

Comparative Predictive Accuracies of the Simplified Mortality Score for the Intensive Care Unit, Sepsis Severity Score, and Standard Severity Scores for 90-day Mortality in Sepsis Patients

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ABSTRACT

Background: The standard severity scores were used for predicting hospital mortality of intensive care unit (ICU) patients. Recently, the new predictive score, Simplified Mortality Score for the ICU (SMS-ICU), was developed for predicting 90-day mortality.

Objective: To validate the ability of the SMS-ICU and compare with sepsis severity score (SSS) and original severity scores for predicting 90-day mortality in sepsis patients.

Method: An analysis of retrospective data was conducted in the ICU of a university teaching hospital. Also, 90-day mortality was used for the primary outcome.

Results: A total of 1,161 patients with sepsis were included. The 90-day mortality was 42.4%. The SMS-ICU presented the area under the receiver operating characteristic curve (AUROC) of 0.71, whereas the SSS had significantly higher AUROC than that of the SMS-ICU (AUROC 0.876, $p < 0.001$). The acute physiology and chronic health evaluation (APACHE) II and IV, and the simplified acute physiology scores (SAPS) II demonstrated good discrimination, with an AUROC above 0.90. The SMS-ICU provides poor calibration for 90-day mortality prediction, similar to the SSS and other standard severity scores. Furthermore, 90-day mortality was underestimated by the SMS-ICU, which had a standardized mortality ratio (SMR) of 1.36. The overall performance by Brier score demonstrated that the SMS-ICU was inferior to the SSS (0.222 and 0.169, respectively). Also, SAPS II presented the best overall performance with a Brier score of 0.092.

Conclusion: The SMS-ICU indicated lower performance compared to the SSS, standard severity scores. Consequently, modifications are required to enhance the performance of the SMS-ICU.

Keywords: Intensive care unit, Mortality, Risk prediction, Severity score.

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HIGHLIGHTS

The conventional severity scores were designed to predict in-hospital mortality. However, assessing outcomes through in-hospital mortality might not be suitable as it can be influenced by discharge policies, and critical illness could continue to affect patients' postdischarge. Thus, it is recommended to use extended fixed-time outcomes to determine the outcomes of critically ill patients.

INTRODUCTION

Mortality prediction in patients with critical conditions is challenging, especially in sepsis patients which is the most prevalent issue in the intensive care unit (ICU).¹ One in every five deaths worldwide is associated with sepsis, which has a mortality rate of 20% to more than 50%.^{2,3} Severity scores are tools that provide objective and standardized assistance in the assessment of temporal trends in mortality and the impact of treatment protocols over time. These scores serve as valuable tools for benchmarking, which ultimately helps improve patient care in the ICU setting through the identification of areas of improvement by medical personnel and the application of evidence-based practices to determine the appropriate level of care.⁴⁻⁶

The acute physiology and chronic health evaluation (APACHE) and simplified acute physiology score (SAPS) are the two models

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that are frequently used to determine the severity of illness in ICU patients.^{6,7} Nevertheless, both APACHE and SAPS are intricate models, necessitating a multitude of laboratory parameters and consuming significant time.⁸

The sepsis severity score (SSS) was formulated specifically to explicitly predict mortality in sepsis patients. The surviving sepsis campaign database served as the source of the SSS and demonstrated commendable performance in estimating the

in-hospital mortality of sepsis patients. A prior investigation conducted in our ICU revealed that the SSS exhibited good discrimination comparable to that of conventional severity scores.^{9,10} However, external validation of these severity scores in our previous study demonstrated poor calibration.¹⁰

Sepsis and septic shock impact both immediate survival and long-term consequences. After hospitalization for sepsis, these patients may experience chronic health issues and an increased mortality risk.¹¹ Thus, long-term sequelae of sepsis should receive more attention. Despite discharge policies and the potential impact of critical illness on patients after hospital discharge, it may not be appropriate to quantify outcomes based on in-hospital mortality. Therefore, the longer fixed-time outcome is recommended to measure the outcomes in critically ill patients.¹²

The SMS-ICU is a new, simple clinical prediction model that has been developed, by using data from 4,086 patients in three randomized controlled trials in sepsis patients and two large cohort studies in critically ill patients, to estimate 90-day mortality among adult patients in the ICU.¹³ The SMS-ICU uses only seven readily available variables within the 24 hours of ICU admission, comprising two numeric parameters (age and lowest systolic blood pressure) and five binary factors (presence of hematologic malignancy/metastatic cancer, surgical admission, administration of vasoactive or inotropic agents, requirement for mechanical ventilator support, and need for renal replacement therapy). External evaluation of the SMS-ICU vs SAPS 3 demonstrated that SMS-ICU discrimination was good, although somewhat lower than that of SAPS 3.¹⁴ Thus, the SMS-ICU was developed for long-term mortality prediction in critically ill patients and represents a simple tool with minimal expected missing data.

