ORIGINAL ARTICLE

Comparison of National Early Warning Score 2, Sepsis-related Organ Failure Assessment, and Quick Sequential Organ Failure Assessment Scores in Detecting Sepsis-induced Organ Dysfunction and Predicting the Outcome in Sepsis: A Prospective Observational Study

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Abstract

Background: We intended to compare the National Early Warning Score 2 (NEWS2), sepsis-related organ failure assessment (SOFA), and quick sequential organ failure assessment (qSOFA) scores for their ability to detect sepsis-induced organ dysfunction and to predict in-hospital mortality and length of hospital stay (LOHS) of survivors in sepsis patients, as such studies have been lacking in the literature.

Materials and methods: This is a prospective observational study of patients ≥ 18 years of age with suspected or documented infection and fulfilling SIRS criteria of ≥ 2. NEWS2, SOFA, and qSOFA scores were compared using the receiver operating characteristic (ROC) curve.

Results: We had 140 patients in the study. The SOFA score had the highest area under the curve (AUC) in identifying sepsis-induced organ dysfunction, followed by NEWS2 and qSOFA. NEWS2 on day 2, followed by qSOFA on day 2, had the highest AUC in predicting in-hospital mortality, but without a statistically significant difference between them ($p = 0.2720$). NEWS2 on day 2, followed by qSOFA on day 2, had the highest AUC in predicting LOHS among survivors, but without a statistically significant difference between them ($p = 0.1015$).

Conclusion: Among the on-admission scores, NEWS2 predicted in-hospital sepsis mortality the best. Overall, the day 2 NEWS2 and qSOFA were better than the on-admission scores in predicting both mortality and LOHS of survivors. However, the AUC difference between the scores was not statistically significant. So, we conclude that compared to NEWS2 and SOFA, qSOFA is still a simpler and quicker way to prognosticate sepsis patients. SOFA was better at identifying sepsis-induced organ dysfunction.

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Introduction

Sepsis, a critical condition characterized by organ dysfunction arising from an abnormal and dysregulated host immune response to infection, is often the terminal complication leading to death from various infections globally. Delayed recognition can result in progression to septic shock, development of multiorgan failure, and eventual mortality.[1,2] Early detection and prognostication of sepsis are of clinical importance, as they guide clinicians in choosing the appropriate level of care and management. Several scoring systems have been established to facilitate the early identification and prognostication of sepsis, including the systemic inflammatory response syndrome (SIRS), sepsis-related organ failure assessment (SOFA), quick sequential organ failure assessment (qSOFA), and National Early Warning Score 2 (NEWS2).[2–5] Although studies comparing various scores in sepsis mortality are available in the literature, studies comparing NEWS2, SOFA, and qSOFA are limited. In this study, we aimed to compare the NEWS2, SOFA, and qSOFA scores for their ability to detect sepsis-induced organ dysfunction and to predict in-hospital mortality and the length of hospital stay (LOHS) among survivors with sepsis.

Materials and Methods

A prospective observational study design was adopted, and the study was conducted in the Department of Internal Medicine at a tertiary care hospital (Kauvery Hospital, Tennur, Trichy, India) during the period from September 2022 to November 2023.

Inclusion Criteria

Any patient aged ≥18 years with both of the following: (i) suspected or documented infection, and (ii) a SIRS score ≥2. The "Sepsis-1" definition formed the basis of our inclusion criteria.[2,6]

Exclusion Criteria

- Trauma patients.
- Patients with a hospital stay of <2 days.
- Patients who succumbed on the day of admission.
- Patients discharged against medical advice.

The study received ethical approval from the Institutional Ethics Committee, and written informed consent was obtained from all enrolled participants.

Various clinical (vital) parameters and laboratory values were noted, and NEWS, SOFA, and qSOFA scores were calculated on admission. On day 2 of hospitalization, NEWS2 and qSOFA scores were calculated. The SOFA score in our study refers only to the on-admission score, as we did not calculate the SOFA score on day 2.

Patients with organ dysfunction were identified. NEWS2, SOFA, and qSOFA scores on admission were compared using the receiver operating characteristic (ROC) curve for the prediction of organ dysfunction. NEWS2, SOFA, and qSOFA scores on admission, as well as NEWS2 and qSOFA scores on day 2, were compared using the ROC curve for outcome prediction. In-hospital mortality was considered the outcome. The LOHS of survivors was divided into two groups: >5 days and ≤5 days. Prolonged length of stay

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was defined as an LOHS >5 days. The NEWS2, SOFA, and qSOFA scores on admission, along with NEWS2 and qSOFA scores on day 2, were compared using the ROC curve for predicting an LOHS of >5 days among survivors.

