (95% CI)*	*P* value
Constant	-1.722	0.442	15.212	-	
Age	0.327	0.126	6.718	1.387 (1.083-1.776)	0.009
AKI staging	0.696	0.188	13.716	2.006 (1.388-2.899)	<0.001
SOFA	0.583	0.177	10.811	1.791 (1.266-2.536)	0.001
PCT	0.440	0.146	9.057	1.553 (1.166-2.068)	0.003
APTT	0.255	0.110	5.348	1.290 (1.040-1.602)	0.021

2.3 Prediction model

According to the results of multivariate analysis, assuming that the risk index of hospitalized death in patients with sepsis combined with AKI is C-index, it can be seen that C-index = -1.722 + 0.327 × (age) + 0.696 × (AKI stage) + 0.583 × (SOFA) + 0.440 × (PCT) + 0.255 × (APTT). ROC curve showed that the AUC of C-index for predicting in-hospital death in elderly patients with sepsis combined with AKI was 0.876 (95% *CI*: 0.837-0.915), with an accuracy of 81.22%, a sensitivity of 78.69%, and a specificity of 82.42%, as shown in **Figure 1**.

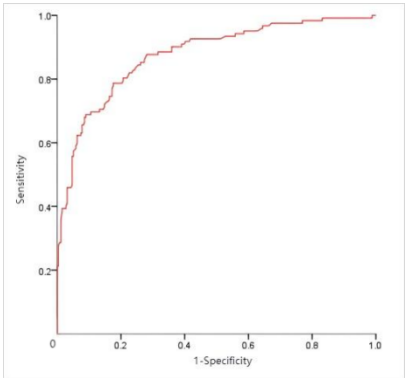

Fig.1 ROC curve for predicting in-hospital mortality in elderly sepsis patients with AKI using the model

3 Discussion

Sepsis in elderly has its own characteristics, such as atypical symptoms, susceptibility to multi-organ disorder, and the occurrence of AKI is more common. After the emergence of AKI, due to the sharp decline in renal function, it can lead to various metabolic toxic substances can not be excreted from the body and re-enter the circulation, which then exacerbates the severity of sepsis and further aggravates the multi-organ damage, and even leads to the death of the patient. Reports show that AKI is an independent risk factor for sepsis death, and the mortality rate can reach 80% if hemodialysis is needed[1]. In clinical practice, the mortality during hospitalization of patients with sepsis AKI varies in different studies due to factors such as patients' underlying conditions, medical conditions, and disease severity. White *et al.*[5] in a retrospective cohort study included 84,528 patients in 12 ICUs from 2015 to 2021, of which 13,451 met the diagnostic criteria for sepsis combined with AKI, and the mortality rate of such patients had a mortality rate of 18% during hospitalization. A study included 2,192 patients with sepsis-combined AKI in the MIMIC-IV database between 2008 and 2019, and the mortality rate during hospitalization ranged from 28.3% to 41.3%. The results of this study showed that 32.28% of patients with sepsis combined with AKI died during hospitalization, which is in line with the above report and similar to the results of previous data from our center (35.23%) [6], suggesting that patients with sepsis combined with AKI still face a high threat of death during hospitalization, and that it is important to strengthen the identification of high-risk groups.

The results of this study showed that age >70 years, SOFA score >10, PCT >3.67 ng/mL, AKI stage III, and APTT >40 s were independent risk factors for all-cause mortality during hospitalization in elderly patients with sepsis combined with AKI. Advanced age is one of the susceptibility factors for AKI, with age, multiple organ functions gradually decrease, and most of them are combined with underlying diseases, which further increase the damage to the kidneys[10]. In addition, after the development of AKI, elderly people may be unfavorable to early diagnosis and treatment due to the fact that their symptoms are masked by the underlying diseases, which increases the risk of death. A study based on the clinical data of 14,240 patients with sepsis in the MIMIC-IV database analyzed the risk factors for death in such patients and found that advanced age directly increased both immediate and long-term mortality[11]. A retrospective cohort study found that age >70 years was an independent risk factor for sepsis death in the elderly, and a model based on five indicators, including age and lactate, allowed early identification of individuals at high risk of death[12]. Clinical management of elderly patients with sepsis AKI should be strengthened and renal function should be closely monitored for early identification of individuals at high risk of death.

