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Comparison of the accuracy of three early warning scores with SOFA score for predicting mortality in adult sepsis and septic shock patients admitted to intensive care unit

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ABSTRACT

Background: The purpose of this study was to compare the accuracy of the Modified Early Warning Score (MEWS), National Early Warning Score (NEWS) and Search Out Severity (SOS), with the quick Sequential Organ Failure Assessment (qSOFA) and SOFA scores, to predict outcomes in sepsis patients.
Methods: A retrospective study was conducted in intensive care unit of university teaching hospital.
Results: A total of 1,589 sepsis patients were enrolled. The SOFA score had the best accuracy to predict hospital mortality, with an area under the receiver operating characteristic curve (AUC) of 0.880 followed by SOS (0.878), MEWS (0.858), qSOFA (0.847) and NEWS (0.833). The SOS score provided a similar performance with SOFA score in predicting mortality.
Conclusion: The SOS presents nearly as good as the SOFA score, to predict mortality among sepsis patients admitted to the ICU. The early warning score is another, alternative tool to use for risk stratification and sepsis screening for ICU sepsis patients.

Introduction

Sepsis is one of the major causes of morbidity and mortality around the world.[1–5] Several studies have reported an increased incidence of sepsis,[3,6] with a trend of slightly decreased mortality.[6,7] Early detection along with the use of sepsis care bundles is associated with lower mortality.[8–10]

One of the key strategies for improving sepsis management is to identify the subgroup of patients with infection who are at high risk of developing adverse outcomes. This may help clinicians to initiate early treatment such as; early antibiotic administration and fluid resuscitation. The early warning scores (EWS) were developed for bedside evaluation, as track and trigger systems, to allow for early detection of patient deterioration.[11] The most popular EWS were; the Modified Early Warning Score (MEWS) and National Early Warning Score (NEWS).[11–13] MEWS has been validated in several critically ill patients and showed that this score could predict hospital admission and mortality outcome.[14,15] NEWS has been adopted by the Royal College of Physicians for standard EWS in England.[16] Several studies evaluated the accuracy of NEWS in sepsis patient in emergency department and wards and revealed that NEWS could be used to predict death and ICU admission.[17,18] Champunot and colleagues created the Search Out Severity (SOS) score, by modified MEWS, as a screening tool to help early sepsis diagnosis and management.[10] The author found that screening with SOS and implementing a checklist of sepsis bundles could decrease mortality in sepsis patients in Thailand.

Recently, the Society of Critical Care Medicine (SCCM) and the European Society of Critical Care Medicine (ESICM) promoted a Third International Consensus Definitions for Sepsis (Sepsis-3).[19] Sepsis is now diagnosed by an increase of the Sequential Organ Failure Assessment (SOFA) score at least two points in patients with suspected infection. Sepsis with persisting hypotension requiring vasoactive agents to maintain mean arterial pressure at least 65 mmHg and having serum lactate more than 2 mmol/L were classified as septic shock.[19] The SCCM/ESICM recommended using the quick SOFA

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; AUC, area under the receiver operating characteristic curve; EWS, Early warning scores; ICU, intensive care unit; GCS, Glasgow Coma Score; MEWS, Modified Early Warning Score; NEWS, National Early Warning Score; qSOFA, quick Sequential Organ Failure Assessment; SOS, Search Out Severity; SOFA, Sequential Organ Failure Assessment; SAPS, Simplified Acute Physiology Score; SBP, systolic blood pressure

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(qSOFA) to screen for sepsis in non- intensive care unit settings (ICU).[19] The qSOFA criteria were defined by; systolic blood pressure (SBP) $\leq$ 100 mmHg, respiratory rate $\geq$ 22 breath/min and Glasgow Coma Score (GCS) $\leq$ 13.[19,20]

EWS are simple, bedside tools, based on physiologic parameter changes and do not require laboratory results as does the SOFA score. However, these scores are commonly implemented for risk assessment and stratification tools in clinical practice in wards or emergency department. The aim of this study was to evaluate and compare the accuracy of EWS (MEWS, NEWS and SOS), with both the qSOFA and SOFA score for predicting adverse outcomes in sepsis patients admitted to the ICU.