This study was conducted with two objectives: (A) to assess the SMS-ICU performance and (B) to compare the ability of the SMS-ICU with disease-specific scores such as the SSS, as well as other widely used severity scores in predicting 90-day mortality among sepsis patients.

Methods

A retrospective study was undertaken using a prospective registry database of patients diagnosed with sepsis, alongside the evaluation of severity scoring systems, within the medical ICU of the university hospital. This study was approved by our Human Research Ethics Committee (REC 63-293-14-1). The retrospective design led to the waiver of informed consent.

The study included individuals aged 15 years and above who were diagnosed with sepsis and hospitalized in the ICU from 1 January 2017 to 30 June 2021. Sepsis or septic shock was diagnosed using the Sepsis-3 criteria.¹⁵ Readmission episodes to the ICU during a single hospitalization were excluded.

All parameters required for the SMS-ICU (Supplementary Table S1), SSS (Supplementary Table S2), APACHE II, APACHE IV, SAPS II, and sequential organ failure assessment (SOFA) calculations as reported in the original studies were collected. The scores were computed using the most unfavorable physiological data obtained within the initial 24 hours following ICU. The probability of mortality was predicted using previously validated algorithms based on the SMS-ICU, SSS, APACHE II, and SAPS II.^{9,13,16,17} The predictions for hospital mortality using APACHE IV were acquired via <https://intensivecarenetwork.com/Calculators/Files/Apache4.html>. The primary outcome was the 90-day mortality. Hospital mortality was used to assess the performance of these scores for secondary outcome.

The scores were assessed based on discrimination, calibration, and overall performance. Discrimination is the scoring system's capacity to differentiate between high and low-risk patients by identifying patients who have died and those who have survived, as measured by the area under the receiver operating characteristic curve (AUROC) with a 95% confidence interval (CI).^{18,19} Furthermore, AUROCs of above 0.90, 0.80–0.89, and 0.70–0.79 are considered excellent, good, and moderate, respectively.²⁰ Comparison of the AUROCs were conducted using the approach recommended by DeLong et al.²¹ Calibration was performed to assess the model's prognostic accuracy across various risk levels. The standardized mortality ratio (SMR) and the Hosmer–Lemeshow goodness of fit H and C statistics were used to assess the calibrations.¹⁸ The disparity between the patient groups' observed and anticipated mortality rates was evaluated using goodness-of-fit statistics. Good calibration was defined as a goodness-of-fit test *p*-value above 0.05. The SMR referred to the ratio of the actual number of deaths and the number of deaths that the severity score predicted. An overestimation of mortality is indicated by an SMR less than 1, whereas an underestimation is shown by an SMR greater than 1. Plotting the expected mortality rates stratified by 10% increments in the anticipated mortality vs actual mortality rates allowed calibration curves to be created. Concerning discrimination and calibration, the Brier score offers a comprehensive assessment of the overall performance.^{4,18} Higher accuracy was reflected by a lower score. The statistical analysis was performed using Stata 15.

RESULTS

A total of 1,161 sepsis patients were enrolled. Septic shock was diagnosed in 641 (55.2%) patients. The 90-day mortality rates were 42.4%, whereas in-hospital mortality rates were 41.5%. Pre-existing diseases affected 452 patients (38.9%), with the three most prevalent being hematologic malignancies (10.8%), immunocompromised conditions (7.8%), and solid tumors with metastases (6.6%). Respiratory tract infections (58.6%) were the most common source, followed by primary bloodstream infections (10.5%), gastrointestinal tract infections (10.4%), and urinary tract infections (10.2%). Microorganisms were identified in 941 (81%) patients. Positive blood cultures were detected in 27.6% of the patients. Most patients (89.2%) required mechanical ventilation. Patient characteristics and severity scores stratified by 90-day mortality are displayed in [Table 1](#).