The SOFA score is the most commonly used clinical system for assessing critical illness and its severity, and it

is particularly applicable to patients with organ failure. He *et al.* [13] evaluated the correlation between the SOFA score and AKI due to sepsis by using different machine learning models, and found that the change in the SOFA score from day 1 to day 3 could help to predict the onset of acute kidney disease including AKI, and it has a good recognition value for AKI. Luo *et al.* [14] in their study based on the clinical data of 12,132 patients with sepsis-induced AKI from the MIMIC-IV database, found that as the SOFA score increased, the in-hospital mortality increased. Previous studies have shown that monitoring SOFA changes can help in early identification of trends in renal function in patients with sepsis-induced AKI and early development of interventions[6]. Screening of patients with septic AKI is facilitated by SOFA score in order to identify individuals at high risk of death.

PCT is a traditional inflammatory marker and injury due to inflammatory response plays a dominant role in the development of AKI, and the index has a higher specificity for sepsis, and its level changes significantly only in severe infections. Therefore, an elevated level of PCT suggests that there is a high level of inflammatory response in the patient, and their risk of AKI increases. Xu *et al.* [6] showed that PCT was an independent risk factor for death in patients with sepsis-associated AKI, with a 39.8% increase in the risk of in-hospital death for each unit of elevation. Lai *et al.* [15] constructed a model based on PCT, hypertension, diabetes mellitus and C-reactive protein that had a high discriminatory ability for individuals with sepsis-associated AKI and death at 28 days. The effect of PCT on the predictive ability of the model has the most significant effect on the predictive ability of the model. The inflammatory state of patients with sepsis-associated AKI combined with elevated PCT should be promptly corrected to reduce mortality.

AKI staging measures changes in renal function, with higher stages indicating more severe renal injury and causing irreversible damage and increased risk of death. Xing *et al.*[11] analyzed the causes of death in elderly sepsis patients and found that the proportion of AKI stage III was significantly higher in the death group, and after correcting for confounders, sepsis patients with AKI stage III were found to have a 98.2% increased risk of death. A cohort study based on 2,066 patients with sepsis combined with AKI from the MIMIC III database showed a significant positive correlation between AKI stage and risk of death[16]. Therefore, patients with higher AKI stage should be actively intervened to prevent further progression of the disease.

Abnormal coagulation is one of the common systemic manifestations in sepsis patients and is closely related to disease regression, manifested by prolonged APTT and PT, low platelet counts, and a hypercoagulable state of the blood leading to microthrombosis, which further aggravates renal lesions and systemic multiorgan damage. A study included 615 patients admitted to ICU with sepsis and showed that elevated APTT was an independent risk factor for developing AKI and had a predictive value for the risk of near-term mortality in patients with septic AKI [15]. A retrospective cohort study showed that among septic AKI patients, the death group had a higher level of APTT than the survival group, and there was a positive correlation between prolonged APTT and significantly shorter survival rate and survival time, and multivariate analysis confirmed that an APTT of >40 s was an independent risk factor for death in septic AKI patients[17]. It is suggested that monitoring the changes of coagulation indexes in septic AKI patients can help to predict their clinical regression.

