The Comparison between Sepsis 1.0 and Sepsis 3.0 in Database of Severe Infection in Critical Illness: A Retrospective Study

Wei Zhang (✉ zhangwei_hxicu@163.com)

Affiliated Hospital of Zunyi Medical College <https://orcid.org/0000-0002-8706-6082>

Yan Zheng

Linyi People's Hospital

Juan Gu

Zunyi Medical University

Yan Kang

Sichuan University West China Hospital

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Abstract

Objective To compared the Sepsis 1.0 critierial with the Sepsis 3.0 criteria predict the efficacy of all-caused mortality of in-hospital in critically ill patients with severe infection.

Design This is a retrospective and cohort study based on the database of severe infection.

Setting A 48-bed general intensive care unit in affiliated hospital of University. Patients Critically ill patients with suspected infection based on the electronic health records from 1 January to 31 December, 2015.

Interventions None.

Measurements The variables of exposures included: quick sequential organ failure assessment (qSOFA), systemic inflammatory response syndrome (SIRS) score and sequential organ failure assessment (SOFA). Main outcomes and measures: for predictive validity, we found that the discrimination for hospital mortality was more common with sepsis than with uncomplicated infections. Results are reported as the area under the receiver operating characteristic curve (AUROC).

Main Results In the primary cohort, 873 patients had suspected infection cohort (n=634), of whom 188 (29.7%) died; and with the non-infection cohort (n=239), 26 patients died (10.9%). Among intensive care unit (ICU) cases in the infection cohort, the predictive validity for hospital mortality was higher for Sepsis 3.0 (SOFA) criteria (AUROC=0.702; 95%CI, 0.665 –0.737; $p \leq 0.01$ for both) than for Sepsis 1.0 (SIRS) criteria (AUROC=0.533; 95% confidence interval [95%CI], 0.493–0.572).

Conclusions In our study, we found the Sepsis 3.0 criteria is able to accurately predict the prognosis in critically ill patients with severe infection, and its predictive efficacy is superior to Sepsis 1.0 criteria.

Materials And Methods

Study design

This is a retrospective cohort study, and it was approved by the Biomedical Ethics Committee. This study was registered at the Chinese Clinical Trial Register (CCTR number: ChiCTR-ORC-16010138, registered 12 December 2016). URL: <http://www.chictr.org.cn/listbycreator.aspx>. Written informed consent was not obtained from the patients or their relatives due to the retrospective study design of using the electronic health records and no additional interventions were given to the subjects.

Setting

We conducted the study in a 48-bed general intensive care unit (GICU) of Sichuan University West China Hospital, (Chengdu, Sichuan Province, China). The periods of recruitment in the study included one whole year from *1 January to 31 December 2015*. We identified those with suspected infection for the purpose

of criteria comparison among 1243 electronic health records. The deadline for follow-up time was defined as the end of in-hospital for every patient according to the electronic health records.

Participants

The included criteria of participants:

1. The participants with suspected infection need to simultaneously meet the following three requirements (17). Firstly, the initial episode of suspected infection was defined as a combination of body fluid cultures and antibiotics. Secondly, it is necessary that the combination of antibiotics and culture sampling occurred within a specific time limits. If the antibiotic was administered first, the culture sampling must have been obtained within 24 hours. If the culture sampling occurred first, antibiotic administration must have been instigated within 72 hours. Finally, the “onset” of infection included the time when the first of the 2 events took place.

2. Age $\geq$ 18 years.

3. Length of stay in GICU $\geq$ 24 hours.

Outcome Variables

In the study, we followed up all patients after hospital discharge using their medical records and all-cause in-hospital mortality was the primary outcome. The secondary outcome was the risks of an ICU stay of 3 or more days. The exposures of risk factors for in-hospital death included scores of SIRS, qSOFA and SOFA.

Effect Modifiers and Potential Confounders

The major effect modifiers were age and acute physiology and chronic health evaluation (APACHE) II in the study due to the hospital mortality gradually increased with the increasing age and APACHE II; sex was the potential confounders due to the difference between male and female was evident in hospital mortality.

Data Sources and Bias Control

Each component of SIRS, qSOFA and SOFA derived from indicators of every medical record. For the time window from 48 hours before to 24 hours after the onset of infection, we calculated the maximum score of SIRS, qSOFA, and SOFA (17). In sepsis occurring before, near the moment of, or after infection, organ dysfunction is recognized by clinicians. Before to up to 24 hours after the onset of infection, we calculated a change of 2 points or more in the SOFA score from up to 48 hours.

The researchers in this study collected general information from medical records of patients admitted to the ICU: medical identification, demographic characteristics, vital signs, and results of laboratory tests.

We calculated the qSOFA, SIRS and SOFA scores for each patient using those data. Acute Physiology and APACHE II collected to assess the illness severity of members of the enrolled participant.