Methods

This study was conducted in a medical ICU of a tertiary university teaching hospital in Thailand. We retrospectively analysis of consecutive sepsis and septic shock patients admitted into our unit during the period of January 2011 to December 2017. Our ICU contains 10 beds and is covered by three, full-time, board-certified intensivists. This study was approved by our Institutional Review Board (REC 60-224-14-1).

Patient demographic data included; age, gender, source of ICU admission, type and sites of infection, ICU and hospital length of stay, initial serum lactate, and physiologic variables of Acute Physiology and Chronic Health Evaluation (APACHE) II, III scores, and Simplified Acute Physiology Score II (SAPS II) were collected. Co-morbidities were derived from APACHE II component. All components of the variables of; MEWS, NEWS, SOS, qSOFA SOFA scores were prospectively recorded, capturing the highest and lowest value during the first 24 h of ICU admission.[21,22] MEWS (range 0–17),[14] NEWS (range 0–20),[17] SOS (range 0–18),[10] SOFA (range 0–24)[20] and qSOFA (range 0–3)[20] were calculated using the worst value of physiological data, as described by previously published papers (detailed in supplement Table S1-4).

The primary outcome was in-hospital mortality, whilst the secondary outcomes were ICU mortality, 30-day mortality and multiple organ failures. Organ failure was defined by an increase in the SOFA score of at least two points in each organ system,[23] and multiple organ failure defined as having developed in two or more organ failures.

Descriptive data were presented as mean $\pm$ standard deviation (SD) or median (interquartile range) for continuous variables and as percentage for categorical variables. Chi-square and Wilcoxon's rank sum test were used to compare category variables along with the continuous variables, respectively. The area under the receiver operating characteristic curve (AUC), with a 95% confidence interval (CI), was used to evaluate the discrimination performance of each score. The analyzing of the difference between the AUCs of each scores was conducted by using the method of Delong et al.[24] The sensitivity and specificity was calculated for each score. Statistical analyses were performed with Stata software version 11 (Stata, College Station, Texas, USA), and two-sided, a $p < 0.05$ was considered statistically significance.

Results

There were 1589 sepsis patients admitted into our ICU during the study period, of which 925 (58.2%) patients were classified to septic shock. The ICU, 30-day, and in-hospital mortality rates were 31.9%, 45.1% and 46%, respectively. Organ failure was found in 1573 (98.9%) patients, however, 1332 (83.8%) developed multiple organ failures. Cardiovascular failure (84.8%) was the most common organ failure follow by respiratory failure (61.9%) and then neurological failure (48%). ICU admission sources were from the wards (54.1%) and emergency department (45.9%). Co-morbidities were found in 581 patients (36.5%). The common co-morbidities were hematologic malignancy (10.8%), immunocompromised (7.3%) and liver cirrhosis (4.9%), respectively. Hemocultures were positive for 475 patients (30%), and micro-organisms were isolated from 1261 patients (79.3%). Patient demographic data, stratified by hospital outcome are summarized in Table 1.

The distributions of the EWS (MEWS, NEWS and SOS), qSOFA and SOFA score coupled with correlation of hospital mortality are shown in the supplement Figures S1–S5. All sepsis patients with MEWS $\leq$ 2 (N = 24) or NEWS $\leq$ 5 (N = 42) or SOS $\leq$ 2 (N = 20) survived, whereas all patients with MEWS $\geq$ 15 (N = 40) or SOS $\geq$ 16 (N = 18) or SOFA $\geq$ 20 (N = 8) died in the hospital. The hospital mortality gradually increased according to the range of each score increasing (Fig. 1).

The performance of the MEWS, NEWS, SOS, qSOFA and SOFA scores are presented in Table 2. The SOFA score provided the highest AUC for predicting in-hospital and 30-day mortality followed by SOS, MEWS, qSOFA and was lowest for NEWS. The performance for predict hospital mortality as well as ICU and 30-day mortality of SOS was similar to the SOFA score (Tables 2 and 3). The AUCs of hospital and 30-day mortality of SOFA and SOS were significantly higher than that of other scores (Fig. 2). For predicting ICU mortality, SOS presented the highest AUC, followed by SOFA, MEWS, NEWS and qSOFA. There were no difference performances in predicting ICU mortality between; SOS *vs.* SOFA, along with SOFA *vs.* MEWS. However, SOS showed better discrimination for ICU mortality than MEWS, NEWS and qSOFA (Table 3). Similarly, the SOFA score had the best accuracy for the prediction of multiple organ failures. Also, the AUC of the SOFA and SOS were statistically higher than other scores in predicting multiple organ failures (Table S5).