Currently, researchers have developed many models for sepsis, such as Xing *et al.*[11] established a prediction model for all-cause mortality during hospitalization for elderly sepsis based on age, lactate, and AKI stage. Li *et al.* [18] developed a prediction model for the occurrence of AKI in sepsis patients, and they pointed out that the inflammatory state should be corrected in time to reduce the occurrence of AKI. Lin [19] and Zhao *et al.* [20] developed a column chart of 28-d mortality in patients with sepsis-induced AKI based on the screening of clinical data, which could help to identify patients at high risk of death at an early stage. However, both studies did not target the elderly, and the sample sizes were small, resulting in unstable analysis results. In the present study, we established a prediction model of death during hospitalization in elderly patients with sepsis-induced AKI, which consisted of 5 indicators, namely, age, SOFA score, PCT, AKI stage, and APTT, which could assess the severity of sepsis and renal lesions from multiple dimensions and then predict the risk of death, and was evaluated to have a high accuracy in identifying high-risk patients, which has a potential value for clinical application.

In summary, a prediction model based on age, SOFA score, PCT, AKI stage, and APTT can help in early identification of elderly patients with sepsis combined with AKI who are at high risk of death during hospitalization and thus early intervention. Since the model component indicators are all readily available, it is expected to offer healthcare providers a practical tool that can transform patient care and ultimately improve clinical prognosis. However, due to the lack of an independent dataset to externally validate the model in this study, the exact conclusions still require in-depth research.

Conflict of interest None

Reference

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·论　著·

老年脓毒症合并急性肾损伤住院死亡预测模型建立与验证

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摘要：目的　初步建立老年脓毒症合并急性肾损伤（AKI）患者住院期间死亡的预测模型，并进行验证。**方法**　回顾性纳入 2019 年 1 月至 2023 年 12 月于哈尔滨医科大学附属第一医院治疗的 378 例老年脓毒症合并 AKI 患者的临床资料。根据住院期间转归，将其分为死亡组 122 例（32.28%）和生存组 256 例（67.72%）。采用多因素 logistic 回归法筛选脓毒症 AKI 患者住院死亡的独立危险因素，并据此建立预测模型。采用受试者工作特征（ROC）曲线对模型进行评价。**结果**　多因素 logistic 回归结果显示，年龄>70 岁（*OR*=1.387，95%*CI*：1.083～1.776）、AKI Ⅲ期（*OR*=2.006，95%*CI*：1.388～2.899）、SOFA 评分>10 分（*OR*=1.791，95%*CI*：1.266～2.536）、PCT>3.67 ng/mL（*OR*=1.553，95%*CI*：1.166～2.068）、APTT>40 s（*OR*=1.290，95%*CI*：1.040～1.602）是老年脓毒症合并 AKI 患者住院期间全因死亡的独立危险因素（*P*<0.05）。建立脓毒症合并 AKI 患者住院死亡风险（C-index）的方程，即 C-index=−1.722+0.327×（年龄）+0.696×（AKI 分期）+0.583×（SOFA）+0.440×（PCT）+0.255×（APTT）。ROC 曲线显示，C-index 预测老年脓毒症合并 AKI 患者住院死亡的曲线下面积为 0.876（95%*CI*：0.837～0.915），准确率为 81.22%，敏感度为 78.69%，特异度为 82.42%。**结论**　基于年龄、SOFA 评分、PCT、AKI 分期、APTT 建立的预测模型有助于早期识别老年脓毒症合并 AKI 患者住院期间死亡高风险人群，进而早期干预并调整治疗策略，有助于患者预后的改善。

关键词：老年；脓毒症；急性肾损伤；活化部分凝血酶时间；序贯器官衰竭评分

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Abstract: Objective　To initially establish a prediction model for death during hospitalization in elderly patients with sepsis combined with acute kidney injury (AKI) and validate it. **Methods**　Clinical data of 378 elderly patients with sepsis combined with AKI treated in The First Affiliated Hospital of Harbin Medical University from January 2019 to December 2023 were retrospectively included. Based on the outcome during hospitalization, they were divided into death group (122 cases, 32.28%) and survival group (256 cases, 67.72%). Multivariate logistic regression was used to screen the independent risk factors for hospitalized death in septic AKI patients, and a prediction model was established accordingly. The model was evaluated using receiver operating characteristic (ROC) curves. **Results**　The results of multivariate logistic regression showed that age>70 years (*OR*=1.387, 95%*CI*: 1.083-1.776), AKI stage Ⅲ (*OR*=2.006, 95%*CI*: 1.388-2.899), sequential organ failure assessment (SOFA) score>10 (*OR*=1.791, 95%*CI*: 1.266-2.536), procalcitonin (PCT)>3.67 ng/mL (*OR*=1.553, 95%*CI*: 1.166-2.068), and activated partial thromboplastin