The range of scores for sepsis patients was 3–35 for the SMS-ICU and 13–138 for the SSS. Patients with SMS-ICU above 25 or SSS above 90 had 81.3% and 89.1% 90-day mortality rates, respectively. Only 10.6% of the patients had an SMS-ICU score of more than 25, whereas 24.5% of our patients with sepsis had an SSS score greater than 90. The distributions of SMS-ICU and SSS scores coupled with 90-day mortality are shown in [Figures 1](#) and [2](#), respectively.

[Tables 2](#) and [3](#) provide an overview the performance of the SMS-ICU, SSS, and other standard severity scores. In comparison to the SSS, which showed good discrimination (AUROC, 0.876; 95% CI: 0.856–0.896), its AUROC was substantially greater than the SMS-ICU (*p* < 0.001), the SMS-ICU revealed moderate discrimination in its ability to predict 90-day mortality (AUROC, 0.71; 95% CI: 0.680–0.740). Nonetheless, the standard severity scores had the AUROC significantly higher than the SMS-ICU and SSS for predicting both 90-day and in-hospital mortality (*p* < 0.001). Furthermore, APACHE IV had the highest AUROC for predicting both outcomes, whereas SMS-ICU had the lowest AUROC ([Table 2](#) and [Fig. 3](#)).

Table 1: Clinical demographic data*

	All patients (n = 1,161)	Survivors at 90 days (n = 669)	Death within 90 days (n = 492)	p-value
Age	65 (51–77)	65 (50–77)	65 (54–77)	0.25
Male [n (%)]	674 (58)	373 (55.75)	301 (61.18)	0.06
Comorbidities [n (%)]	452 (38.9)	189 (28.25)	263 (53.46)	<0.001
Hematologic malignancy	125 (10.8)	37 (5.53)	88 (17.89)	<0.001
Immunocompromised	91 (7.8)	51 (7.62)	40 (8.13)	0.75
Metastatic cancer	76 (6.6)	24 (3.59)	52 (10.57)	<0.001
<i>Site of infection</i>				
Respiratory tract	681 (58.8)	382 (57.1)	299 (60.77)	0.21
Primary bloodstream	122 (10.5)	54 (8.07)	68 (13.82)	0.002
Gastrointestinal tract	121 (10.4)	74 (11.06)	47 (9.55)	0.41
Urinary tract	118 (10.2)	77 (11.51)	41 (8.33)	0.08
<i>Severity scores</i>				
SMS-ICU	18 (13–22)	17 (13–20)	22 (17–25)	<0.001
SSS	71 (49–90)	54 (39–71)	91 (77–107)	<0.001
APACHE II	22 (15–31)	17 (13–21)	33 (27–37)	<0.001
APACHE IV	78 (56–120)	60 (47–72)	124 (105.5–142)	<0.001
SAPS II	51 (39–69)	41 (33–49)	72 (64–82)	<0.001
SOFA	10 (6–13)	7 (4–10)	13 (11–15)	<0.001
Lactate (mmol/L)	4.7 ± 5.3	3.3 ± 4.3	6.7 ± 5.8	<0.001
ICU LOS (days)	4 (2–8)	4 (2–8)	4 (2–9)	0.78
Hospital LOS (days)	18 (9–33)	19 (10–36)	16 (6–31)	<0.001

*Unless otherwise indicated, the data are presented as medians with interquartile ranges. APACHE, acute physiology and chronic health evaluation; ICU, intensive care unit; LOS, length of stay; SAPS, simplified acute physiology score; SOFA, sequential organ failure assessment; SMS-ICU, simplified mortality score for the intensive care unit; SSS, sepsis severity score