These study designers did not participate in the data collection, and those who participated in data collection of the study were blind to the study design.

Comparability of Assessment Methods

The comparable cohorts including Sepsis 1.0 and Sepsis 3.0 were generated from the database of critically ill patients with infection. We compared with the baseline characteristics and in-hospital death of both cohorts.

Statistical Analysis

Descriptive variables with a normal distribution were expressed as means $\pm$ standard deviations and were analysed using an independent sample *t* test. We expressed variables with a skewed distribution as medians and quartiles and analysed them using the Mann-Whitney *U* test. We employed the χ^2 test for comparison of frequencies. To assess the baseline risk of outcomes, we analysed the demographic variables that significantly differed among patients with opposite outcomes by means of univariate and multivariate logistic regression analysis; we determined the independent predictors. We constructed and compared the area under the curve of receiver operating characteristic (AUROC) was determined to assess predictive values.

We performed all the statistical analyses using MedCalc® (version 15.8) statistical software ([18](#)), and Empower Stats software. All the statistical tests were two-tailed, and $P < 0.05$ was considered significant. We considered the area under the receiver operating characteristic curve (AUROC) to be poor at 0.6 – 0.7, adequate at 0.7 – 0.8, good at 0.8 – 0.9, and excellent at 0.9 or higher ([19](#)).

Discussion

In the present study from the data of severe infection in GICU, we found the predictive validity of prognostic assessment is higher for the Sepsis 3.0 criteria than the Sepsis 1.0 criteria. In contrast, the predictive efficacy of SOFA and SIRS scores in our study was lower than that of the data from the developed counties.

As noted earlier, sepsis was defined as a “life-threatening organ dysfunction due to a dysregulated host response to infection” by the Third International Consensus Definitions Task Force([8](#)). With its new definitions, the task force constructed potential clinical criteria and validated using the data from the developed countries([15](#)).

Using the qSOFA assessment system as a screening tool, we may miss approximately one-third of patients with infections at high risk of death; that, suggests it may be unfit for critically ill patients with severe infection in ICUs. A similar result was reported in 2016 ([15](#)). In our study, if we use the Sepsis 1.0

criteria, we found that we may miss more than one-sixth of patients with infection at high risk of death. Interestingly, using the Sepsis 3.0 criteria, the rate of exclusion was zero; this suggests that the clinical criteria in the new definitions for sepsis and septic shock may be more appropriate for critically ill patients with infection.

In the present investigation, hospital mortality was reduced to zero in patients with infection and SOFA scores under 5. When SOFA scores exceeded 5 points, it increased sharply (Fig. 1C). Regarding hospital mortality and SIRS scores, the number of patients who died was higher with 0 point than with 1 point, but the difference was not statistically significant ($p>0.05$); hospital mortality was likewise not statistically significant in variance analysis of subgroups with scores of 0-4 points ($p>0.05$) (Fig. 1B). With respect to hospital mortality and qSOFA scores, variance analysis of subgroups with 3 points in a pairwise comparison with those with 2, 1, and 0 points showed statistical significance; the cut-off value of 2 points was optimal (Fig. 1A).

Hitherto, comparative studies on the use of qSOFA as a screening tool in non-ICU settings have demonstrated its efficacy in sepsis diagnosis(9-11 , 13). However, the position was not clear with ICUs? In the present investigation, we found the AUC of qSOFA to be much lower than in the original study for predicting hospital mortality in patients with infection in ICUs (0.585 vs. 0.66) (15). One reason for the discrepancy may be that the illness severity in the cohort of the present study was more severe than that in the matching cohort of the original study.

Strengths

Our study has several strengths. Firstly, the data of our study are current and present over a period of one whole year (2015) due to the time that we designed the study was just at which the Sepsis 3.0 had been published for more than one year. Secondly, the data we collected during the time window of infection or suspected infection consist of physiological or laboratory measurements that were retrospectively collected for routine monitoring data and are therefore unlikely to be biased.

Limitations

This study has several limitations. First, we conducted a single-centre clinical investigation in a province of southwest China. Second, we did not include comorbidities owing to the states of construction of the database, which was still in an initial stage. Third, the high morbidity and mortality in this study may to some extent limit its generalization under the Sepsis 3.0 definition..

Conclusions

In our study, we found the Sepsis 3.0 criteria is able to accurately predict the prognosis in critically ill patients with severe infection, and its predictive efficacy is superior to Sepsis 1,0 criteria.

Declaration

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Sichuan University West China Hospital (No. 315, 2016). Due to the retrospective study design involving electronic health records and no additional interventions, written informed consent was not obtained from the patients or their relatives.

Consent to publish

All authors have read and approved the manuscript version, and agree to submit for consideration for publication in the journal.