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time (APTT) >40 s (*OR* = 1.290, 95%*CI*: 1.040-1.602) were independent risk factors for all-cause mortality during hospitalization in elderly patients with sepsis combined with AKI ($P<0.05$). Based on the results of multivariate analysis, an equation for the risk of in-hospital death (C-index) in patients with sepsis combined with AKI was established, C-index = -1.722+0.327×(age)+0.696×(AKI stage)+0.583×(SOFA)+0.440×(PCT)+0.255×(APTT). The ROC curves showed that the C-index predicted in-hospital death in elderly patients with sepsis combined with AKI with an AUC of 0.876 (95%*CI*: 0.837-0.915), an accuracy of 81.22%, a sensitivity of 78.69% and a specificity of 82.42%. **Conclusion** The prediction model based on age, SOFA score, PCT, AKI staging, and APTT can help to identify the high-risk group of elderly patients with sepsis combined with AKI at an early stage of death during hospitalization, and then intervene and adjust the treatment strategy at an early stage, which can help to improve the prognosis of patients.

Keywords: Elderly; Sepsis; Acute kidney injury; Activate partial thrombin time; Sequential organ failure assessment
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脓毒症是由于感染失调所致的全身综合征,是重症医学科的常见危重症,可引发多系统损伤,短期死亡风险高,是全球性公共卫生领域面临的重要挑战之一。急性肾损伤(acute kidney injury, AKI)是脓毒症最常见的外周器官损伤,表现为急性肾功能下降,脓毒症相关 AKI 约占临床所有 AKI 的 50%,即使进行早期干预,多数病例的肾脏功能难以在短时间内完全恢复,并对患者预后造成不利影响,是 ICU 死亡的重要原因[1-2]。目前,对于 AKI 的预防存在较大困难,常见的 AKI 早期诊断分子标志物也存在敏感性不足的局限性,因此,早期识别 AKI 也具有一定难度。早期干预,减少脓毒症相关 AKI 患者死亡,是临床关注的重点[3]。目前,脓毒症合并 AKI 的相关研究,主要聚焦于此类人群的临床特征分析和 AKI 的诊断方面,而对预后缺少深入分析[4-6]。建立可预测脓毒症 AKI 患者死亡的预测模型,有助于早期识别死亡高风险人群,进而根据危险因素进行针对性干预,不仅可提高诊治效率,也有助于优化医疗资源,具有重要的临床意义。本研究初步建立老年脓毒症合并 AKI 患者住院期间死亡的预测模型,并进行评价,旨在为临床决策提供参考依据。

1　资料与方法

1.1　*研究对象*　经医院伦理委会员批准,回顾性收集 2019 年 1 月至 2023 年 12 月于哈尔滨医科大学附属第一医院住院治疗的 378 例老年脓毒症合并 AKI 患者的临床资料。纳入标准:(1) 符合脓毒症所致的 AKI 相关诊断标准[7-8];(2) 老年人群,年龄≥60 岁;(3) 住院治疗,且住院期间具有明确的临床转归。排除标准:(1) 既往存在肾脏疾病;(2) 合并其他危重症疾病,如急性胰腺炎、重症肺炎等;(3) 存在免疫功能紊乱、血液系统疾病、慢性感染性疾病;(4) 住院时间不足 24 h。

