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# Validation the performance of New York Sepsis Severity Score compared with Sepsis Severity Score in predicting hospital mortality among sepsis patients

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ABSTRACT

*Purpose:* The aim of this study was to compare the performance of the New York Sepsis Severity Score (NYSSS) with the Sepsis Severity Score (SSS) and Acute Physiology and Chronic Health Evaluation and Simplified Acute Physiology Scores for predicting mortality in sepsis patients.
*Method:* A retrospective analysis was conducted in the intensive care unit. The primary outcome was in-hospital mortality.
*Results:* Overall 1680 sepsis patients were enrolled. The hospital mortality rate was 44.4%. The NYSSS underestimated actual mortality with standard mortality ratio (SMR) of 1.28 (95%CI 1.19–1.38). However, the SSS slightly overestimated the actual mortality with an SMR of 0.94 (0.88–1.01). The NYSSS had moderate discrimination with an AUC of 0.772 (0.750–0.794), in contrast to the SSS which had good discrimination with an AUC of 0.889 (0.873–0.904). The AUC of the SSS was statistically higher than that of the NYSSS. The AUCs of both the NYSSS and SSS were significantly lower than other standard severity scores. The calibrations for all severity scores were poor. The SSS had better overall performance than the NYSSS (Brier score 0.149 and 0.201, respectively).
*Conclusion:* The SSS had better discrimination and overall performance than the NYSSS. However, both sepsis severity scores were poorly calibrated.



## 1. Introduction

Sepsis, defined as severe infection with organ dysfunction, is one of the common causes of intensive care unit (ICU) admission and can lead to multiple organ failures and death [1-3]. Early recognition [4,5] and aggressive treatment of sepsis can improve outcomes and increase the chance of survival [6,7].

Severity scoring systems have been designed to evaluate severity of illness and estimated mortality outcome of critically-ill patients [8,9]. Also, severity scores can be used for assessment of ICU performance, quality measurement and clinical research [10-12]. The Acute Physiology and Chronic Health Evaluation (APACHE) and Simplified Acute Physiology Score (SAPS) are the most commonly used scoring systems for critically-ill patients [9,13]. These scores were developed for general critically-ill populations but not specifically for sepsis patients.

In 2014, a severity score specific for sepsis was developed to predict mortality in sepsis patients specifically. The Sepsis Severity Score (SSS) was derived from the Surviving Sepsis Campaign database [14]. This scoring system was tested and found to have good performance for estimating hospital mortality in sepsis patients. A previous study from our ICU showed that the SSS had as good discrimination as the APACHE II, SAPS II and SAPS-3 scores in predicting mortality in ICU sepsis patients [15]. More recently, the New York Sepsis Severity Score (NYSSS) was devised based on the records of 43,200 sepsis patients from 179 New York State hospitals to predict mortality in sepsis. The NYSSS demonstrated good discrimination and calibration to predict hospital mortality in adult patients with severe sepsis and septic shock [16].

Our hypothesis is that the performance of the NYSSS equal to the SSS and both scores may be provided better performance than general standard severity scores to predict mortality in sepsis patients. However, various studies have found that the performance of severity scores declines when applied to other populations than those for which the scores were specifically developed [15,17-19]. Therefore, this study was conducted to compare the performance of the NYSSS with SSS for predicting hospital mortality in adult sepsis patients. The secondary purpose of this study was to compare the performance of both sepsis

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severity score with general severity scores (APACHE II-IV, SAPS II and SAPS-3) to predict mortality in sepsis patients admitted into the ICU.

## 2. Methods

This study was a retrospective analysis of a prospective registry database of severity scoring systems and sepsis database of patients admitted to our medical ICU. Our ICU had a 10 to 12-bed within an 842-bed of tertiary referral university teaching hospital at Prince of Songkla University, Thailand. Our ICU is run by three full-time, board-certified intensivists and nurse to patient ratio was 1:1-2. The study was approved by our Institutional Human Research Ethics Committee (REC 61-306-14-1) with a waiver of informed consent.

Patients 18 years of age or older diagnosed with sepsis admitted to the ICU between 2011 and 2017 were included. Sepsis was defined by suspected or documented infection with a Sequential Organ Failure Assessment (SOFA) score of at least 2 [20]. Septic shock was defined by sepsis with persistent hypotension requiring vasoactive agents to maintain a mean arterial pressure of at least 65 mmHg and having serum lactate ≥2 mmol/L. Patients for whom a serum lactate level within 24 h of diagnosis of sepsis was not in the records and who had been re-admitted to the ICU during their hospital stay were excluded.