Sensitivity and specificity of three EWS, qSOFA and SOFA scores to predict mortality at different thresholds, is presented in the supplement Table S6. Using the median value of hospital-surviving patients, SOFA $\geq$ 7 had sensitivity 95.3%, specificity of 49.4% as well as SOS $\geq$ 8 providing sensitivity of 95.9% and specificity of 44.5%, for hospital mortality.

Discussion

This study showed that the SOFA score present the best predictive ability for in-hospital and 30-day mortality as well as multiple organ failures among sepsis patients admitted to the ICU. We also found that all EWS were not equal, our results established that only SOS has comparable accuracy as a SOFA score to predict mortality in ICU sepsis patients.

Our results are consistent with previous studies, which have shown that; SOFA score provide the best discrimination to predict hospital mortality, than other scores in ICU sepsis patients.[5,20,21] The two large studies, from different parts of the world (the USA, Australian and New Zealand) reported the SOFA score present a better discriminative ability for hospital mortality, than qSOFA and systemic inflammatory response syndrome (SIRS) criteria.[20,21] In addition, the SOFA score presented a better performance to predict outcomes in sepsis patients outside of the ICU. Szakmany and co-workers validated the predictive ability of SOFA, with qSOFA and NEWS for predicting 30-day mortality in sepsis patient at both wards and emergency department.[25] The SOFA score presented the best AUC (0.69), followed by NEWS (AUC 0.58), and qSOFA (AUC 0.56).

EWS are track and triggers of physiological parameters, which allow early detection of patient deterioration at many healthcare levels (pre-hospital, emergency department and wards).[12,17,26] Various variations of the EWS have been introduced into clinical practice. However, the most popular used versions of EWS are still; MEWS and NEWS.[11–13] MEWS and NEWS both include; temperature, respiratory rate, heart rate, blood pressure and level of consciousness. The

Table 1
Patient data stratified by hospital mortality

	All patients (N = 1589)	Survivors (N = 858)	Non-survivors (N = 731)	p-value
Age	63 (48–76)	62 (46–75)	64 (50–77)	0.07
Male [N, (%)]	898 (56.5)	475 (52.9)	423 (47.1)	0.31
Community-acquired infection [N, (%)]	1069 (67.3)	688 (64.4)	381 (35.6)	<0.001
On mechanical ventilator [N, (%)]	1427 (89.8)	699 (49)	728 (51)	<0.001
Sepsis [N, (%)]	664 (41.8)	498 (75)	166 (25)	<0.001
Septic shock [N, (%)]	925 (58.2)	360 (38.9)	565 (61.1)	<0.001
Site of infection [N, (%)]				
- Respiratory	816 (51.4)	410 (50.2)	406 (49.8)	0.002
- Gastrointestinal	212 (13.4)	125 (59)	87 (41)	0.12
- Urinary tract	155 (9.7)	102 (65.8)	53 (34.2)	0.002
- Others*	406 (25.5)	222 (54.7)	184 (45.3)	0.80
Physiological parameters				
Temperature (°C)	38.2 (37–39)	38.2 (37.3–39)	38.2 (35.9–39.1)	0.06
Heart rate (/min)	124 (105–143)	119 (98–138)	130 (115–147)	<0.001
Respiratory rate (/min)	30 (26–35)	28 (24–34)	32 (28–36)	<0.001
Systolic blood pressure (mmHg)	91 (80–104)	95 (84–108)	87 (75–99)	<0.001
Glasgow Coma Score	13 (3–15)	15 (14–15)	4 (3–8)	<0.001
Serum creatinine (mg/dL)	1.52 (0.88–3)	1.33 (0.82–2.77)	1.73 (0.96–3.26)	<0.001
Bilirubin (mg/dL)	1 (0.5–2.3)	0.8 (0.5–1.9)	1.1 (0.6–3.5)	<0.001
Platelets ($\times 10^3$/dL)	168 (86–262)	183.5 (109–273)	146 (63–240)	<0.001
Serum lactate (mmol/L)	2.7 (1.4–5.4)	2 (1.2–3.6)	3.7 (2.1–8.7)	<0.001
Scores				
APACHE II	23 (16–32)	17(13–22)	32 (26–36)	<0.001
APACHE III	84 (59–122)	61 (48–76)	124 (104–143)	<0.001
SAPS II	53 (39–72)	40.5 (32–49)	73 (62–84)	<0.001
MEWS	9 (6–11)	7 (5–9)	11 (9–12)	<0.001
NEWS	13 (11–16)	11 (9–14)	16 (14–17)	<0.001
SOS	10 (7–12)	8 (6–10)	12 (10–13)	<0.001
qSOFA	2 (2–3)	2 (2–2)	3 (3–3)	<0.001
SOFA	9 (6–12)	7 (5–9)	12 (10–15)	<0.001
ICU LOS (days)	4 (2–8)	4 (2–7)	4 (2–8)	0.17
Hospital LOS (days)	16 (7–32)	19 (9–37)	13 (5–26)	<0.001