1.2　*方法*

1.2.1　资料收集　通过在线病历收集患者的基线临床资料,主要包括人口信息学特征、合并症、脓毒症严重程度、入院时血液学指标及 AKI 分期。其中,人口信息学特征包括性别、年龄、吸烟、饮酒等;合并症包括糖尿病、高血压;脓毒症严重程度主要为急性生理与慢性健康评分(APACHE)Ⅱ、序贯器官衰竭(SOFA)评分;血液学指标包括血常规(白细胞、血小板)、肝功能[白蛋白、丙氨酸氨基转移酶(ALT)、天门冬氨酸氨基转移酶(AST)、乳酸]、肾功能(尿酸)、炎症因子[C 反应蛋白(CRP)、降钙素原(PCT)、白细胞介素 17(IL-17)]、凝血功能[纤维蛋白原、D-二聚体、凝血酶原时间(PT)、活化部分凝血酶时间(APTT)]等。

1.2.2　研究分组　根据住院期间转归,将脓毒症 AKI 患者分为死亡组 122 例(32.28%)和生存组 256 例(67.72%)。

1.3　*统计学方法*　采用 R 软件进行统计分析。连续变量采用 $\bar{x}\pm s$ 描述,组间比较采用独立样本 t 检验;分类变量采用例(%)描述,组间比较行 χ^2 检验。采用多因素 logistic 回归法筛选脓毒症 AKI 患者住院死亡的独立危险因素,并据此建立预测模型。采用受试者工作特征(ROC)曲线对模型进行评价。$P<0.05$ 为差异有统计学意义。

2　结　果

2.1　*脓毒症合并 AKI 患者死亡的单因素分析*　与生存组比较,死亡组年龄>70 岁、冠心病、AKI Ⅲ期占比高,SOFA 评分、乳酸、PCT、IL-17、纤维蛋白原、APTT 水平高,白蛋白水平低,差异有统计学意义($P<$

0.05)；两组性别、基础共患疾病等差异无统计学意义(P>0.05)。见表 1。

2.2　脓毒症合并 AKI 患者死亡的多因素分析　将单因素分析中 P<0.05 的指标进一步采用多因素 logistic 回归法筛查脓毒症合并 AKI 患者住院死亡的影响因素。变量赋值见表 2。结果显示，年龄>70 岁、SOFA 评分>10 分、PCT>3.67 ng/mL、AKI Ⅲ期、APTT>40 s 是老年脓毒症合并 AKI 患者住院期间全因死亡的独立危险因素(P<0.05)。见表 3。

2.3　预测模型　根据多因素分析结果，假设脓毒症合并 AKI 患者住院死亡的风险指数为 C-index，可知 C-index=−1.722+0.327×年龄+0.696×AKI 分期+0.583×SOFA+0.440×PCT+0.255×APTT。ROC 曲线显示，C-index 预测老年脓毒症合并 AKI 患者住院死亡的曲线下面积为 0.876(95% CI：0.837～0.915)，准确率为 81.22%，敏感度为 78.69%，特异度为82.42%。见图 1。

表 1　死亡组和生存组临床资料比较
Tab. 1　Comparison of clinical data between the death group and the survival group

