## **Research Article**

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# Exploring the predictive value of multiple scoring systems for 30-day prognosis in ICU patients with sepsis - A retrospective study base on mimic-iv database

Binfei Tang\*; An Zhang

### \*Corresponding Author: Binfei Tang

Department of Critical Care Medicine, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, 400010, China.

Email: 2656103267@qq.com

## Abstract

**Object:** To evaluate the efficacy of Acute Physiologic Score III (APS III) score, the Logistic Organ Dysfunction Score (LODS), the Oxford Acute Severity of Illness Score (OASIS), the Simplified Acute Physiology Score (SAPS II), the Systemic Inflammatory Response Syndrome (SIRS) criteria, Sequential Organ Failure Assessment (SOFA) score and partial combined score in prediction of the mortality within 30 days in patients with sepsis in ICU. **Methods:** Based on the diagnostic criteria of sepsis 3.0, patients who met the diagnostic criteria in the intensive care unit database of Beth Israel Deaconess Medical Center (MIMIC- IV) were included according to the inclusion criteria. The survival status was judged by the readmissions of patients, and the early efficacy of those scores in predicting the in-hospital mortality of ICU sepsis patients was analyzed by Receiver Operating Characteristic (ROC) curve. The clinical application value of each scoring system was compared by decision curve analysis (DCA). Those scoring systems with higher predictive value were combined and analyzed with ROC curve and DCA. **Results:** Finally, there were 7082 patients with sepsis who met the criteria were included for analysis, with a median age of 63 [interguartile range (IQR)] 52-73] years, among them, 3904 (55.1%) were males and 1517 (21.4%) patients died within 30 days. AUC values of all scoring systems were as follows: the APS III [0.775, 95% (CI) 0.765-0.785] and the LODS [0.766, 95% CI 0.756-0.776)] were better than OASIS [0.736, 95% CI 0.726-0.746)], SAPS II [ (0.721, 95% CI 0.710-0.731)], SIRS [ (0.578, 95% CI 0.566-0.590)] and SOFA [ (0.722, 95% CI 0.711-0.732)] (with all P < 0.05) in predicting the 30-day mortality of sepsis patients. However, there was no significant difference in AUC area between the two scores (P>0.05), while the predictive value of APS III combined with LODs was higher than that of both alone (P<0.05). **Conclusion:** The predictive value of APS III and LODS scores are superior than that of SAPS II, SIRS, OASIS and SOFA score in predicting the 30-day mortality of ICU sepsis patients, the combination of the two was of best prediction effect and greater clinical application value.

# **Keywords**

Sepsis 3.0; Scoring system; Prognosis; Mimic database; ICU.

# Introduction

Sepsis is a life-threatening organ dysfunction caused by the dysregulated host response to infection [1]. Currently, sepsis has long been the focus of global health [2]. Studies [3] have shown that the in-hospital mortality of sepsis patients in high-income countries is as high as 17%. In 2015, there were 1,025,997 sepsis related deaths in China [4], which has caused an overwhelming burden on China's public health and economic development. Therefore, early prediction of the prognosis of patients with sepsis is of great value. This study is mainly based on the intensive care unit database (MIMIC- IV) of Beth Israel Deaconess Medical Center in the United States. We evaluated the predictive value of the Acute Physiologic Score (III (APS III) score, the Logistic Organ Dysfunction Score (LODS), the Oxford Acute Severity of Illness Score (OASIS), the Simplified Acute Physiology Score (SAPS II), the Systemic Inflammatory Response Syndrome (SIRS) criteria, Sequential Organ Failure Assessment (SOFA) score [5,6] for the prognosis of sepsis patients. Besides, the predictive value of the combination of some scoring systems was preliminarily explored.

#### **Study projects**

This study was based on the intensive care unit database (MIMIC- IV) of Beth Israel Deaconess Medical Center, obtaining SQL statements from GitHub website (https://github.com/MIT-LCP/mimic-iv), and patients meeting the diagnostic criteria of sepsis 3.0 were selected according to the inclusion and exclusion criteria.

Inclusion criteria: (1). Patients were 18 to 85 years of age. (2). Patients met the diagnostic criteria of sepsis 3.0, namely, infection was suspected with increased SOFA by  $\geq$  2 points and admitted into ICU for the first time (If there were multiple ICU records in the database, and only the first stay was taken).

Exclusion criteria: (1). The first ICU length of stay less than 24 hours. (2). Patients had those combined diseases like myocardial infarction, malignant tumors and metastatic solid tumors that a great impact on patients' short-term prognosis. (3). The information of patients' survival state within 30 days was lack. (4). Patients with missing records or possible errors were excluded (The process for patient selection was shown on Figure 1).