Unless otherwise indicated, numbers are given as medians with interquartile range.
APACHE: Acute Physiology and Chronic Health Evaluation; ICU: intensive care unit; LOS length of stay; MEWS: Modified Earning Warning Score; NEWS: National Early Warning Score; qSOFA: quick Sequential Organ Failure Assessment; SAPS: Simplified Acute Physiology Score; SOFA: Sequential Organ Failure Assessment; SOS: Search Out Severity.
* Others (N): primary bacteremia (154), skin and soft tissue (65), acute undifferentiated fever (51), central nervous system (26), bone and joint (20), infective endocarditis (14), catheter-related (12), obstetrics/gynecological (3), not identified (61).

difference between the score is that MEWS includes a scoring for urine output, whereas the NEWS uses oxygen saturation and oxygen supplement. There is still inconsistent data for the accuracy of EWS for predicting mortality or adverse outcomes in sepsis patients. A meta-analysis, from six studies (4298 patients) showed that EWS are not accurate in the prediction of mortality, with a summary of AUC at 0.68 (sensitivity 66% and specificity 62%).[13] Tirotta et al. evaluated the ability of MEWS to predict hospital mortality in septic patients

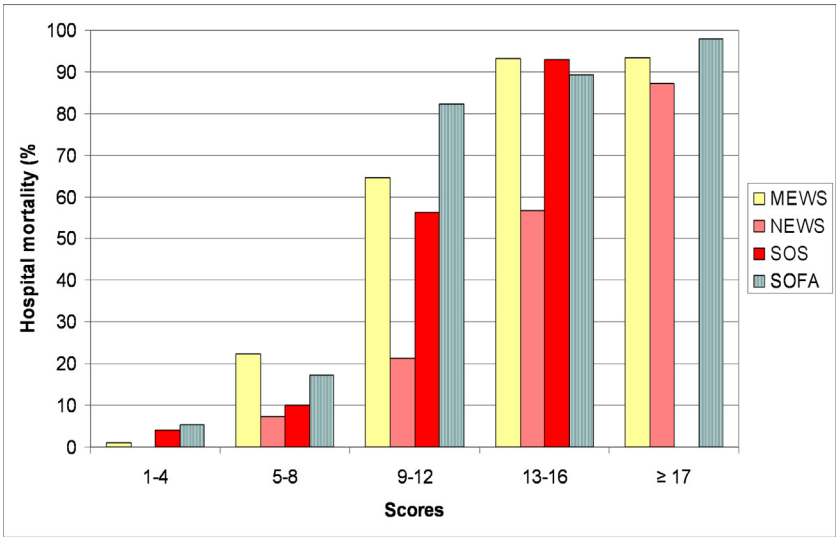

Fig. 1. Comparison the distribution of MEWS, NEWS, SOS and SOFA score with in-hospital mortality.
Range of score: MEWS 1–17, NEWS 2–20, SOS 1–16, SOFA 2–22.