指标	死亡组(n=122)	生存组(n=256)	t/χ^2 值	P 值
性别[例(%)]				
男性	78(63.93)	149(58.20)	1.131	0.288
女性	44(36.07)	107(41.80)		
年龄[例(%)]				
≤70 岁	32(26.23)	99(38.67)	5.648	0.018
>70 岁	90(73.78)	157(61.33)		
糖尿病[例(%)]	43(35.25)	77(30.08)	1.018	0.312
高血压[例(%)]	50(40.98)	81(31.64)	3.185	0.074
冠心病[例(%)]	23(18.85)	26(10.16)	6.154	0.013
吸烟[例(%)]	48(39.34)	91(35.54)	0.512	0.474
饮酒[例(%)]	49(40.16)	112(43.75)	0.435	0.510
AKI 分期[例(%)]				
Ⅰ	24(19.67)	115(44.92)		
Ⅱ	36(29.51)	84(32.81)	36.008	<0.001
Ⅲ	62(50.82)	57(22.27)		
APACHEⅡ($\bar{x}\pm s$)	27.35±5.84	26.13±5.37	1.952	0.052
SOFA($\bar{x}\pm s$)	10.53±2.76	9.11±2.32	5.091	<0.001
血小板($\times10^9$/L, $\bar{x}\pm s$)	116.33±27.91	122.15±30.06	1.746	0.082
白蛋白(g/L, $\bar{x}\pm s$)	28.89±5.17	30.12±4.94	2.167	0.031
白细胞($\times10^9$/L, $\bar{x}\pm s$)	14.98±3.56	14.21±3.69	1.862	0.064
ALT(u/L, $\bar{x}\pm s$)	36.17±7.62	34.92±8.15	1.380	0.168
AST(u/L, $\bar{x}\pm s$)	43.78±12.39	41.80±10.11	1.610	0.108
尿酸(μmol/L, $\bar{x}\pm s$)	323.59±68.13	308.77±72.16	1.843	0.066
乳酸(mmol/L, $\bar{x}\pm s$)	2.60±0.51	2.48±0.49	2.135	0.033
CRP(mg/L, $\bar{x}\pm s$)	49.38±12.17	47.56±10.91	1.421	0.156
PCT(ng/mL, $\bar{x}\pm s$)	3.82±1.13	3.29±0.84	4.990	<0.001
IL-17(ng/L, $\bar{x}\pm s$)	32.12±7.91	30.40±6.58	2.166	0.031
纤维蛋白原(g/L, $\bar{x}\pm s$)	4.80±1.22	4.29±1.43	3.287	0.001
D-二聚体(mg/L, $\bar{x}\pm s$)	4.21±0.95	4.10±0.92	1.045	0.297
PT(s, $\bar{x}\pm s$)	21.59±5.83	20.37±5.56	1.908	0.057
APTT(s, $\bar{x}\pm s$)	41.32±6.76	38.67±5.49	3.962	<0.001

表 2　脓毒症合并 AKI 患者死亡的多因素分析变量说明
Tab. 2　Multivariate analysis variables for mortality in sepsis patients with AKI

变量	赋值说明
Y(因变量)	住院期间死亡=1，生存=0
自变量	
X1(年龄)	>70 岁=1，≤70 岁=0
X2(冠心病)	是=1，否=0
X3(AKI 分期)	Ⅲ期=1，Ⅰ～Ⅱ=0
X4(SOFA)	>10 分=1，≤10 分=0
X5(白蛋白)	>30 g/L=1，≤30 g/L=0
X6(乳酸)	>2.56 mmol/L=1，≤2.56 mmol/L=0
X7(PCT)	>3.67 ng/mL=1，≤3.67 ng/mL=0
X8(IL-17)	>32 ng/L=1，≤32 ng/L=0
X9(纤维蛋白原)	>4.50 g/L=1，≤4.50 g/L=0
X10(APTT)	>40 s=1，≤40 s=0

表 3　脓毒症合并 AKI 患者死亡的多因素 logistic 回归分析
Tab. 3　Multivariate logistic regression analysis of mortality in sepsis patients with AKI

变量	β	SE	$Wald$	OR(95%CI)	P 值
常量	−1.722	0.442	15.212	—	
年龄	0.327	0.126	6.718	1.387(1.083～1.776)	0.009
AKI 分期	0.696	0.188	13.716	2.006(1.388～2.899)	<0.001
SOFA	0.583	0.177	10.811	1.791(1.266～2.536)	0.001
PCT	0.440	0.146	9.057	1.553(1.166～2.068)	0.003
APTT	0.255	0.110	5.348	1.290(1.040～1.602)	0.021