# **Study Methods**

#### **Clinical data collection**

In this study, the SQL language in Navicat premium 15 was used to extract the data, part of the code was obtained from GitHub website, and the extracted data was preliminarily processed with Excel. The extracted data including age, gender and weight. Monitoring parameters within 24 hours after ICU admission: heart rate, noninvasive systolic blood pressure, noninvasive diastolic blood pressure and noninvasive mean arterial pressure. Laboratory test results, APS III, LODS, OASIS, SAPS II, SIRS and SOFA

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scores. According to the international classification of diseases ICD 9 and ICD 10 codes, patients with septic shock were collected. Partial complication data were collected with official codes. Complications included congestive heart failure, myocardial infarction, chronic lung diseases, severe liver diseases, diabetes with or without ketosis, kidney diseases, metastatic solid tumors, and malignant tumors. The access to the MIMIC - IV database and the acquisition of data in this study were approved by the Beth Israel Deaconess Medical Center and Massachusetts Institute of Technology (No. 47940551). The patients in the database were anonymous, therefore, the ethical approval statement and the need for informed consent were waived for this study.

#### **Related definitions**

The clinical data within 24h of ICU admission was extracted from the database based on the SQL code on the official website. If the same variable had multiple value records within 24h on the day of admission, the maximum value of the day was extracted except the minimum value of platelet.

Because the out of hospital follow-up of the MIMIC database was not available, in this study, we inferred the survival status of patients through the readmission of patients. During that period, the author found that some patients were hospitalized immediately after a death event, and there was no death event at the time of readmission, which may be related to the operation mode of the database. Therefore, for patients hospitalized for many times, the length of stay of the death event shall prevail; If there was no death event in multiple hospitalizations, the last hospitalization shall prevail.



**Figure 1:** Patients' selection process (Note: in the process of exclusion, 2 patients with systolic blood pressure greater than 1000mmHg were excluded due to missing blood pressure in consideration of recording error. In addition, the death time of two evolved patients was missing, and the last discharge time was considered as the death time).

#### **Statistics**

SPSS (Version 25.0) statistical software was used for general data statistical analysis. The measurement variables were described by mean ± standard deviation (M ± SD) or median with interquartile range (IQR) [M ( $Q_L$ ,  $Q_u$ )] according to whether they were distributed normally or not. The independent sample t-test or Mann Whitney U-test were used for comparison. The categorical variables were expressed as numbers and percentages and compared using the Chi-square test or Fisher exact probability. The receiver operating characteristic curves (ROC) were drawn by Medcalc software (Ver 20.1.0.0) and Delong test was used for the comparison of the area under the curve (AUC). We also performed the decision curve analysis (DCA) to evaluate the clinical benefit of each scoring system by R software (Ver 4.1.3) rmda package. Then the two scoring systems with the greatest value were combined and compared with each other separately by the ROC and DCA curves. Bilateral two tailed test was used and P value < 0.05 was considered statistically significant.

## **Results**

#### Comparison of patients' baseline data

This study finally included 7082 patients with sepsis who met the inclusion and exclusion criteria in the MIMIC- IV database. Among them, 3904 cases (55.1%) were male, the overall median age was 63 (52,73) years, and 1517 cases (21.4%) died within 30 days. The age, heart rate, noninvasive diastolic blood pressure, leukocyte count and all the scores in the death group were higher than those in the survival group. While the body weight and platelet count were lower than those in the survival group. Besides, more patients in the death group were complicated with septic shock, congestive heart failure, diabetes (whether combined with ketosis or not), kidney diseases, severe liver diseases and other complications (all with p <0.05), and the rest of the baseline data were not statistically significant (p>0.05) (Table 1).

Characteristics	Total (n=7082)	Survival group (n=5565)	Death group (n=1517)	$z/\chi^2$	P value		
Baseline data							
Age (years)	63 (52,73)	62 (51,72)	67 (55,77)	-10.583	< 0.001		
Male (%)	3904 (55.1%)	3084 (55.4%)	820 (54.1%)	0.896	0.344		
Weight (kg)	81.43 (68,97.7)	82.15 (68.70,98.18)	78.90 (65.60,95.78)	-4.919	< 0.001		
Heart rate (bpm)	106 (92,121)	105 (91,120)	109 (95,125)	-6.853	< 0.001		
Non-invasive SBP (mmHg)	138 (122,156)	138 (122,156)	139 (122,156)	-0.074	0.941		
Non-invasive DBP (mmHg)	83 (71,98)	83 (71,97)	85 (71,99)	-2.007	0.045		
Non-invasive BP (mmHg)	95 (82,110)	95 (82,110)	96 (82,111)	-1.909	0.056		
White blood cell $(10^9/L)$	13 (6.4, 17.8)	12.6 (8.8,17.3)	14.7 (10.1,19.9)	-9.470	< 0.001		
Hemoglobin (g/dL)	10.9 (9.5,12.3)	10.9 (9.5,12.2)	10.8 (9.2,12.5)	-0.604	0.546		
Platelets (10 <sup>9</sup> /L)	167 (110,235)	169 (115,237)	157 (92,226)	-5.774	< 0.001		
Complications							
Septic shock	630 (8.9%)	369 (6.6%)	261 (17.2%)	164.465	< 0.001		
Congestive heart failure	1917 (27.1%)	1443 (25.9%)	474 (31.2%)	17.064	< 0.001		