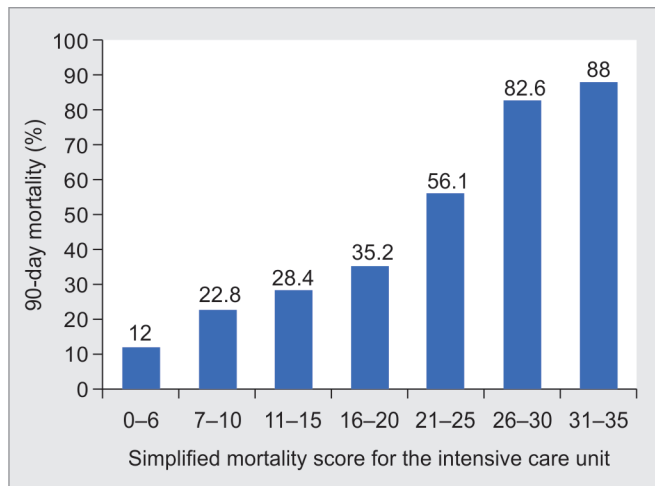


Fig. 1: The 90-day mortality stratified by the SMS-ICU

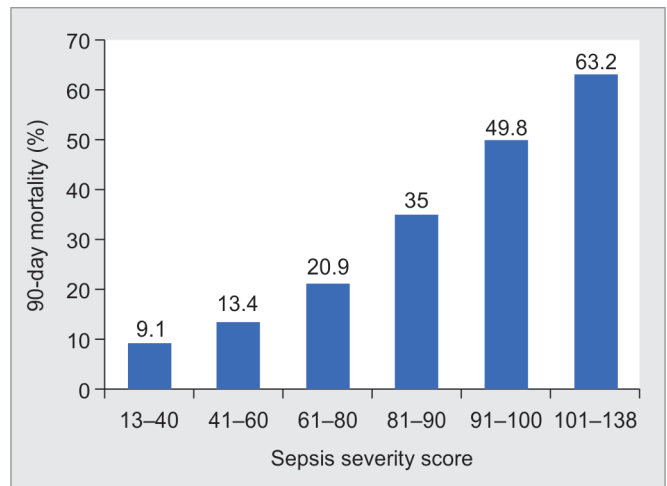


Fig. 2: The 90-day mortality stratified by the SSS

For the calibration assessment, the SMS-ICU reported SMRs of 1.36 (95% CI: 1.24–1.48) for the 90-day and 1.33 (95% CI: 1.22–1.46) for in-hospital mortalities, which were underestimated in both mortalities, whereas the APACHE II, SAPS II, and SSS had SMRs between 0.95 and 1.01, which represented appropriate estimations for the 90-day and in-hospital mortalities (Tables 2 and 3). However, the APACHE IV overpredicted the 90-day and in-hospital mortalities with an SMR of 0.92 (95% CI: 0.84–1.01) and 0.90 (95% CI: 0.82–0.99), consecutively. The SMS-ICU demonstrated poor calibration in

predicting the 90-day and in-hospital mortalities, similar to that seen with both the disease-specific SSS and commonly used standard severity scores according to the Hosmer–Lemeshow goodness-of-fit H; $p < 0.05$ (Tables 2 and 3). None of these scores showed good calibration for forecasting the 90-day mortality, as shown in the calibration graph (Fig. 4).

According to the Brier scores, which represent the overall performance, the SMS-ICU had inferior overall performance than the SSS in both 90-day and in-hospital mortality predictions

Table 2: Predictive performance of the SMS-ICU, SSS, APACHE II, APACHE IV, and SAPS II for 90-day mortality

Severity score	AUROC (95% CI)	SMR (95% CI)	H- χ^2 , p-value	C- χ^2 , p-value	Brier score
SMS-ICU	0.710 (0.680–0.740)	1.36 (1.24–1.48)	102.1, <0.0001	79.0, <0.0001	0.222
SSS	0.876 (0.856–0.896)	1.01 (0.93–1.11)	45.3, <0.0001	8.3, 0.60	0.169
APACHE II	0.936 (0.922–0.950)	0.97 (0.89–1.06)	43.1, <0.0001	5.6, 0.85	0.099
APACHE IV	0.957 (0.946–0.968)	0.92 (0.84–1.01)	89.9, <0.0001	10.9, 0.37	0.111
SAPS II	0.950 (0.938–0.962)	0.96 (0.88–1.05)	74.2, <0.0001	7.3, 0.70	0.092

APACHE, acute physiology and chronic health evaluation; AUROC, area under the receiver operating characteristic; C, Hosmer–Lemeshow goodness-of-fit C test; CI, confidence interval; H, Hosmer–Lemeshow goodness-of-fit H test; SAPS, simplified acute physiology score; SMS-ICU, simplified mortality score for the intensive care unit; SSS, sepsis severity score

Table 3: Predictive performance of the SMS-ICU, SSS, APACHE II, APACHE IV, and SAPS II for in-hospital mortality

Severity score	AUROC (95% CI)	SMR (95% CI)	H- χ^2 , p-value	C- χ^2 , p-value	Brier score
SMS-ICU	0.696 (0.664–0.726)	1.33 (1.22–1.46)	92.5, <0.0001	68.4, <0.0001	0.224
SSS	0.879 (0.859–0.898)	0.99 (0.91–1.09)	46.2, <0.0001	7.25, 0.70	0.168
APACHE II	0.941 (0.927–0.954)	0.95 (0.87–1.04)	52.4, <0.0001	5.87, 0.83	0.096
APACHE IV	0.959 (0.948–0.970)	0.90 (0.82–0.99)	88.4, <0.0001	13.4, 0.20	0.112
SAPS II	0.952 (0.940–0.963)	0.95 (0.86–1.03)	81.2, <0.0001	7.6, 0.67	0.091