The databases contained prospectively data collection, acquired as part of the severity scoring systems (APACHE and SAPS scores) and sepsis registry in our unit, were collected by a single well-trained research assistant with previous experience in this process [3,15,21]. On a quarterly basis, 20% of the data sheets and clinical charts were randomly selected by the corresponding author to assess the reliability of data collection. All parameters required by the SSS [14], NYSSS [16] as described in the original studies were abstracted for analysis (Supplemental Tables S1–2). We modified patient pay items in the NYSSS as they were affected by the Thailand public health care insurance (details in Supplemental Table S3). The physiological data record in the SSS, NYSSS, APACHE II-IV [22-24], and SAPS II [25] instruments were based on the worst values within the first 24 h after ICU admission, while the physiological data of the SAPS-3 [26] were based on the first hour before or after ICU admission. For the individual SOFA items, the worst SOFA values during the first 24 h were used [20]. The probability of hospital mortalities based on the SSS, NYSSS, APACHE II, SAPS II and SAPS-3 scores were calculated by previously validated algorithms [14,16,22,25,26]. The APACHE III and IV predictions of hospital mortality were obtained from the Cerner Corporation via https://apachefoundations.cernerworks.com/apachefoundations. The primary outcome was in-hospital mortality.

We conducted a hypothesis test against the null hypothesis that the performance of two sepsis severity score may not different than 8%. Based on previous study in our ICU, the area under the receiver operating characteristic curves (AUC) of SSS was 0.892 [15]. With 80% power and 5% type I error, the minimum of sample size was 1422 cases.

Descriptive continuous variable data are reported as means ± standard deviations, and median (interquartile range) and discrete variable data are presented as percentages. Chi-square and Wilcoxon's rank sum were used to compare categorical and continuous variable data, respectively. The performance of the severity scores was evaluated by discrimination, calibration, and overall performance. Discrimination refers to the ability of the scoring model to discriminate between patients who died from those who survived and was evaluated by the AUC [8,13]. Pairwise comparisons of the AUCs were performed based on the method purposed by Delong et al. [27]. Calibration assesses the degree of correspondence between the estimated probabilities of mortality and actual mortality. Calibrations of severity scores were tested by the Hosmer-Lemeshow goodness of fit H and C statistics and standardized mortality ratio (SMR) [8,13]. A p-value > .05 for the goodness of fit test was used to indicate good calibration. The SMR is a ratio between the observed number of deaths in the study population and the number of deaths which would be expected from a severity score. An SMR >1 indicates an underestimation, while an SMR lower than 1 indicates an overestimation of the mortality by the predictive score. Calibration curves were constructed by plotting predicted mortality rates, stratified by 10% increments of predicted mortality versus actual mortality rates. The Brier score offers an overall assessment of performance, involving elements of both discrimination and calibration. The Brier score is the mean squared difference between the probability of death and the actual outcome [8]. A lower score represents high accuracy. Stata 11 software was used for statistical analysis.

## 3. Results

There were 1810 sepsis patients admitted within our ICU during study period. After exclusion of 130 patients (Fig. 1), 1680 patients were included into the study analysis. A total of 895 patients (53.3%) were classified as septic shock. The actual hospital mortality rate was 44.4%. The most common source of infection was respiratory tract infection (51.8%). The clinical characteristics of the study patients classified by in-hospital mortality are presented in Table 1. Non-survivors had more co-morbidities and higher severity scores than survivors.

Hospital mortality rate as classified by NYSSS and SSS are shown in Fig. 2 and Fig. 3, respectively. Hospital mortality increased in patients with higher scores. NYSSS of <100 had a hospital mortality rate of about 20%, rising to almost 90% in patients with an NYSSS over 400 (Fig. 2). All patients with SSS less 40 survived. A hospital mortality rate of about 8% was noted in patients with SSS <60, while the hospital mortality rate was >85% in those patients with an SSS of >110 (Fig. 3). The performance of the NYSSS, SSS, APACHE II-IV, SAPS II and SAPS-3 scores are summarized in Table 2. The SMRs of the severity scores varied between 0.82 and 1.28. The NYSSS predicted hospital mortality of 34.6 ± 21.5%, which underestimated the actual figure with an SMR of 1.28 (95%CI 1.19–1.38). However, the SSS predicted hospital mortality of 47 ± 22.2%, which slightly overestimated the actual mortality giving an SMR of 0.94 (95%CI 0.88–1.01). All scores had good discrimination with AUCs of 0.889 to 0.937 except for the NYSSS that had only moderate discrimination with an AUC of 0.772 (95%CI 0.750–0.794) (Table 2 and Fig. 4). The AUC of the SSS was statistically significantly higher than that the NYSSS ($p < 0.0001$). However, the AUCs of both the NYSSS and SSS were significantly lower than the other standard severity scores ($p < 0.001$ for all). The APACHE IV and SAPS II showed the best discrimination with AUC of 0.937. The NYSSS ≥190 had a sensitivity 60.2% and specificity of 71.1% as well as SSS ≥ 89 providing a sensitivity of 72.6% and specificity of 80.1%, for hospital mortality.

