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Construction of a predictive model for the severity of sepsis based on APACHE Ⅱ score, IL-6, and T lymphocyte subsets

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Abstract: Objective: To construct a predictive model for the severity of sepsis using the Acute Physiology and Chronic Health Evaluation Ⅱ (APACHE Ⅱ) score, interleukin-6 (IL-6), and T lymphocyte subsets, and to evaluate the model's effectiveness. **Methods** A total of 225 patients with sepsis admitted to the Anqing Municipal Hospital from January 2021 to September 2023 were selected as the study subjects. IL-6, T lymphocyte subsets ($CD4^+$, $CD8^+$, $CD4^+/CD8^+$), C-reactive protein (CRP), procalcitonin (PCT), and APACHE Ⅱ scores were measured within 24 hours after diagnosis. Based on the Sepsis-3.0 diagnostic criteria, patients were divided into the sepsis group (109 cases) and the septic shock group (116 cases). Logistic regression analysis was used to select variables and construct a predictive model for the severity of sepsis. Calibration plots and decision curve analysis were employed to evaluate the model's fit and clinical value. **Results** The levels of $CD4^+$ and $CD4^+/CD8^+$ in the septic shock group were lower than those in the sepsis group, while CRP, PCT, IL-6, and APACHE Ⅱ scores were higher in the septic shock group than in the sepsis group ($P<0.05$). The constructed predictive model was as follows: $\ln[P/(1-P)] = 0.999 + 0.054 \times$ APACHE Ⅱ score $- 0.054 \times CD4^+ - 0.180 \times CD4^+/CD8^+ + 0.001 \times$ IL-6. Calibration plots and decision curve analyses indicated that the model had good fit and clinical value. **Conclusion**: The predictive model composed of $CD4^+$, $CD4^+/CD8^+$, IL-6, and APACHE Ⅱ score can be used for early assessment of the severity of sepsis, providing assistance for clinical diagnosis and treatment.

Keywords: Interleukin-6; T lymphocyte subsets; Acute Physiology and Chronic Health Evaluation score; Sepsis; Predictive model
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Sepsis refers to a syndrome of organ dysfunction caused by dysregulated host response to infection, typically presenting with clinical symptoms such as altered consciousness, chills, fever, etc. If not promptly treated with effective interventions, the condition may progress to septic shock, which poses a life-threatening risk [1]. Early assessment of the disease severity and timely, appropriate intervention can improve the prognosis of sepsis patients. Currently, there is no available effective biomarker for accurate prediction and analysis of sepsis. Traditional biomarkers, such as C-reactive protein (CRP) and procalcitonin (PCT), have their limitations, necessitating the development of new predictive models for early evaluation of the severity of sepsis [2]. Previous studies have shown that sepsis can lead to immune stress responses and inflammatory changes in the body [3]. Among these, T lymphocyte subsets, including $CD4^+$ and $CD8^+$ cells, are common indicators reflecting inflammatory changes and are typically used to assess the severity of the disease, with immunosuppressed patients showing more severe illness and higher mortality. Thus, these markers can be used to assess disease severity and prognosis in the early stages [4]. Interleukin-6 (IL-6) directly participates in the body's inflammatory response process and is closely related to the degree of infection and inflammation [5]. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score can be used to assess disease severity. Based on these factors, this study aims to develop a preliminary predictive model for sepsis severity by combining the APACHE II score, IL-6, and T lymphocyte subsets.

1 Materials and Methods

1.1 Study Subjects

This study enrolled 225 sepsis patients admitted to the Department of Intensive Care Medicine at Anqing Municipal Hospital between January 2021 and September 2023. Among them, 127 were male and 98 were female, with a median age of 70 (58, 78) years and a median body mass index (BMI) of 21.7 (19.5, 22.75) kg/m². A total of 104 patients required invasive mechanical ventilation. The median APACHE II score was 16 (15, 22). This study was approved by the hospital's ethics committee (2024045).

Inclusion criteria: patients meeting the diagnostic criteria for sepsis as defined in Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) [6]; age>18 years; complete clinical data and follow-up information.

Exclusion criteria: patients with malignancies who have received chemotherapy or radiotherapy within the past 3 months; patients who have taken glucocorticoids, immunosuppressants, or other drugs that suppress immune function within the past 3 months; pregnant or postpartum women; patients with hematologic diseases, malignancies, or autoimmune diseases.