Table 2
The area under the receiving operating characteristic curve with 95%CI of early warning scores, qSOFA and SOFA score to predict hospital, ICU and 30-day mortality and multiple organ failures

Scores	Hospital mortality	ICU mortality	30-day mortality	Multiple organ failures
MEWS	0.858 (0.840–0.876)	0.861 (0.842–0.879)	0.854 (0.835–0.872)	0.779 (0.752–0.805)
NEWS	0.833 (0.813–0.852)	0.825 (0.805–0.846)	0.829 (0.809–0.848)	0.799 (0.771–0.827)
SOS	0.878 (0.861–0.894)	0.875 (0.858–0.892)	0.873 (0.856–0.889)	0.831 (0.807–0.855)
qSOFA	0.847 (0.829–0.864)	0.812 (0.794–0.830)	0.842 (0.825–0.860)	0.776 (0.748–0.803)
SOFA	0.880 (0.863–0.896)	0.867 (0.849–0.885)	0.876 (0.859–0.893)	0.978 (0.972–0.984)

ICU: intensive care unit; MEWS: Modified Earning Warning Score; NEWS: National Early Warning Score; qSOFA: quick Sequential Organ Failure Assessment; SAPS: Simplified Acute Physiology Score; SOFA: Sequential Organ Failure Assessment; SOS: Search Out Severity.

admitted into medical wards. The study found that MEWS limited the prediction of hospital mortality, with an AUC of 0.596.[27] Nevertheless, NEWS showed to be similar to AUC for predicting hospital mortality, with qSOFA in sepsis outside the ICU.[18,25] A large recent study to comparing the performance of two EWS (MEWS and NEWS), with qSOFA and SIRS was conducted in 30677 patients with suspected infection in emergency department or hospital wards,[17] and this study showed that NEWS presents the best discrimination for hospital mortality (AUC 0.77), followed by MEWS (AUC 0.73), and then by qSOFA (0.69) and SIRS (0.65). This study demonstrated that conventional track and trigger EWS may detect adverse outcomes better than that of the qSOFA criteria in sepsis patients outside the ICU. Prospective trials comparing various strategies for early sepsis detection by qSOFA, EWS as well as SOFA score along with their impact on clinical outcomes should be further studies for definite optimal screening methods.

Different versions of EWS often have minor modifications or variation in specific cut-off values. The SOS score was derived by some modified parameters (vasopressor and mechanical ventilator use) and threshold values of MEWS by Champunot and coworkers.[10] The authors used SOS for a sepsis screening tool, with implemented sepsis checklist management for sepsis care, and found that these strategies decreased the mortality of sepsis patients in Phitsanulok, Thailand from 47% to 37%. Therefore, SOS is one of the most popular sepsis screening tools or EWS in Thailand. Qin et al. modified MEWS by adding age and oxygen saturation to the conventional MEWS checklist, and revealed that, this modified MEWS has superiority in the prediction of 28-day mortality, than that of the conventional MEWS for septic shock patients (AUC 0.731 *vs.* 0.652).[15] Our results suggested that standard EWS should be validated before application in some specific populations or for some specific purposes. Minor modifications or recalibration of cut-point values of each physiological parameter may improve the ability for predicting adverse outcomes.

There are possible reasons to explain the different performances of the EWS for predicting mortality in sepsis patients. One of these is that; NEWS has parameters in concerns to part of the same organ dysfunction, for example; respiratory rate and oxygen saturation. When we omitted the oxygen saturation parameter, the performance of the modified NEWS had a slightly higher accurate for predicting hospital mortality, compare with the original NEWS (AUC 0.840 *vs.* 0.833, p = 0.07, data not shown). The threshold value may relate to the performance of each score. MEWS and SOS start to score for SBP $\leq$ 100 mmHg, thus detecting an earlier degree of hypotension, whereas NEWS initiated at SBP $\leq$ 110 mmHg.