The calibration of all severity scores was poor according to the Hosmer-Lemeshow goodness-of-fit H test <0.05 (Table 2). The calibration graph showed that none of these tests had good calibration (Fig. 5 and Supplemental Fig. S1).

Overall performance as assessed by Brier scores revealed that the SSS was better than the NYSSS with Brier scores of 0.149 and 0.201, respectively. However, the APACHE IV had the best overall performance with a Brier score of 0.107 (Table 2).

## 4. Discussion

In this study, the SSS had better discrimination and overall performance than the NYSSS for predicting hospital mortality in sepsis patients admitted to the ICU. However, the APACHE IV had the best discrimination and overall performance. Nevertheless, the calibration of both specific sepsis severity scores (NYSSS and SSS) and the other general severity scores performed poorly in terms of being able to predict hospital mortality in sepsis patients.

The SSS was developed by Osborn et al. to estimate the probability of hospital mortality among sepsis patients [14]. This score was derived from the database of the Surviving Sepsis Campaign. They reported AUCs of 0.736 in the development group and 0.748 in the validation group, respectively, with good calibration as measured by the

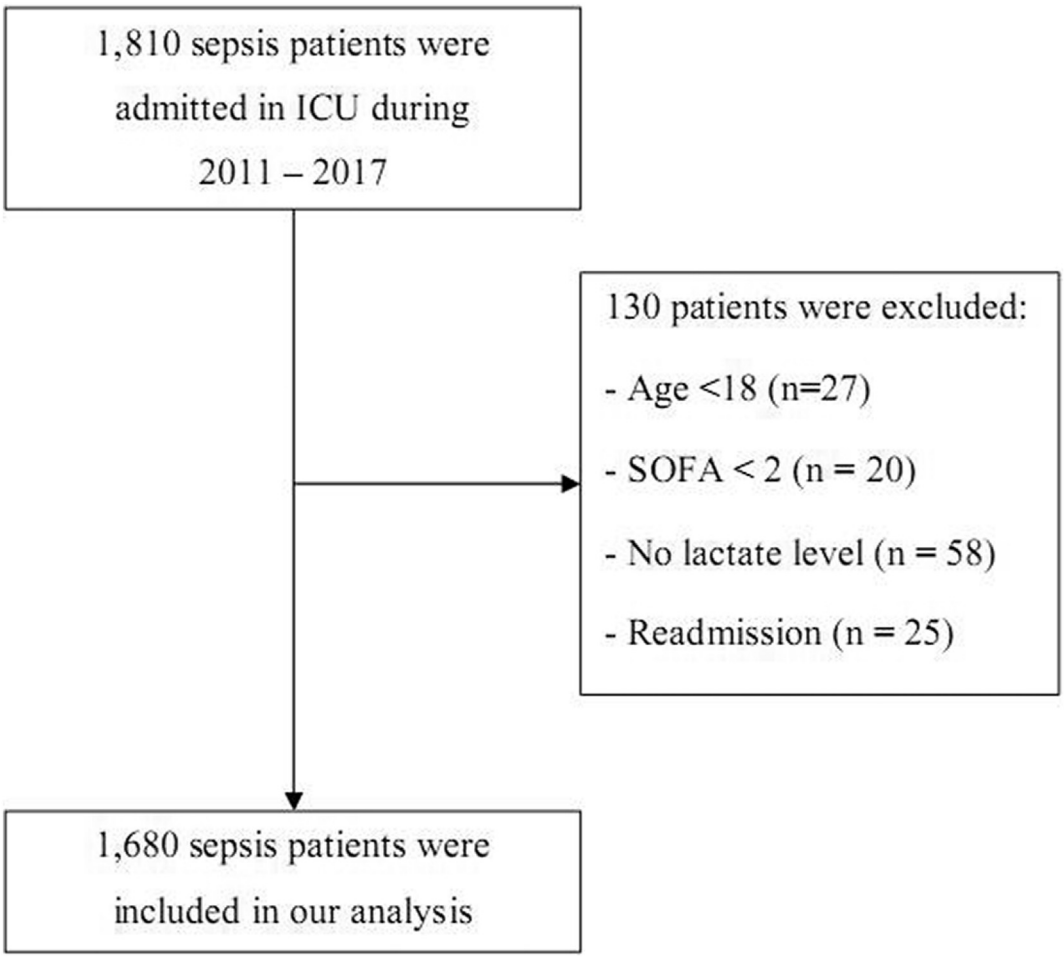


**Fig. 1.** Flow chart of study population.

**Table 1**
Clinical demographic data.

| | All patients (n = 1680) | Survivors (n = 934) | Non-survivors (n = 746) | p-Value |
|---|---|---|---|---|
| Age | 63 (48–76) | 62 (46–75) | 64 (50–77) | 0.09 |
| Male (n [%]) | 943 (56.1) | 512 (54.3) | 431 (45.7) | 0.22 |
| Co-morbidities (n [%]) | 611 (36.4) | 261 (42.7) | 350 (57.3) | <0.001 |
| - Hematologic malignancy | 171 (28) | 58 (33.9) | 113 (66.1) | <0.001 |
| - Immunocompromised | 124 (20.3) | 73 (58.9) | 51 (41.1) | 0.45 |
| - Liver cirrhosis | 84 (13.7) | 29 (34.5) | 55 (65.5) | <0.001 |
| Site of infection | | | | |
| - Respiratory | 870 (51.8) | 454 (52.2) | 416 (47.8) | 0.004 |
| - Gastrointestinal | 219 (13) | 130 (59.4) | 89 (40.6) | 0.23 |
| - Primary blood stream | 157 (9.4) | 62 (39.5) | 95 (60.5) | <0.001 |
| Severity scores | | | | |
| - SSS | 84 (69–100) | 73 (62–85) | 99 (87–112) | <0.001 |
| - NYSSS | 180 (130.5–226) | 161 (109–201) | 206 (160–268) | <0.001 |