1.2 Laboratory Tests

Within 24 hours of sepsis diagnosis, venous blood was collected from patients for the following laboratory tests:
(1) Immunoturbidimetric method was used to detect CRP levels (Roche Fully Automated Immunoassay Analyzer). Chemiluminescence was used to measure PCT (Mindray chemiluminescence analyzer) and IL-6 levels (Hotgen chemiluminescence analyzer).
(2) T lymphocyte subsets ($CD4^+$ and $CD8^+$ cells) were detected using fluorescence labeling (Beckman Coulter flow cytometer), and the $CD4^+/CD8^+$ ratio was calculated, following the manufacturer's guidelines.

1.3 Grouping

According to the Sepsis-3.0 diagnostic criteria [6], septic shock is defined as sepsis with persistent hypotension despite adequate fluid resuscitation, with two of the following criteria met: (1) mean arterial pressure ≥ 65 mmHg with the use of vasopressors, and (2) serum lactate level>2 mmol/L. Based on whether the patient progressed to septic shock, the patients were divided into two groups: the sepsis group (n=109) and the septic shock group (n=116).

1.4 Statistical Methods

Data were processed using R4.2.3 software. Normally distributed continuous variables were expressed as $\bar{x}\pm s$, and differences between groups were compared using the independent t-test. Non-normally distributed continuous variables were expressed as M (P_{25}, P_{75}), and differences between groups were compared using the rank-sum test. Categorical data were expressed as count (%) and compared using the chi-square test. Logistic regression was used to analyze factors related to sepsis severity, and a predictive model for diagnosing septic shock was developed and visualized as a nomogram. The model's calibration was assessed using a calibration plot, and its clinical value was evaluated using decision curve analysis (DCA). P<0.05 was considered statistically significant.

2 Results

2.1 Baseline Data

There was no significant difference in age, BMI, gender, and length of ICU stay between two groups (P>0.05). The APACHE II score and the proportion of invasive mechanical ventilation in the sepsis group were lower than those in the septic shock group, and the differences were significant (P<0.05) **[Table 1]**.

2.2 Laboratory Indicators

Compared with sepsis group, the levels of IL-6, CRP, and PCT were higher, and $CD4^+$ and $CD4^+/CD8^+$ ratio were lower in the septic shock group (P<0.05). There was no significant difference in $CD8^+$ between two groups (P>0.05) **[Table 2]**.

Tab.1 Comparison of the basic clinical data between two groups

Group	Case	Age(year)[a]	Male [case(%)]	BMI (kg/m²)[a]	Invasive Mechanical Ventilation [case(%)]	APACHE II[a]	Length of ICU Stay (d)[a]
Sepsis Group	109	68(58, 77)	58(53.2)	22.10(19.90,22.90)	39(35.78)	16(12, 21)	5(3, 9)
Septic Shock Group	116	72(59, 79)	69(59.5)	21.50(19.30, 22.60)	65(56.03)	17(15, 23)	5(3, 9)
***Z*/χ^2/*t* value**		1.484	0.899	1.647	8.443	3.146	0.595
***P* value**		0.138	0.416	0.100	0.004	0.002	0.552

Note: [a] meant the data was represent in the form of $M(P_{25}, P_{75})$.

Tab.2 Comparison of laboratory indexes between two groups

Group	Case	IL-6(pg/mL)[a]	$CD4^+$(%)[b]	$CD8^+$(%)[b]	$CD4^+/CD8^+$[a]	CRP(mg/L)[b]	PCT(mg/mL)[a]
Sepsis Group	109	63.20(15.9,183.0)	37.37±12.49	18.00±9.92	2.09(1.38,3.58)	113.7±81.05	5.12(1.40,23.85)
Septic Shock Group	116	158.75(44.8,1 000.0)	27.73±11.22	20.04±9.35	1.44(0.87.2.33)	140.89±89.46	15.55(2.44,46.99)
***Z* /*t* value**		4.529	6.097	1.583	4.251	2.384	3.148
***P* value**		<0.001	<0.001	0.115	<0.001	0.018	0.002

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

2.3 ROC Analysis of Laboratory Indicators to Predict the Severity of Sepsis

ROC showed that $CD4^+$, IL-6, and $CD4^+/CD8^+$ were more effective than CRP and PCT in predicting the severity of sepsis **[Figure 1]**.