Competing interests

(1) All authors have no relationships with companies that might have an interest in the submitted work over the previous 5 years; (2) their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and (3) none of the authors have nonfinancial interests that may be relevant to the submitted work.

There are no ethical/legal conflicts involved in the article.

Availability of data and materials

We stated that all the data and materials were true and available in the study. The data in the study were deposited to the Chinese Clinical Trial Register Center (URL: <http://www.chictr.org.cn/listbycreator.aspx>).

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Authors' Contributions

Wei Zhang had full access to all of the data in the study and accepts responsibility for the data management and accuracy of the data analysis. Study concept and design: Wei Zhang and Yan Kang. Acquisition, analysis, and interpretation of data: Wei Zhang, Juan Gu, and Yan Zheng. Drafting of the manuscript: Wei Zhang, Yan Zheng, and Juan Gu. Critical revision of the manuscript for important intellectual content: Juan Gu and Yan Zheng. Administrative, technical, or material support: Wei Zhang and Yan Zheng. Study supervision: Juan Gu and Yan Kang. All authors agreed to the final version before submission. Wei Zhang is the study guarantor.

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Tables

Table 1. Baseline characteristics of the study cohort

Characteristic	Entire cohort N=634	Sepsis 1.0 N=540	Sepsis 3.0 N=631	P value	Survivors N=446	Non-survivors N=188	P value
Age, years	58.4 ± 17.6	57.7 ± 17.7	58.4 ± 17.6	0.744	56.4 ± 17.1	62.3 ± 18.0	<0.001
male Sex, (N-%)	418 (65.9)	360 (66.7)	417 (66.1)	0.675	287 (64.3%)	131 (69.7%)	0.196
APACHEII	24.6 ± 7.2	24.9 ± 7.4	24.7 ± 7.2	0.660	22.9 ± 6.6	28.8 ± 7.1	<0.001
SOFA	9.7 ± 3.9	9.8 ± 3.9	9.7 ± 3.8	0.452	8.9 ± 3.6	11.7 ± 3.7	<0.001
SIRS	2.6 ± 1.0	2.9 ± 0.8	2.6 ± 1.0	<0.001	2.5 ± 1.0	2.6 ± 1.0	0.173
qSOFA	1.8 ± 0.8	1.9 ± 0.7	1.8 ± 0.8	0.068	1.7 ± 0.8	2.0 ± 0.7	<0.001
Hospital length of stay, median (IQR), d	22 (12.2-35)	21.0 (12.0-35.0)	21.0 (12.0-33.0)	0.824	25 (15-39)	16 (8.8-25)	<0.001
ICU length of stay, median (IQR), d	13 (7-24)	11.0 (6.0-21.0)	11.0 (6.0-21.0)	0.774	14 (7.2-26)	11.5 (6-20)	0.002
28-days mechanical ventilation, median (IQR), d	8 (4-16)	6.0 (3.0-14.8)	6.0 (3.0-14.0)	0.649	8 (3-15)	10.5 (6-18)	<0.001
Duration of CRRT, median (IQR), d	10 (5-20)	8.0 (4.0-16.5)	9.0 (4.2-17.0)	0.872	9.5 (5.2-23.5)	10 (5-15)	0.381
Mechanical ventilation, (N-%)	573 (90.4%)	489 (90.6)	573 (90.8)	0.767	389 (87.2)	184 (97.9)	<0.001
**CRRT (N-%)	109 (17.2)	96 (17.8)	109 (17.3)	0.652	56 (12.6)	53 (28.2)	<0.001
Hospital mortality, (N-%)	188 (29.7)	168 (31.1)	188 (29.8)	0.331	NA	NA	NA
Vasopressin, (N-%)	212 (33.4)	189 (35)	212 (33.6)	0.316	119 (26.7)	93 (49.5)	<0.001

Abbreviation: APACHE Acute Physiology and Chronic Health Evaluation; SOFA Sepsis-related Organ Failure Assessment; SIRS Systemic Inflammatory Response Syndrome; qSOFA quick Sepsis-related

Organ Failure Assessment; CRRT Continuous renal replacement therapy. Normal distributed data are expressed as mean $\pm$ standard deviation

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Table 2. Outcomes of univariate analysis for hospital mortality and ICU length of stay 3 days or more