| - APACHE II | 22 (15–31) | 16 (13−21) | 32 (26–36) | <0.001 |
| - APACHE III | 81 (57–120) | 60 (47–76) | 124 (104–142) | <0.001 |
| - SAPS II | 52 (38–71) | 40 (31–49) | 72 (62–84) | <0.001 |
| - SAPS- 3 | 71 (59–88) | 61 (54–69) | 90 (81–99) | <0.001 |
| SOFA | 9 (6–12) | 6 (4–9) | 12 (10–15) | <0.001 |
| Lactate (mmol/L) | 2.5 (1.3–5.1) | 1.8 (1–3.5) | 3.6 (2.1–8.5) | <0.001 |
| ICU LOS (days) | 4 (2–8) | 3 (2–7) | 4 (2–8) | 0.79 |

Unless otherwise indicated, numbers are given as medians with interquartile ranges.
APACHE: Acute Physiology and Chronic Health Evaluation; ICU: Intensive Care Unit; LOS: length of stay; NYSSS: New York Sepsis Severity Score; SAPS: Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment; SSS: Sepsis Severity Score.

Hosmer-Lemeshow goodness-of-fit test ($p = 0.94$). In our study, the discrimination of the SSS was higher than that of the original study (AUC 0.889) but the calibration was poor.

Recently, a new severity score specific for sepsis was devised from a large clinical database of 179 New York State hospitals [16]. They reported the AUC of the validation group was 0.773, indicating moderate discrimination, but this score had good calibration assessed by the Hosmer-Lemeshow goodness of fit test. In our study, the discrimination of the NYSSS (AUC 0.772) was similar to the original study but the calibration was poor with a Hosmer-Lemeshow goodness-of-fit H test <0.05.

The reason of the SSS has better discrimination and overall performance than the NYSSS may be from differences in the categorical variables used. The SSS model has 34 categorical variables while, the NYSSS has only 17 items within 13 categorical variables. The SSS has vital signs parameters such as hypothermia, hyperthermia, tachypnea, and responsive or unresponsive hypotension. Importantly, the SSS provides parameters indicating organ failures, the same as the SOFA score. Previous studies found that the SOFA offers good discrimination in predicting hospital mortality in sepsis patients [3,28]. Moreover, the SSS and NYSSS have obvious differences in the categorical details involving mechanical ventilation. The SSS includes mechanical ventilation details such as plateau pressure and organ failure, while the NYSSS record only whether the patient is on a mechanical ventilator or not.