APACHE, acute physiology and chronic health evaluation; AUROC, area under the receiver operating characteristic; C, Hosmer–Lemeshow goodness-of-fit C test; CI, confidence interval; H, Hosmer–Lemeshow goodness-of-fit H test; SAPS, simplified acute physiology score; SMS-ICU, simplified mortality score for the intensive care unit; SSS, sepsis severity score

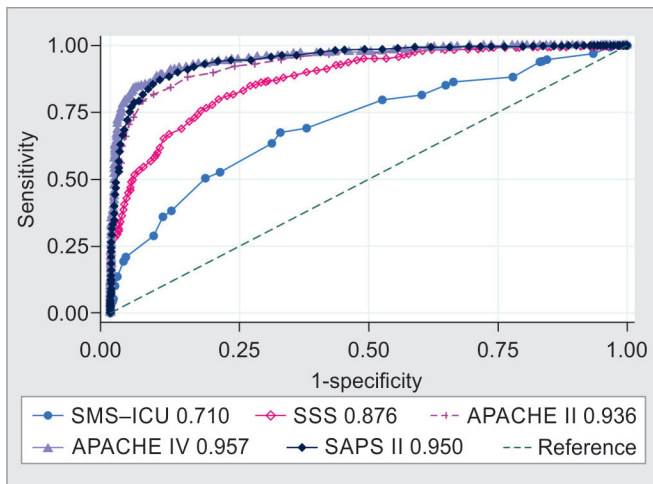


Fig. 3: Comparison of the AUROC of the SMS-ICU, SSS, and other severity scores for the 90-day mortality prediction in sepsis patients

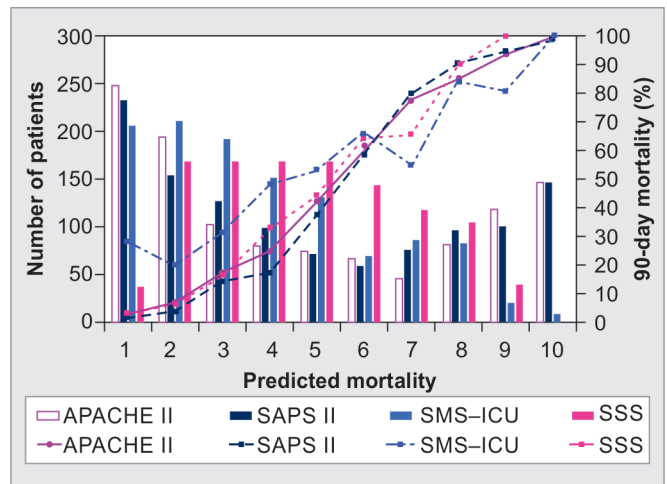


Fig. 4: Comparison of the calibration of the SMS-ICU, SSS, and other standard severity scores for 90-day mortality prediction in sepsis patients

(Tables 2 and 3). The SAPS II presented the best overall performance with Brier score 0.092.

DISCUSSION

For the prediction of 90-day mortality in ICU-admitted sepsis patients, this study demonstrated that the SMS-ICU had moderate discrimination. In comparison to disease-specific severity scores such as SSS and standard severity scores such as SAPS II, APACHE II, and APACHE IV, the SMS-ICU demonstrated lower overall performance and discrimination.

The intricacy of frequently using standard severity scores gradually lessens their clinical usefulness over time.²² Therefore, the development of a simple severity score may be a strategy to improve the use of severity score in ICU patients. Granholm et al.

developed the SMS-ICU to predict 90-day mortality.¹³ This score was obtained from a database of cohort studies and randomized controlled trials that primarily included patients with sepsis. The SMS-ICU contained seven clinical and physiological variables that ranged from 0 to 42. Internal validation showed that the instrument had a high calibration and discrimination of 0.72.¹³ However, SMS-ICU had lower discrimination than SAPS II, which revealed an AUROC of 0.88 in 1993,¹⁷ and SAPS 3, which showed an AUROC of 0.848 in 2005.²³

The SMS-ICU was tested for external validation in critically ill patients in Brazil, which was recently published in 2020 and compared with the SAPS 3.¹⁵ The findings from the validation cohort demonstrated that the discrimination of the SMS-ICU was good (AUROC, 0.817), although slightly lower than that of the SAPS 3

with an AUROC of 0.845. In terms of calibration, the customized predictions generated by the SMS-ICU showed similarity to those produced by the SAPS 3. However, in the subgroup analysis of Brazilian ICU patients admitted due to infection, the SMS-ICU's discrimination declined to 0.785, which is a moderate discrimination comparable to that of the SMS-ICU in our investigation and the original.