2.4 Predictive Model

A risk prediction model was established based on logistic regression analysis. The formula for the model was as follows: $\ln[P/(1-P)] = 0.999+0.054\times$APACHE II score $-0.054\times CD4^+ -0.180\times CD4^+/CD8^+ +0.001\times$IL-6.

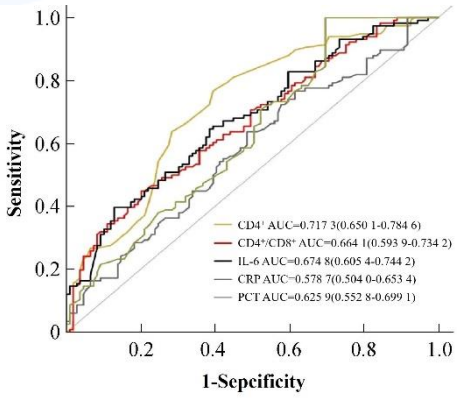

Fig.1 Related laboratory indicators predict the severity of sepsis in ROC curve

2.5 Nomogram Construction

A nomogram for predicting the occurrence of septic shock in sepsis patients was constructed based on the predictive factors identified in the model. The nomogram is shown in **Figure 2**.

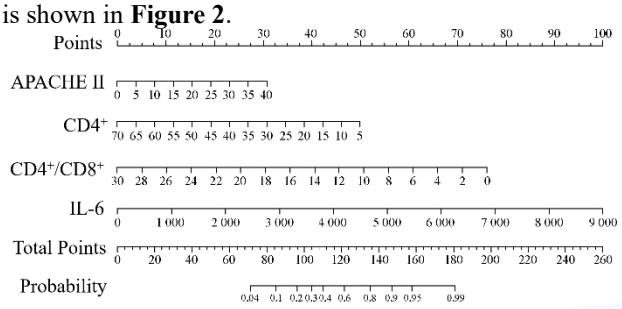

Fig.2 Predict the severity of sepsis in the column chart

2.6 Model Performance Evaluation

Goodness of fit evaluation: The Hosmer-Lemeshow test indicated that the model's predicted severity of sepsis closely matched the ideal curve (P = 0.253), suggesting good model fit **[Figure 3]**.

Clinical value evaluation: The decision curve analysis for the model's prediction of sepsis severity showed that when the high-risk threshold range was 0 to 0.99, Model 1 had a net benefit rate over 0, indicating clinical significance. The net benefit rate was negatively correlated with the high-risk threshold **[Figure 4]**.

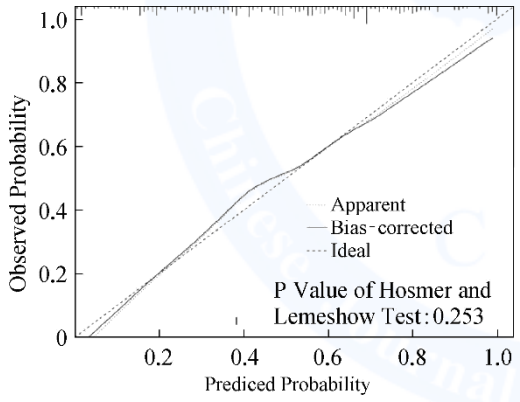

Fig.3 Model predict the severity of sepsis in the calibration graph

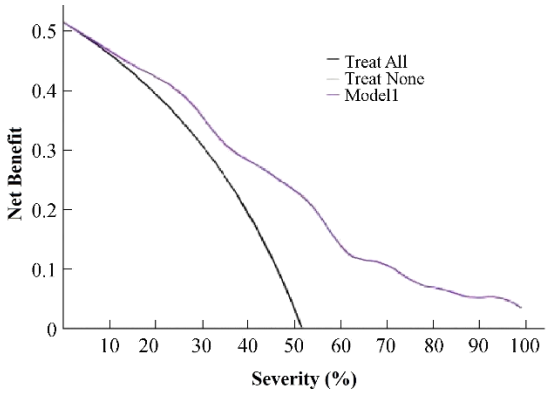

Fig.4 Model predict the severity of sepsis in DCA curves

3 Discussion

Sepsis is a systemic inflammatory response syndrome caused by various microbial infections, characterized by high incidence and mortality rates. Studies have shown that without timely treatment, sepsis can progress to septic shock, which not only threatens the patient's life but also impacts various bodily functions. Some surviving patients may develop complications such as cognitive dysfunction, affecting daily life and increasing the burden on families [7]. Therefore, early detection and treatment are crucial.