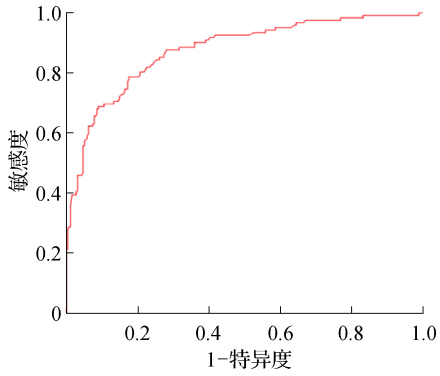

图 1　模型预测老年脓毒症合并 AKI 患者住院死亡的 ROC 曲线
Fig. 1　ROC curve for predicting in-hospital mortality in elderly sepsis patients with AKI using the model

3　讨　论

老年脓毒症具有其自身特点，如症状不典型、易发生多器官障碍，发生 AKI 更为常见。出现 AKI 后，由于肾脏功能急剧降低，可导致各种代谢毒性物质无法排出体外而重新进入体循环，继而加剧脓毒症严重程度，并进一步加重多器官损伤，甚至导致患者死亡。报道显示，AKI 是脓毒症死亡的独立危险因素，如需血液透析，死亡率可达 80%[1]。临床实践中，受患者基础状况、医疗条件、疾病严重程度等因素的影响，不

同研究中脓毒症 AKI 患者住院期间死亡率具有一定差异。White 等[5]在回顾性队列研究纳入了 2015 年至 2021 年 12 个 ICU 的 84 528 例患者,其中 13 451 例符合脓毒症合并 AKI 的诊断标准,此类患者住院期间死亡率为 18%。一项研究纳入 2008 年至 2019 年期间 MIMIC-Ⅳ数据库中 2 192 例脓毒症合并 AKI 患者,住院期间死亡率为 28.3%~41.3%。本研究结果显示,32.28%的脓毒症合并 AKI 患者在住院期间发生死亡,与上述报道符合,且与本中心既往数据结果相近(35.23%)[6],提示脓毒症合并 AKI 患者在住院期间仍面临较高的死亡威胁,加强高危人群的识别显得尤为重要。

本研究结果显示,年龄>70 岁、SOFA>10 分、PCT>3.67 ng/mL、AKI Ⅲ期、APTT>40 s 是老年脓毒症合并 AKI 患者住院期间全因死亡的独立危险因素。高龄是 AKI 的易感因素之一,随着年龄增长,多种器官功能逐渐降低,且多数合并基础疾病,进一步加大了对肾脏的损伤[9];此外,发生 AKI 后,高龄老人可能由于症状被基础疾病所掩盖,从而不利于早期诊治,增加死亡风险。一项基于 MIMIC-Ⅳ数据库中 14 240 例脓毒症患者临床资料的研究发现,高龄可直接增加近期和远期死亡率[10]。回顾性队列研究发现,年龄>70 岁是老年脓毒症死亡的独立危险因素,基于年龄、乳酸等 5 项指标建立的模型可早期识别死亡高风险个体[11]。一项对北京 28 家医院 30 个 ICU 的 AKI 患者的前瞻性观察性研究显示,高龄是脓毒症合并 AKI 患者死亡的独立危险因素[12]。应加强老年脓毒症 AKI 患者的临床管理,严密监测肾功能,以早期识别死亡高风险个体。

SOFA 评分是临床最常用的危重症及其严重程度评估体系,对器官衰竭患者尤为适用。He 等[13]采用不同的机器学习模型评估了 SOFA 评分与脓毒症所致 AKI 的相关性,发现第 1~3 天 SOFA 评分变化有助于预测急性肾脏疾病(包括 AKI)的发生,对 AKI 具有良好的识别价值。Luo 等[14]基于 MIMIC-Ⅳ数据库中 12 132 例脓毒症所致 AKI 患者的临床资料,发现随着 SOFA 评分增加,住院死亡率随之升高。既往研究表明,监测 SOFA 变化有助于早期识别脓毒症 AKI 患者的肾功能变化趋势,并早期制定干预措施[6]。SOFA 评分有助于对脓毒症 AKI 患者进行筛查,以便识别死亡高风险个体。