Our study found that the AUCs of the NYSSS and SSS were both significantly lower than the standard severity scores. In contrast, a previous study from our ICU found that the discrimination of the SSS was comparable to the APACHE II, SAPS II and SAPS-3 [15]. There are several factors may affect the different between two studies such as differences

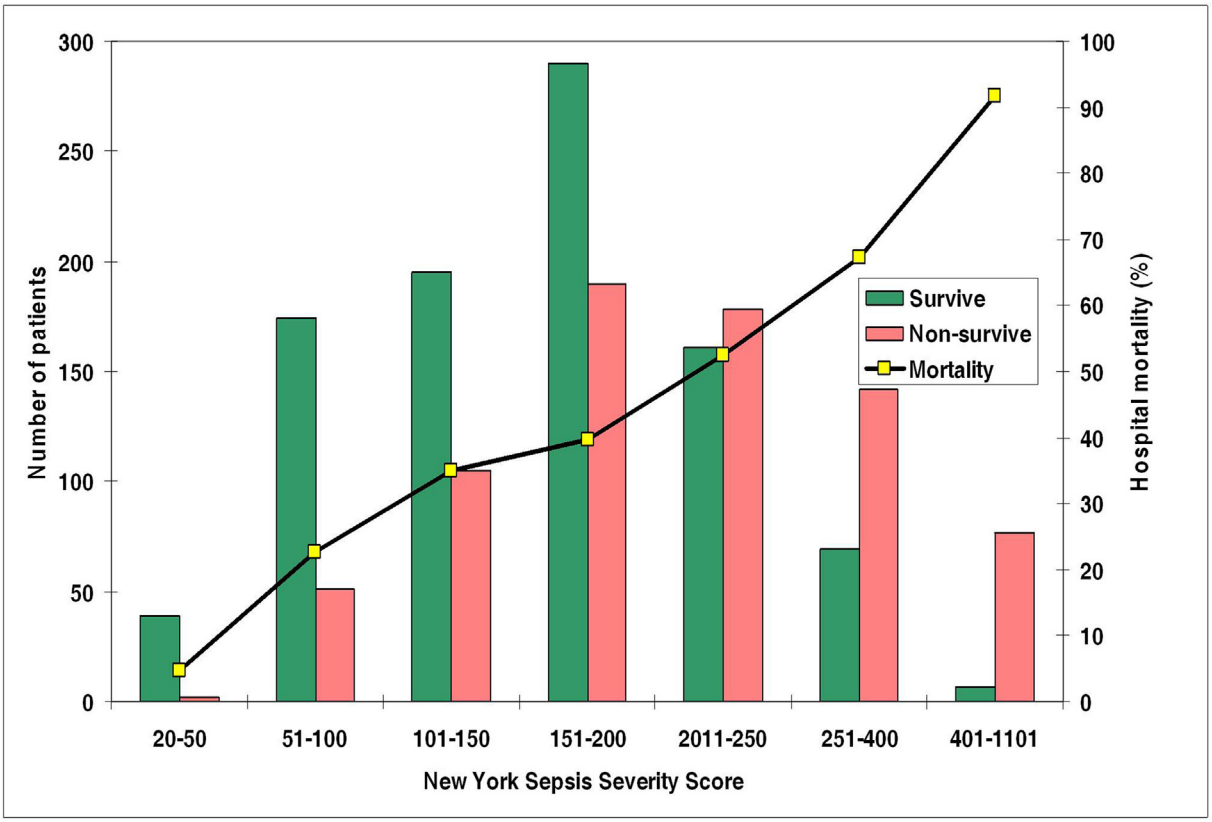


**Fig. 2.** Hospital mortality rate arranged by New York Sepsis Severity Score (NYSSS).

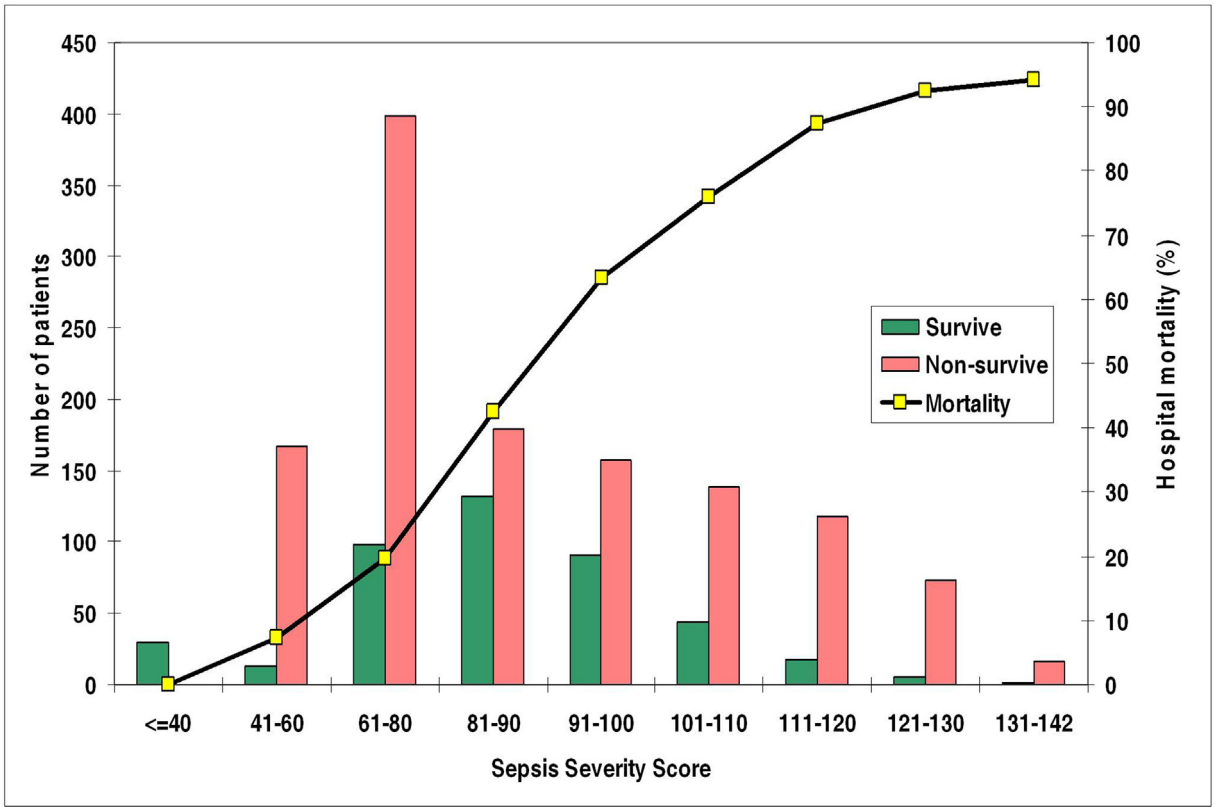


**Fig. 3.** Hospital mortality rate arranged by Sepsis Severity Score (SSS).

**Table 2**
The performance of SSS, NYSSS, APACHE II, III, IV, SAPS II, and SAPS 3.

| | AUC (95% CI) | SMR (95% CI) | H Chi-2, p-value | C Chi-2, p-value | Brier score |
|---|---|---|---|---|---|
| SSS | 0.889 (0.873–0.904) | 0.94 (0.88–1.01) | 144.7, <0.0001 | 18.7, 0.04 | 0.149 |
| NYSSS | 0.772 (0.750–0.794) | 1.28 (1.19–1.38) | 73.5, <0.0001 | 73.4, <0.0001 | 0.201 |
| APACHE II | 0.923 (0.910–0.936) | 0.9 (0.84–0.97) | 150.6, <0.0001 | 22.4, 0.01 | 0.120 |
| APACHE III | 0.922 (0.908–0.935) | 1.08 (1.00–1.16) | 85.9, <0.0001 | 14.5, 0.15 | 0.112 |
| APACHE IV | 0.937 (0.926–0.948) | 0.97 (0.91–1.05) | 112.6, <0.0001 | 6.8, 0.74 | 0.107 |
| SAPS II | 0.937 (0.926–0.949) | 0.86 (0.80–0.92) | 143.6, <0.0001 | 42.1, <0.0001 | 0.109 |
| SAPS-3 | 0.926 (0.913–0.939) | 0.82 (0.76–0.88) | 290.7, <0.0001 | 122.6, <0.0001 | 0.141 |

APACHE: Acute Physiology and Chronic Health Evaluation; AUC: 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; NYSSS: New York Sepsis Severity Score; SAPS: Simplified Acute Physiology Score; SMR: standardized mortality ratio; SSS: Sepsis Severity Score.

in study populations or severity of disease and clinical sepsis care processes. However, the AUC of the APACHE IV score in a previous study was statistically greater than the SSS, which was also found in this study [5]. The better discrimination of the APACHE IV than the SSS may be from the inclusion of age, co-morbidities and more predictor variables.