This study showed that the $CD4^+$ and $CD4^+/CD8^+$ levels in the septic shock group were lower than those in the sepsis group, while IL-6, CRP, and PCT levels were higher in the septic shock group. Furthermore, $CD4^+$, $CD4^+/CD8^+$, and IL-6 were better predictors of sepsis severity than CRP and PCT. This may be because CRP has low specificity and cannot distinguish between infectious and sterile inflammatory diseases, while PCT can also be elevated in conditions like renal insufficiency, heat shock, and cardiogenic shock. Current research suggests that immune dysfunction is a major pathophysiological process in sepsis. Sepsis triggers immune responses, but in septic shock, there is an immune suppression state [8-9]. T lymphocytes are key immune cells in the body's defense against infections. They are divided into $CD4^+$ and $CD8^+$ subsets based on surface differentiation markers [10]. The apoptosis of these cells plays a critical role in the immune function. In sepsis, the body may experience immune suppression, evidenced by changes in the number and proportion of T lymphocyte subsets. Abnormal apoptosis of immune cells leads to immune suppression and paralysis [11]. This is because, in a state of immune suppression, sepsis patients cannot effectively regulate specific immune functions, making them vulnerable to pathogen infections, which worsen the infection and lead to septic shock and other complications, endangering life. This aligns with previous studies [12].

IL-6, a major pro-inflammatory cytokine, is a commonly used serum marker for evaluating inflammatory diseases [13]. Studies have shown that IL-6 has superior diagnostic and prognostic value for sepsis and septic shock compared to PCT and CRP [5]. It is positively correlated with the severity of the condition. Prolonged elevation of IL-6 indicates the presence of septic shock and a poor prognosis. IL-6 is one of the most effective biomarkers for diagnosing and assessing sepsis severity. It can guide antibiotic use and help clinicians adopt more appropriate treatment strategies to achieve the desired therapeutic goals [14].

This study established a predictive model combining IL-6, T lymphocyte subsets, and the APACHE II score, suggesting that lower $CD4^+$ and $CD4^+/CD8^+$ ratios, and higher IL-6 and APACHE II scores, indicate a more severe sepsis condition and higher mortality risk. The performance of the model was evaluated, and the model based on $CD4^+$, $CD4^+/CD8^+$, IL-6, and APACHE II scores showed high goodness of fit and clinical value, assisting in the early prediction of sepsis progression.

However, this study has some limitations. First, it is

a single-center study with a relatively small sample size. Future studies should collect data from multiple centers to validate the results. Second, the study did not include additional inflammatory markers. Although the inclusion of $CD4^+$, $CD4^+/CD8^+$, IL-6, and APACHE II scores simplifies the model and increases its practicality, it may reduce the model's performance. Lastly, since this is a retrospective study, further prospective studies are needed to optimize the model.

In summary, $CD4^+$, $CD4^+/CD8^+$, IL-6, and APACHE II scores can be used to construct a predictive model for sepsis severity, which can assist clinical practice. However, further validation with large multi-center studies and continuous prospective research is needed to optimize the model.

The authors report no conflict of interest

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·论　著·

APACHEⅡ评分、IL-6 与 T 淋巴细胞亚群联合构建脓毒症病情严重程度的预测模型

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摘要：目的　急性生理学和慢性健康状况评分（APACHEⅡ评分）、白介素-6（IL-6）与 T 淋巴细胞亚群联合构建脓毒症病情严重程度的预测模型，并评价模型的效能。**方法**　选取 2021 年 1 月至 2023 年 9 月安庆市立医院收治的脓毒症患者 225 例为研究对象，测定确诊后 24 h 内 IL-6、T 淋巴细胞亚群（$CD4^+$、$CD8^+$、$CD4^+/CD8^+$）、C-反应蛋白（CRP）、降钙素原（PCT）和 APACHEⅡ评分；依据 Sepsis-3.0 诊断标准将其分为脓毒症组（109 例）和脓毒性休克组（116 例），根据 logistic 回归分析选择变量并构建脓毒症病情严重程度的预测模型，采用校准图和决策曲线分析评价模型的拟合度和临床价值。**结果**　脓毒性休克组 $CD4^+$、$CD4^+/CD8^+$ 水平低于脓毒症组，CPR、PCT、IL-6、APACHEⅡ评分高于脓毒症组（$P<0.05$）；构建的脓毒症严重程度预测模型为：$\ln[P/(1-P)]=0.999+0.054\times$APACHEⅡ评分$-0.054\times CD4^+-0.18\times CD4^+/CD8^++0.001\times$IL-6。校准图和决策曲线图表明模型具有良好的拟合度和临床价值。**结论**　由 $CD4^+$、$CD4^+/CD8^+$、IL-6 和 APACHEⅡ评分构建的预测模型可用于早期评估脓毒症病情的严重程度，为临床诊断及治疗提供帮助。