Regarding calibration, the present study showed that the 90-day and in-hospital mortality rates were underestimated by the SMS-ICU. Underestimating the risk could result in inaccurate admission policies and an undervaluation of care quality, performance, and effectiveness, particularly when utilized for benchmarking purposes.²⁴ The reason for the poor calibration may be that the SMS-ICU contained only seven parameters with five dichotomous variables that could not be assessed in detail in our critical sepsis patients, who had high severity scores and higher mortality rates than those in the original study. The 90-day mortality rates of the populations in our study and the original study were 42.4 and 34.3% respectively. Various studies have revealed a correlation between the dose of vasopressors/inotropic agents and mortality;^{25–28} however, the SMS-ICU only recorded whether vasopressors/inotropes were used. Furthermore, the SMS-ICU only evaluates the usage of respiratory support, and the PaO₂/FiO₂ ratio is generally one of the measures that correlates with the severity and mortality of respiratory problems.^{29–31} Our population did not require acute surgical admission, which is one of the domains in the SMS-ICU scoring. Therefore, customizing changes by converting some dichotomous variables to ordinal parameters, such as the stratified dose of vasopressors/inotropic agents, PaO₂/FiO₂ ratio instead of recording only the use of respiratory support, and considering the collected lactate levels, which revealed significant differences between survivors and deaths on day 90 in our study population, may improve the overall performance of the SMS-ICU. Finally, the accuracy of the performance of these scores in our study of sepsis diagnosis by Sepsis-3 criteria that were developed in 2016 may not be the same result as using alternative sepsis definitions from the original study that developed the SMS-ICU and investigated sepsis/septic shock patients between 2009 and 2016.

Compared to the disease-specific SSS, the SMS-ICU showed moderate discrimination, whereas the SSS showed good discrimination. The SSS model had 34 categorical variables, whereas the SMS-ICU model featured seven domains with five dichotomous variables. The SSS included vital sign parameters for responding to hypotension, tachypnea, and assessing body temperature. In addition, the SSS also contains specific mechanical ventilator parameters, including plateau pressure, as well as crucial parameters related to organ failure, similar to the SOFA score comprising the domain of organ failure, which presented a good discrimination in forecasting hospital death among patients with sepsis.^{32,33}

According to the findings of our study, conventional scoring systems could be employed in populations with sepsis because they provide good discriminating with an AUC above 0.9. Although APACHE IV had the best discrimination, its practical application is difficult due to its reliance on 142 physiological parameters and the need for proprietary computer software to compute the expected mortality. On the contrary, the SAPS II had the best overall performance and was simpler to use because it had fewer variables and the ability to gather these parameters during ICU care, and it

had comparable discrimination to APACHE IV. Therefore, the SAPS II may be appropriate for use in ICU sepsis patients.

There were some limitations in our study. First, because the investigation was performed solely in a medical ICU, it is essential to recognize that our findings might not be universally applicable or generalizable to other ICU settings. Therefore, prospective multicenter studies are warranted. Second, this study evaluated sepsis patients solely in the medical ICU; hence, our results could not be representative of surgical ICU sepsis patients for acute surgical admission.

CONCLUSION

The SMS-ICU indicated lower discrimination and overall performance than the disease-specific SSS and other original severity scores. The calibration of the SMS-ICU was poor and revealed an underestimation when predicting the 90-day mortality in sepsis patients. Consequently, customization of the SMS-ICU is imperative to enhance its performance.

Ethical Approval

This study was approved by the Human Research Ethics Committee of the Faculty of Medicine at Prince of Songkla University, Hat Yai, Songkhla, Thailand (REC 63-293-14-1). The requirement for informed consent was waived because of the retrospective design.

AUTHORS' CONTRIBUTION

BK: Conceptualization, data collection, data curation, formal analysis, review and editing manuscript.

NS: formal analysis, manuscript draft.

All authors read and approved the manuscript.

SUPPLEMENTARY MATERIALS

All the supplementary materials are available online on the website of <https://www.ijccm.org/journalDetails/IJCCM>.

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