Several scoring systems are available and can be used for severity stratification in sepsis patients. qSOFA is simple and easy to use for alerting clinicians to consider possible sepsis.[19] However, studies showed that qSOFA has a limited accuracy for predicting adverse outcomes in sepsis patients.[5,17,21,25] The severity scoring systems (APACHE or SAPS) or organ dysfunction score (SOFA) may be superior to the EWS, in assessing mortality outcomes. Nevertheless, these scores are complex, time consuming, require blood tests and could not be routinely calculated as early as EWS. Our study showed that SOS has a good ability to predict mortality in sepsis patient in the ICU. Therefore, SOS should be considered as another tool for risk stratification and a guide prognosis for ICU sepsis patients.

There are some limitations that should be address in our study. First, we studied sepsis patients admitted into a medical ICU, therefore, our results may be limited in the application to other ICUs such as; a surgical ICU and could not be extrapolated for sepsis patients in wards or emergency department. Second, data of the EWS and SOFA scores were collected within the first 24 h of ICU admission, consequently, these data could not be confirmed at the exact time of sepsis diagnosis. Third, the accuracy of EWS and SOFA scores for predicting mortality in sepsis patients diagnosed according to new criteria (Sepsis-3), may not be the same as those diagnosed using the previous criteria (Sepsis-1 or 2).

Table 3
p-values for comparison between the scores

Scores	MEWS			NEWS			SOS			qSOFA		
	Hospital mortality	ICU mortality	30-d mortality	Hospital mortality	ICU mortality	30-d mortality	Hospital mortality	ICU mortality	30-d mortality	Hospital mortality	ICU mortality	30-d mortality
NEWS	<0.001	<0.001	<0.001									
SOS	<0.001	0.005	<0.001	<0.001	<0.001	<0.001						
qSOFA	0.25	<0.001	0.25	0.11	0.16	0.12	<0.001	<0.001	<0.001			
SOFA	0.03	0.57	0.03	<0.001	<0.001	<0.001	0.78	0.38	0.72	<0.001	<0.001	<0.001

ICU: intensive care unit; MEWS: Modified Earning Warning Score; NEWS: National Early Warning Score; qSOFA: quick Sequential Organ Failure Assessment; SAPS: Simplified Acute Physiology Score; SOFA: Sequential Organ Failure Assessment; SOS: Search Out Severity.

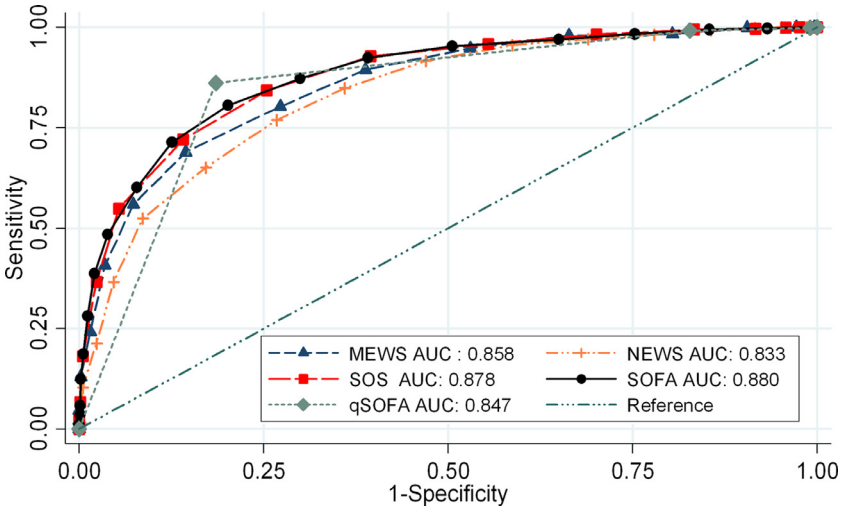

Fig. 2. Comparison the area under the receiver operating characteristic curves to discriminate in-hospital mortality for MEWS, NEWS, SOS, qSOFA and SOFA score.

Conclusion

SOS showed a similar ability as that of the SOFA score in predicting ICU, 30-day and in-hospital mortality among sepsis patients admitted to the ICU. Our results suggest that the implication of EWS, by SOS may be an alternative tool for risk stratification and sepsis screening in ICU sepsis patients.

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Conflict of interest

None

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.hrtlng.2019.02.005.

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