关键词：白介素-6；T 淋巴细胞亚群；急性生理学和慢性健康状况评分；脓毒症；预测模型

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Abstract: Objective　To construct a predictive model for the severity of sepsis using the Acute Physiology and Chronic Health Evaluation Ⅱ (APACHEⅡ) score, interleukin-6 (IL-6), and T lymphocyte subsets, and to evaluate the model's effectiveness. **Methods**　A total of 225 patients with sepsis admitted to the Anqing Municipal Hospital from January 2021 to September 2023 were selected as the study subjects. IL-6, T lymphocyte subsets ($CD4^+$, $CD8^+$, $CD4^+/CD8^+$), C-reactive protein (CRP), procalcitonin (PCT), and APACHE Ⅱ scores were measured within 24 hours after diagnosis. Based on the Sepsis-3.0 diagnostic criteria, patients were divided into the sepsis group (109 cases) and the septic shock group (116 cases). Logistic regression analysis was used to select variables and construct a predictive model for the severity of sepsis. Calibration plots and decision curve analysis were employed to evaluate the model's fit and clinical value. **Results**　The levels of $CD4^+$ and $CD4^+/CD8^+$ in the septic shock group were lower than those in the sepsis group, while CRP, PCT, IL-6, and APACHEⅡ scores were higher in the septic shock group than in the sepsis group ($P<0.05$). The constructed predictive model was as follows: $\ln[P/(1-P)]=0.999+0.054\times$APACHEⅡ score$-0.054\times CD4^+-0.18\times CD4^+/CD8^++0.001\times$IL-6. Calibration plots and decision curve analyses indicated that the model had

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good fit and clinical value. **Conclusion**　The predictive model composed of $CD4^+$, $CD4^+/CD8^+$, IL-6, and APACHEⅡ score can be used for early assessment of the severity of sepsis, providing assistance for clinical diagnosis and treatment.

Keywords: Interleukin-6; T lymphocyte subsets; Acute Physiology and Chronic Health Evaluation score; Sepsis; Predictive model

Fund program: Science and Technology Plan Project of Anqing Science and Technology Bureau of Anhui Province (2021Z2015); University-Level Scientific Research Project of Wannan Medical College (WK2023JXYY026)

脓毒症如未采取及时有效的治疗措施,则可致疾病进一步发展为脓毒性休克,危及生命安全[1]。尽早判断疾病的严重程度,并采取及时合理的干预治疗,可改善脓毒症患者预后。目前尚无有效的生物标记物能够对脓毒症进行精准的预测分析,传统的 C 反应蛋白(CRP)、降钙素原(PCT)均有各自的局限性,还需要新的预测模型早期评估脓毒症的病情严重程度[2]。既往研究发现,脓毒症可致人体发生免疫应激反应与炎症改变[3]。其中,T 淋巴细胞亚群是反映人体炎症改变的常见指标,包括 $CD4^+$、$CD8^+$等指标,通常表现出免疫抑制的患者疾病更加严重,死亡率更高,因此可用于早期判断疾病的病情严重程度与预后评估[4]。白介素-6(IL-6)能直接参与机体炎症反应过程,与机体的感染程度及炎症反应有直接关联[5]。急性生理学和慢性健康评分(APACHE Ⅱ 评分)可评估病情的严重程度。基于此,本研究通过结合 APACHE Ⅱ 评分、IL-6 与 T 淋巴细胞亚群三项指标,初步建立一种脓毒症病情严重程度的预测模型。