Sepsis patients are heterogeneous in severity of illness, and severity scores are important tools for risk assessment and, mortality prediction as well as resource allocation. The SSS is better than the NYSSS for assessing risk stratification in sepsis patients. Similar to previous studies, we found that the calibration of all severity scoring systems was poor for predicting mortality in sepsis patients. The possible causes for poor calibration may be differences in the case mixes or progression of sepsis care over time. Therefore, new sepsis severity scores or customization of the SSS or NYSSS may improve the performance of outcome prediction in sepsis patients. Several studies have reported significantly improved calibration after customization of severity scores [17,21,29]. The performance of the SSS may be improved by secondary customization by using new variable parameters such as age, co-morbidities and/or new physiological variables. The NYSSS may be modified for better accuracy by adding new hemodynamic parameters or bio-markers.

We can deduce from our study results that non-disease specific scoring systems such as APACHE IV and SAPS II could be used in sepsis populations due to the best discrimination. Although, APACHE IV had the best discrimination and overall performance, this score is not easy to use because it requires a large amount of detailed physiological data (142 variables) and proprietary computer software to calculate the predicted mortality. SAPS II may be suitable to use for sepsis patients in an ICU as it has good discrimination and is easy to use because has fewer variables and these parameters can collected during the ICU care.

To the best of our knowledge, this is the first external validation of the performance of the NYSSS in predicting hospital mortality in sepsis patients, and it is also the first attempt to compare NYSSS with SSS along with other standard severity scores. Our study has some limitations. First, the nature of retrospective design may be carries risk of bias to establish outcome. The data for this analysis were not primarily collected for the study purpose. Second, this was a study involving a single medical ICU, and other ICUs may have differences in case-mixes and ICU care policies. So our results may have limited generalizability to other ICUs, and each ICU should validate or customize the severity score equation to develop the most suitable prognostic model for their particular situation. Prospective multicenter studies are needed to validate our results.