PCT 是传统炎症标志物,而炎症反应所致的损伤在 AKI 的发生中发挥主导作用,而且该指标对脓毒症具有更高的特异度,在严重感染时其水平才会有显著变化,因此,PCT 水平升高提示患者存在高水平炎症反应,其发生 AKI 的风险也随之增加。许彩虹等[6]研究显示,PCT 是脓毒症合并 AKI 患者死亡的独立危险因素,其每升高一个单位,院内死亡风险增加 39.8%。Lai 等[15]基于 PCT、高血压、糖尿病、CRP 等指标建立的模型对脓毒症相关 AKI 及 28 d 死亡个体具有较高的识别能力,且 PCT 对模型预测能力的影响最为显著。应及时纠正 PCT 升高脓毒症 AKI 患者的炎症状态,以降低死亡率。

AKI 分期可衡量肾功能变化,分期越高表示肾损伤越严重,并引起不可逆性损伤,增加死亡风险。邢冬梅等[11]对老年脓毒症患者死亡原因进行了分析,发现死亡组 AKI Ⅲ期的比例显著升高,校正混杂因素后发现 AKI Ⅲ期的脓毒症患者死亡风险增加了 98.2%。一项基于 MIMIC Ⅲ数据库中 2 066 例脓毒症合并 AKI 患者的队列研究显示,AKI 分期与死亡风险存在显著正相关[16]。因此对于 AKI 分期较高的患者,应积极干预,以防止病情进一步进展。

凝血功能异常是脓毒症患者常见的全身表现之一,且与疾病转归密切相关,表现为 APTT、PT 延长,血小板低下,血液高凝状态导致微血栓形成,进一步加重肾脏病变和全身多器官损伤。一项研究纳入了 615 例入住 ICU 脓毒症的患者,结果显示 APTT 升高是发生 AKI 的独立危险因素,且对脓毒症 AKI 患者近期死亡风险具有一定预测价值[15]。一项回顾性队列研究显示,脓毒症 AKI 患者中,死亡组比生存组具有更高水平的 APTT,且 APTT 延长与生存率、生存时间明显缩短存在正相关,多因素分析证实 APTT>40 s 是脓毒症 AKI 患者死亡的独立危险因素[17]。提示,监测脓毒症 AKI 患者凝血指标变化有助于预测其临床转归。

目前,研究者针对脓毒症已经开发了诸多模型,如邢冬梅等[11]基于年龄、乳酸、AKI 分期等指标建立了老年脓毒症住院期间全因死亡的预测模型。李雅琳等[18]建立了脓毒症患者发生 AKI 的预测模型,其指出应及时纠正炎症状态,以减少 AKI 发生。林泽华[19]、赵丽等[20]基于临床资料筛选,建立了脓毒症所致 AKI 患者 28 d 死亡的列线图,从而有助于早期识别死亡高风险患者。但此两项研究均没有针对老年人,且样本量均较小,导致分析结果不稳定。本研究建立针对老年脓毒症 AKI 患者住院期间死亡的预测模型,该模型由年龄、SOFA 评分、PCT、AKI 分期、APTT 5 项指标构成,可从多维度评估脓毒症严重程度和肾脏病变,继而预测死亡风险,经评价,识别高危

人群具有较高的准确率，具有潜在的临床应用价值。

综上所述，基于年龄、SOFA 评分、PCT、AKI 分期、APTT 建立的预测模型有助于早期识别老年脓毒症合并 AKI 患者住院期间死亡高风险人群，进而早期干预。由于模型组成指标均易获得，有望为医疗保健者提供一种能够改变患者护理并最终改善临床预后的实用工具。但由于本研究缺乏独立数据集对模型进行外部验证，因此确切结论仍需深入研究。

利益冲突　无

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