1　资料与方法

1.1　*研究对象*　选取 2021 年 1 月至 2023 年 9 月安庆市立医院重症医学科收治的脓毒症患者 225 例为研究对象,其中男性 127 例,女性 98 例,年龄 70(58, 78)岁,BMI 21.70(19.50, 22.75)kg/m^2,有创机械通气例数 104 例,APACHE Ⅱ 评分 16(15, 22)分。本研究经医院伦理委员会批准(2024045)。纳入标准:符合《脓毒症和脓毒性休克的第三个国际共识定义》中脓毒症相关诊断标准[6];年龄>18 岁;临床资料及随访预后信息完整。排除标准:近 3 个月内接受放化疗的恶性肿瘤患者;近 3 个月内服用糖皮质激素、免疫抑制剂或其他免疫功能抑制状态者;孕产妇患者;有血液系统疾病、恶性肿瘤及自身免疫性疾病的患者。

1.2　*实验室检查*　脓毒症患者确诊 24 h 内采集静脉血,并检测以下实验室指标,(1) 采用免疫透射比浊法(罗氏全自动生化免疫分析仪)检测 CRP 水平;采用化学发光法(迈瑞化学发光分析仪)检测 PCT 水平;采用化学发光法(热景化学发光分析仪)检测 IL-6 水平,均严格按照说明书操作。(2) 采用荧光标记法(Beckman 公司流式细胞仪)检测 $CD4^+$、$CD8^+$ T 淋巴细胞比例,计算 $CD4^+/CD8^+$比值。均严格按照说明书操作。

1.3　*分组*　依据脓毒症 3.0 的诊断标准[6],根据是否进展为脓毒性休克分为脓毒症组($n=109$)与脓毒性休克组($n=116$)。

1.4　*统计学方法*　采用 R 4.2.3 软件处理数据。服从正态分布的计量资料用 $\bar{x}\pm s$ 表示,两组间比较采用成组 t 检验;非正态分布的计量资料用 $M(P_{25}, P_{75})$表示,两组间比较采用秩和检验;计数资料用例(%)表示,两组间比较行 χ^2 检验。采用 logistic 回归分析脓毒症病情严重程度的相关因素,建立诊断脓毒性休克的预测模型,并以此可视化为列线图,采用校准图评价模型拟合度,用决策曲线分析(DCA)评价模型临床价值。$P<0.05$ 为差异有统计学意义。

2　结　果

2.1　*两组基线资料比较*　两组年龄、BMI、性别、ICU 住院天数比较差异无统计学意义($P>0.05$)。脓毒症组 APACHE Ⅱ 评分和有创机械通气占比均低于脓毒性休克组($P<0.05$)。见表 1。

2.2　*两组实验室指标比较*　脓毒性休克组 IL-6、CRP、PCT 水平高于脓毒症组($P<0.05$),$CD4^+$、$CD4^+/CD8^+$低于脓毒症组($P<0.05$),两组间 $CD8^+$水平差异无统计学意义($P>0.05$)。见表 2。

表 1　两组基本临床资料比较

Tab. 1　Comparison of the basic clinical data between two groups

组别	例数	年龄[岁, $M(P_{25}, P_{75})$]	男性[例(%)]	BMI [kg/m^2, $M(P_{25}, P_{75})$]	机械通气[例(%)]	APACHE Ⅱ 评分[$M(P_{25}, P_{75})$]	ICU 住院天数[d, $M(P_{25}, P_{75})$]
脓毒症组	109	68(58, 77)	58(53.2)	22.10(19.90, 22.90)	39(35.78)	16(12, 21)	5(3, 9)
脓毒性休克组	116	72(59, 79)	69(59.5)	21.50(19.30, 22.60)	65(56.03)	17(15, 23)	5(3, 9)
χ^2/Z 值		1.484	0.899	1.647	8.443	3.146	0.595
P 值		0.138	0.416	0.100	0.004	0.002	0.552