 Table 1: The patients' characteristics in the death group and survival group.

Chronic lung diseases	1962 (28%)	1537 (27.6%)	425 (28%)	0.094	0.760		
Diabetes without ketosis	1734 (24.5%)	1396 (25.1%)	338 (22.3%)	5.071	0.024		
Diabetes with ketosis	738 (10.4%)	609 (10.9%)	129 (8.5%)	7.061	0.006		
Kidney diseases	1626 (23.0%)	1264 (22.7%)	362 (23.9%)	0.890	0.345		
Severe liver diseases	854 (12.1%)	562 (10.1%)	292 (19.2%)	94.105	<0.001		
Scoring systems							
APSIII	55 (40,76)	50 (37,67)	80 (61,101)	-32.926	<0.001		
LODS	3 (6,9)	5 (3,7)	9 (7,11)	-31.988	<0.001		
OASIS	35 (29,42)	34 (27,40)	42 (36,48)	-28.241	<0.001		
SAPSII	37 (29,47)	35 (28,44)	46 (37,58)	-26.407	<0.001		
SIRS	3 (2,4)	3 (2,3)	3 (3,4)	-9.873	<0.001		
SOFA	6 (4,9)	5 (4,8)	9 (6,13)	-26.615	<0.001		

Note: SBP:systolic blood pressure, DBP: diastolic blood pressure; BP: blood pressure; APS III: Acute Physiologic Score III; LODS: Logistic Organ Dysfunction Score; OASIS: the Oxford Acute Severity of Illness Score; SAPS II: Simplified Acute Physiology Score II; SIRS: Systemic Inflammatory Response Syndrome; SOFA: Sequential Organ Failure Assessment.

#### The predictive value of the six scoring systems for 30-day mortality in ICU sepsis patients

The AUC of APS III, LODS, OASIS, SAPS II, SIRS, SOFA were 0.775(95% CI 0.765, 0.785), 0.766(95% CI 0.756, 0.776), 0.736(95% CI 0.726, 0.746), 0.721(95% CI 0.710, 0.731), 0.578(95% CI 0.566, 0.590), 0.722(95% CI 0.711, 0.732), respectively. It could be seen that the six scoring systems were of predictive value (Figure 2 and table 2). Comparing the area under the Delong test curve, we found that the AUC areas of APSIII and LODS scores were the largest, which were significantly higher than that of other scoring systems (p < 0.05), but there was no significant difference in AUC area between them (p > 0.05). The prediction ability of SIRS was the worst (p < 0.05)



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Table 2: Predictive value of each scoring system for 30 day prognosis of patients with sepsis in I						
	APSIII	LODS	OASIS	SAPSII	SIRS	SOFA
APSIII		0.0618	< 0.001	< 0.001	<0.001	< 0.001
LODS			< 0.001	< 0.001	<0.001	< 0.001
OASIS				0.03	<0.001	0.0551
SAPSII					<0.001	0.8960
SIRS						< 0.001
SOFA						

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## Comparison of the DCA curve of six scoring systems on predicting the 30-day mortality risk in patients with sepsis

As we mentioned above, although the AUC of APS II was the largest, there was no statistical difference compared with the LODS. In addition, patients' benefit needed to be taken into consideration clinically. Therefore, six scoring systems were used as clinical decision-making aids through DCA analysis. Taking the net benefit as the ordinate and the High Risk Threshold as the abscissa to draw the DCA curve (Figure 3), the high risk threshold was set to (0,1). The results of decision analysis curve shown that the range of net benefits from high to low was APS III, LODS, OASIS, SOFA, SAPS II and SIRS, respectively. Namely, APS III was the best among the six scoring systems, but it had little difference from LODS (Figure 3).