Variables	Hospital mortality	P value	ICU length of stay ≥ 3 days	P value
	Odds ratio(95%CI)		Odds ratio(95%CI)	
Age, years	1.02(1.01, 1.03)	≤ 0.01	1.00 (0.99, 1.01)	0.91
Sex				
Male	1.0		1.0	
Female	0.79(0.54, 1.13)	0.20	1.07 (0.77, 1.48)	0.71
Hospital length of stay	0.98(0.96, 0.99)	≤ 0.01	1.08 (1.06, 1.10)	≤ 0.01
ICU length of stay	0.99 (0.97, 1.00)	0.09	–	–
28-days mechanical ventilation	1.03 (1.01, 1.05)	0.01	1.31 (1.26, 1.37)	≤ 0.01
Mechanical ventilation, (N-%)	6.74(2.37, 19.16)	≤ 0.01	1.62 (0.94, 2.78)	0.08
Duration of CRRT	0.99(0.96, 1.02)	0.45	1.19 (1.07, 1.31)	≤ 0.01
**CRRT (N-%)	2.73 (1.79, 4.18)	≤ 0.01	1.77 (1.16, 2.71)	≤ 0.01
SOFA	1.22 (1.16, 1.28)	≤ 0.01	0.99 (0.95, 1.03)	0.51
APACHE II	1.14 (1.10, 1.17)	≤ 0.01	1.01 (0.99, 1.03)	0.48
Vasopressors	2.69 (1.89, 3.84)	≤ 0.01	0.78 (0.56, 1.09)	0.14
SIRS	1.13 (0.96, 1.33)	0.15	1.15 (0.98, 1.34)	0.09
qSOFA	1.58 (1.25, 1.99)	≤ 0.01	1.26 (1.02, 1.56)	0.03

Abbreviation: APACHE Acute Physiology and Chronic Health Evaluation; SOFA Sequential Organ Failure Assessment; SIRS Systemic Inflammatory Response Syndrome; qSOFA quick Sequential Organ Failure Assessment; CRRT Continuous renal replacement treatment. Normal distributed data are expressed as mean $\pm$ standard deviation

Table 3. Multivariate regression analysis of the risk of hospital mortality and ICU length of stay 3 days or more

Independent variables	Non-adjusted OR, 95%CI, <i>p</i>	Adjusted I (age and sex) OR,95%CI, <i>p</i>	Adjusted II (APACHE II) OR,95%CI, <i>p</i>
Hospital mortality			
qSOFA	1.58 (1.25, 1.99), <0.01	1.70 (1.34, 2.15), <0.01	1.17 (0.90, 1.53), 0.23
SIRS	1.13 (0.96, 1.33), 0.15	1.24 (1.04, 1.49), 0.02	1.00 (0.84, 1.20), 0.96
SOFA	1.22 (1.16, 1.28), <0.01	1.23 (1.17, 1.29), <0.01	1.12 (1.05, 1.19), <0.01
ICU length of stay 3 days or more			
qSOFA	1.26 (1.02, 1.56), 0.03	1.27 (1.03, 1.57), 0.03	1.27 (1.02, 1.58), 0.04
SIRS	1.15 (0.98, 1.34), 0.09	1.16 (0.99, 1.36), 0.07	1.14 (0.98, 1.33), 0.10
SOFA	0.99 (0.95, 1.03), 0.51	0.99 (0.95, 1.03), 0.53	0.97 (0.92, 1.02), 0.18

Abbreviation: APACHE Acute Physiology and Chronic Health Evaluation; SOFA Sequential Organ Failure Assessment; SIRS Systemic Inflammatory Response Syndrome; qSOFA quick Sequential Organ Failure Assessment

Figures

Figure 1

Distribution of hospital mortality in assessment systems

Suspected infection cohort (N = 634)

	Age	APACHE II	SOFA	qSOFA	SIRS
Age	0.614 (0.575,0.652)	0.031 (0.051,0.174)	0.036 (0.017, 0.159)	0.036 (-0.042,0.101)	0.037 (0.008,0.154)
APACHE II	P < 0.001	0.727 (0.69,0.761)	0.023 (-0.021, 0.07)	0.029 (0.086, 0.198)	0.030 (0.135, 0.253)
SOFA	P = 0.015	P = 0.292	0.702 (0.665 ,0.737)	0.029 (0.06, 0.174)	0.031 (0.109,0.23)
qSOFA	P = 0.415	P < 0.001	P = 0.001	0.585 (0.545,0.623)	0.028 (-0.003,0.107)
SIRS	P = 0.03	P < 0.001	P < 0.001	P = 0.066	0.533 (0.493, 0.572)

ICU indicates intensive care unit; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sepsis-related Organ Failure Assessment; SIRS, Systemic Inflammatory Response Syndrome; qSOFA, quick Sepsis-related Organ Failure Assessment. The area under the receiver operating characteristic curve (AUROC) data in the blue-shaded diagonal cells derive from models that include baseline variables plus candidate criteria. For comparison, the AUROC of the baseline model (Age model is looked as the baseline model) alone is 0.614 (95%CI, 0.575-0.652) in the ICU. Below the AUROC data cells are *P* values for comparisons between criteria, while above the AUROC data cells are Standard Error ^a (with bootstrap 95%confidence intervals), a measure of agreement. ^a DeLong et al., 1988

Figure 2

Area under the receiver operating characteristic curve and 95% confidence intervals for hospital mortality

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