表 2　两组实验室指标的比较

Tab. 2　Comparison of laboratory indexes between two groups

组别	例数	IL-6[pg/mL, $M(P_{25},P_{75})$]	$CD4^+$(%, $\bar{x}\pm s$)	$CD8^+$(%, $\bar{x}\pm s$)	$CD4^+/CD8^+$ [$M(P_{25},P_{75})$]	CRP(mg/L, $\bar{x}\pm s$)	PCT[mg/mL, $M(P_{25},P_{75})$]
脓毒症组	109	63.20(15.90, 183.00)	37.37±12.49	18.00±9.92	2.09(1.38, 3.58)	113.7±81.05	5.12(1.40, 23.85)
脓毒性休克组	116	158.75(44.83, 1 000.00)	27.73±11.22	20.04±9.35	1.44(0.87, 2.33)	140.89±89.46	15.55(2.44, 46.99)
$\chi^2/t/Z$ 值		4.529	6.097	1.583	4.251	2.384	3.148
P 值		<0.001	<0.001	0.115	<0.001	0.018	0.002

2.3　实验室指标预测脓毒症病情严重程度的 ROC 分析　$CD4^+$、IL-6、$CD4^+/CD8^+$在预测脓毒症病情严重程度方面优于 CRP、PCT(图 1)。

2.4　预测模型　根据 logistic 回归分析建立的脓毒症患者发生脓毒性休克的风险预测模型公式如下:$\ln[P/(1-P)]=0.999+0.054\times$APACHE Ⅱ评分$-0.054\times CD4^+-0.18\times CD4^+/CD8^++0.001\times$IL-6。

2.5　列线图的构建　根据预测模型分析的影响因素作为预测变量,构建预测脓毒症患者发生脓毒性休克的列线图,见图 2。

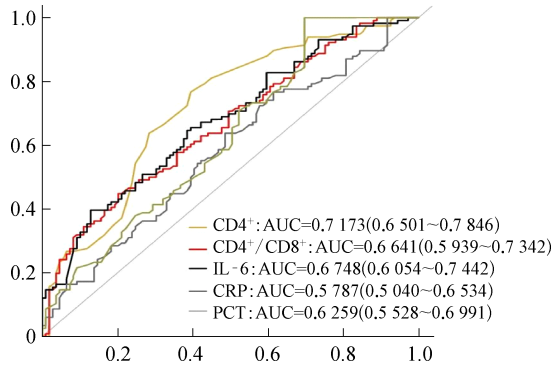

图 1　实验室指标预测脓毒症病情严重程度的 ROC 曲线图

Fig. 1　Laboratory indicators predict the severity of sepsis in ROC curve

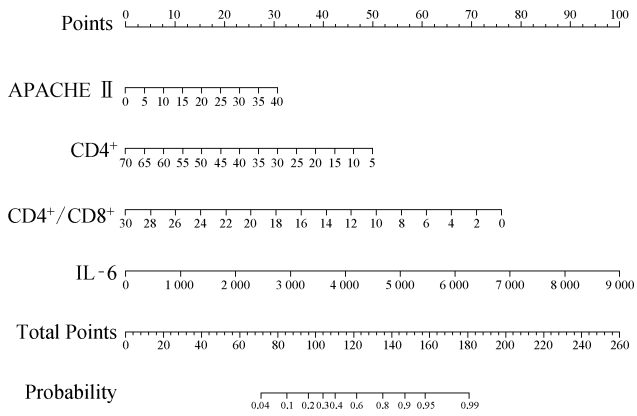

图 2　预测脓毒症病情严重程度的列线图

Fig. 2　The column chart of the severity of sepsis

2.6　模型的效能评价　(1) 拟合度的评价:Hosmer-Lemeshow 检验表明模型预测脓毒症病情严重程度的校正曲线趋近于理想曲线($P=0.253$),表明模型效果拟合较好(图 3)。(2) 临床价值评价:模型预测脓毒症病情严重程度的决策曲线显示,当高风险阈值区间为 0~0.99 时,模型 1 净受益率>0 表明有临床意义,且高风险阈值取值与净受益率呈负相关(图 4)。