Table 2: Comparison of area under ROC curve of each scoring system.							
Scoring systems	AUC (95%CI)	Youden index	sensitivity (%)	specificity(%)	P value	Optimal cut-off	
APSIII	0.775 (0.765,0.785)	0.4275	76.14	66.61	< 0.001	60	
LODS	0.766 (0.756,0.776)	0.4167	75.21	66.45	< 0.001	6	
OASIS	0.736 (0.726,0.746)	0.3508	69.55	65.53	< 0.001	37	
SAPSII	0.721 (0.710,0.731)	0.3146	62.29	69.16	< 0.001	41	
SIRS	0.578(0.566,0.590)	0.1088	76.40	34.48	< 0.001	2	
SOFA	0.722 (0.711,0.732)	0.3317	63.09	70.08	< 0.001	7	



#### Comparison of the predictive value of APSIII combined LODS with that of both alone

The AUC of the combination of the two score systems was 0.784 (95% CI 0.775-0.794), which was higher than that of APSIII or LODS (p < 0.001) (Figure 4), and the clinical net benefit was higher when combined (Figure 5). Collectively, the APS III was better than LODS and other scoring systems in predicting the 30-day mortality for ICU sepsis patients, and its combination with LODS had the optimal predictive efficacy.



## **Discussions**

This study is a retrospective study based on the large clinical database, the MIMIC-IV database. We finally enrolled 7082 patients who met the diagnostic criteria of sepsis 3.0. At present, although the incidence rate and mortality of sepsis have decreased, it is still an important risk factor affecting global health [7]. What' more, a report [8] showed that about 41.9% of sepsis patients died before discharge. Therefore, it is of great clinical significance to early judge the condition and predict the prognosis of ICU sepsis patients. Although some studies [9] had conducted similar investigations based on the MIMIC - IV database, they seemed not to explain how to figure out the 28-day mortality.

Just as the sepsis patients' conditions change rapidly, the scoring systems for predicting the prognosis of patients are also developing rapidly. Proposed in 199, SIRS was once seemed as the diagnostic standard for sepsis patients. However, a better scoring system, the SOFA score was proposed in 2016 and soon been confirmed by studies [10] that the SOFA score was better than SIRS in predicting the prognosis of patients with sepsis. Which was consistent with the conclusion of this study. Similarly, APSIII had also been proved to be superior to SAPSII [5]. APS III is a part of APACHE II score and it is generally difficult to judge the chronic health status of patients in clinic. Therefore, a considerable number of studies have analyzed APSIII alone and recognized its predictive value for the prognosis of patients with sepsis [5]. LODS score was proposed in 1996, which was mainly used for evaluation of organs dysfunction in ICU [11] and its predictive value for the prognosis of patients with sepsis of patients in clinic value for the prognosis dysfunction in ICU [11] and its predictive value for the prognosis of patients with sepsis [5]. DOS score was proposed in 1996, which was mainly used for evaluation of organs dysfunction in ICU [11] and its predictive value for the prognosis of patients in ICU [11] and its predictive value for the prognosis of patients in ICU [11] and its predictive value for the prognosis of patients in ICU [11] and its predictive value for the prognosis of patients in ICU [11] and its predictive value for the prognosis of patients in ICU [11] and its predictive value for the prognosis of patients in ICU [11] and its predictive value for the prognosis of patients in ICU [12] and its predictive value for the prognosis of patients in ICU [20] and its predictive value for the prognosis of patients in ICU [20] and I

parameters based on machine learning raised in 2013 [14] and our study shows that its predictive value is only lower than APSIII and LODS.

We found that the APSIII and LODS were superior than the other four scoring systems in AUCs and net benefit through ROC and DCA curves, especially combining the two scoring systems together. However, whether they are alone or combined, the predictive value of death risk in ICU sepsis patients is relatively low. Besides, some studies considered that even APACHE II / IV system had an average ability in predicting hospitalized mortality in elderly patients with sepsis [15]. Therefore, we believe that we should combine more parameters to launch a better prediction system. In addition, diseases often develop over a period of time rapidly, especially after human intervention, so these factors should also be taken into account.

# Limitations

This study is a retrospective study based on a single center, that would inevitably lead to selective bias. Secondly, due to the defects of the original database itself, there are many excluded cases in this study, which might cause outcome bias. What's more, through the comparison of the general data, it can be seen that there are great differences in the baseline characteristics between the two groups, which are the weaknesses of retrospective survival analysis. We are looking forward to large prospective studies on the prognosis of patients with sepsis in ICU in the future.

## Conclusions

In conclusion, the predictive value of APS III and LODS scores are superior than that of SAPS II, SIRS, OASIS and SOFA score in predicting the 30-day mortality of ICU sepsis patients, the combination of the two was of best prediction effect and greater clinical application value.

# **Declarations**

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**Conflict of interest:** The authors declare that they have no conflicts of interest.

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Authors Information: Binfei Tang\*; An Zhang Department of Critical Care Medicine, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, 400010, China.

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