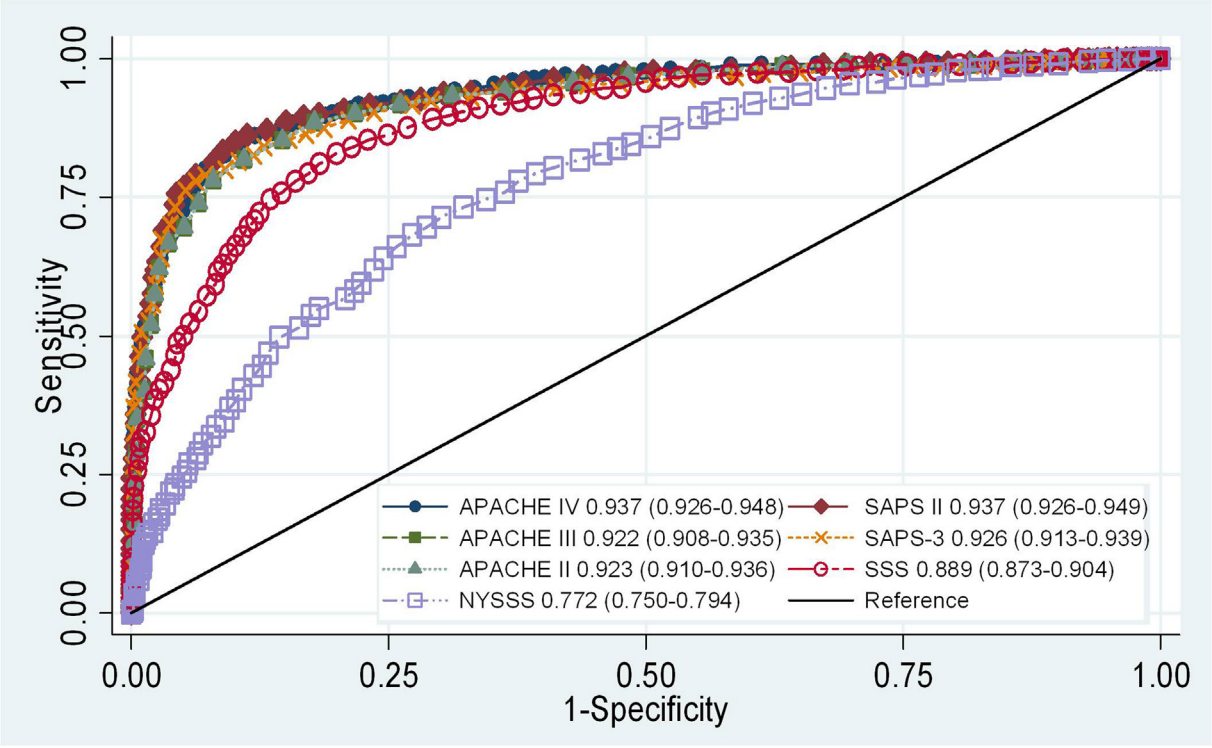


**Fig. 4.** Comparison of the areas under the receiver operating characteristic curves of NYSSS and SSS with other severity scores for predicting hospital mortality in ICU sepsis patients.

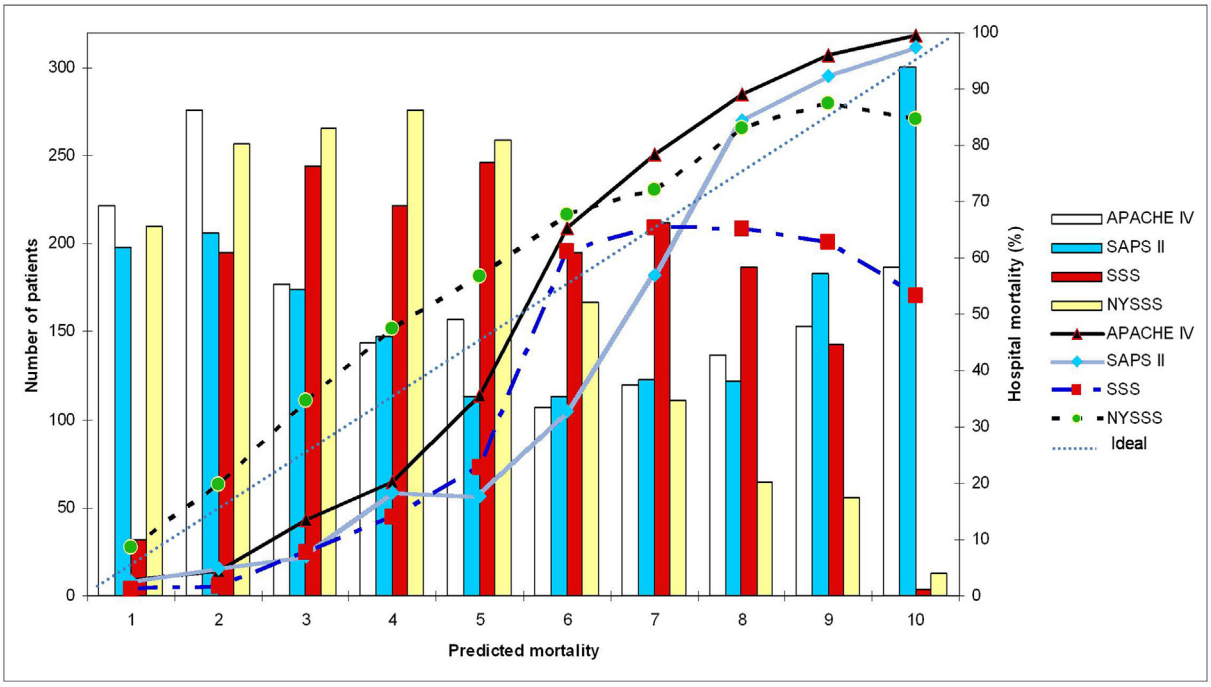


**Fig. 5.** Calibration curves for NYSSS, SSS, APACHE IV and SAPS II.

Third, we only evaluated sepsis patients admitted to a medical ICU; consequently, these results may not apply to surgical or traumatic sepsis patients. Finally, the accuracy of these scores for predicting mortality in sepsis diagnosed by Sepsis-3 criteria may not be the same as those diagnosed using the old Sepsis-1 or 2 criteria.

## 5. Conclusion

The SSS indicated better discrimination and overall performance than the NYSSS. However, the calibrations of both sepsis severity scores and the other standard severity scores were poor. Specific severity scores for sepsis patients need to be modified or customized for improved performance.

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None.

## Declaration of Competing Interests

None.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2019.06.017.

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