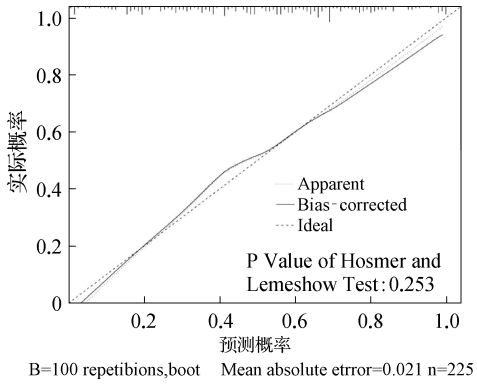

图 3　模型 1 预测脓毒症病情严重程度的校准图

Fig. 3　Model predict the severity of sepsis in the calibration graph

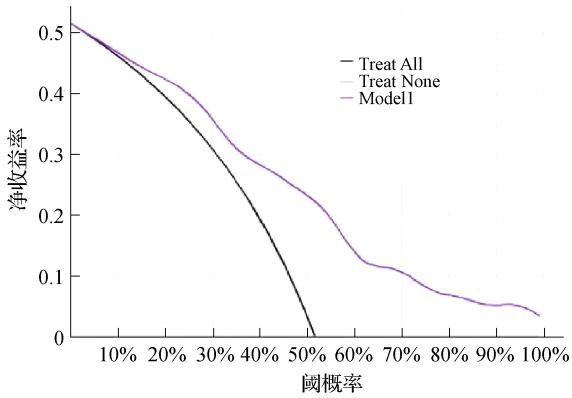

图 4　模型 1 预测脓毒症病情严重程度的 DCA 曲线

Fig. 4　Model predict the severity of sepsis in DCA curves

3　讨　论

本研究显示,脓毒性休克组 $CD4^+$、$CD4^+/CD8^+$低于脓毒症组,IL-6、CRP、PCT 高于脓毒症组,且 $CD4^+$、$CD4^+/CD8^+$、IL-6 在预测脓毒症病情严重程度方面优于 CRP、PCT。这是由于 CRP 具有低特异性,不能鉴别感染性疾病和无菌性炎症性疾病,PCT 则在肾功能不全、热休克、心源性休克等疾病中也可升高。根据目前研究显示,免疫功能障碍是脓毒症发生的主要

病理生理过程，脓毒症的免疫反应被激活，但在脓毒性休克中表现出免疫抑制[8]。T 淋巴细胞是人体抵御感染的主要防御细胞，可分为 $CD4^+$ 和 $CD8^+$ 两大亚群，其凋亡在人体免疫功能中发挥着关键作用[9]，脓毒症发生时，机体可存在免疫抑制状态，在免疫水平表现为 T 淋巴细胞亚群的数量与比例的改变，还会合并免疫细胞异常凋亡导致免疫抑制与麻痹[10]。这是由于脓毒症患者机体处于免疫抑制状态下，无法对特异性免疫功能进行有效调控，因此无法抵抗病原体感染，导致感染加重，引起脓毒性休克等多种并发症，危及生命安全，与相关研究相一致[11]。因此，通过 T 淋巴细胞亚群可以更好的反应疾病的严重程度。

IL-6 是评价炎症性疾病的常用血清标志物[12]，根据研究显示，IL-6 在对脓毒症和脓毒性休克的诊断和预后价值方面优于 PCT、CRP[13]，与病情严重程度成正相关，IL-6 长期处于高水平则提示患者存在脓毒性休克，且预后不良[5]，是诊断和评估脓毒症病情严重程度最有效的标志物，可以监测和指导抗生素的应用，指导临床采取更合理的治疗方案，达到预期的治疗目标[14]。

因此本研究建立了 IL-6、T 淋巴细胞亚群与 APACHEⅡ评分联合的预测模型，提示 $CD4^+$、$CD4^+/CD8^+$ 降低，IL-6、APACHEⅡ评分增高的患者，脓毒症病情严重程度高，死亡风险增加；本研究还对建立的预测模型进行效能评价，基于 $CD4^+$、$CD4^+/CD8^+$、IL-6、APACHEⅡ评分构建的模型具有较高拟合度和临床价值，为早期预测脓毒症的发展提供帮助。

本研究仍存在一定局限性，首先，研究类型属单中心研究，且样本量较小，未来应收集大量多中心研究的数据来验证结果；其次，本研究未纳入更多的炎症标志物，虽然仅纳入 $CD4^+$、$CD4^+/CD8^+$、IL-6、APACHEⅡ评分可简化模型和增加模型的实用性，但有可能降低了模型的性能；最后，该研究为回顾性研究，需要进行更多的前瞻性研究来进一步优化模型。

综上所述，$CD4^+$、$CD4^+/CD8^+$、IL-6、APACHEⅡ评分可构建脓毒症病情严重程度的预测模型，有助于临床实践指导，但仍需通过多中心研究中开展大样本进行验证以及不断进行前瞻性研究来优化模型。

利益冲突　无

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