Statistical Analysis

The MDCalc application was used to calculate the NEWS2, SOFA, and qSOFA scores. Statistical analyses were performed using MedCalc version 22.026 and SPSS version 26. Tables were created using Microsoft Word 2021. Continuous variables were presented as mean ± standard deviation (SD) or median, while discrete variables were expressed as numbers (percentages). The Chi-square test was used to assess associations between categorical variables. Mortality prediction was performed using the ROC curve, and the ROC curve cut-off criterion was determined using the Youden Index. A *p*-value of <0.05 was considered statistically significant.

Definitions

Sepsis as per "Sepsis-1" Criteria

The systemic response to infection is manifested by two or more of the SIRS components: (i) temperature >38°C or <36°C, (ii) heart rate >90/min, (iii) respiratory rate >20/min or $PaCO_2$ <32 mm Hg, and (iv) total white blood cell (WBC) count >12,000/mm^3 or <4,000/mm^3 or >10% immature bands, as a result of infection.[2,6] This definition formed the basis for our inclusion criteria.

Sepsis-induced Organ Dysfunction

The criteria to define "sepsis-induced organ dysfunction" were based on the "severe sepsis" definition provided by the Surviving Sepsis Campaign 2012 guidelines.[7] The presence of any of the following, considered attributable to infection, was taken as indicative of sepsis-induced organ dysfunction:[7] (i) hypotension related to sepsis, (ii) serum lactate levels exceeding the laboratory's upper reference limit, (iii) urine output <0.5 mL/kg/hour for over 2 hours despite adequate fluid resuscitation, (iv) acute lung injury with a PaO_2/FiO_2 ratio <250 when pneumonia was not the presumed infection source, or a PaO_2/FiO_2 ratio <200 when pneumonia was the presumed infection source, (v) serum creatinine >2.0 mg/dL, (vi) total serum bilirubin >2 mg/dL, (vii) platelet count <1 lakh/µL, and (viii) coagulopathy, defined as an international normalized ratio (INR) >1.5.

Results

A total of 140 patients were included in the study. The recruitment process and study methodology are outlined in Figure 1. The baseline clinical characteristics are summarized in Table 1. The genitourinary tract (60%), especially urinary tract infection, was the most common infection source in our sepsis patients (Fig. 2), followed by gastrointestinal infections (12.1%), skin and soft tissue infections (11.4%), and respiratory infections (9.3%). The source of infection could not be determined in 7.1% of patients. The in-hospital mortality rate was 28.6% (*n* = 40). Out of 140 patients, 66 were males (47.14%), and 74 (52.86%) were females. The mean and median days of illness (DOI) on presentation were 6.34 ± 4.49 and 5 days, respectively. The mean and median LOHS among survivors were 7.76 ± 5.17 and 7 days, respectively. Out of 140 patients, 64 (45.7%) had hypotension, i.e., systolic blood pressure ≤ 90 mm Hg. The mortality rates among hypotensive patients, patients who required vasopressors, and patients who required ventilatory support (in the first 2 days) were 48.4%, 48.1%, and 59%, respectively, and the associations were statistically significant (Chi-square test, $p < 0.0001$). The median NEWS2, SOFA, and

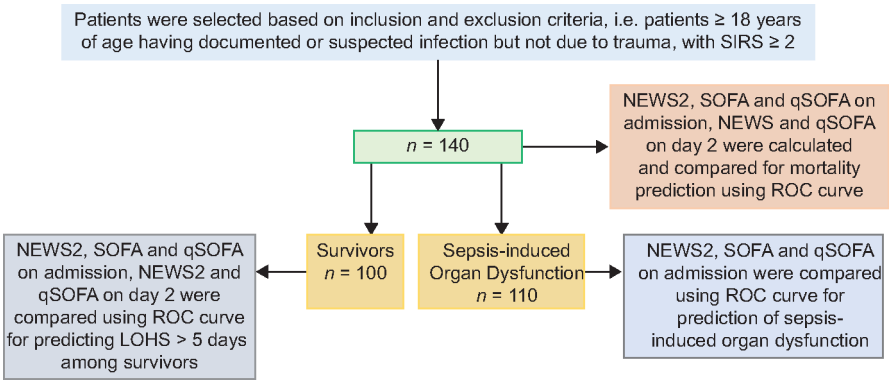

Fig. 1: Flowchart depicting the recruitment of patients and the methodology of our study

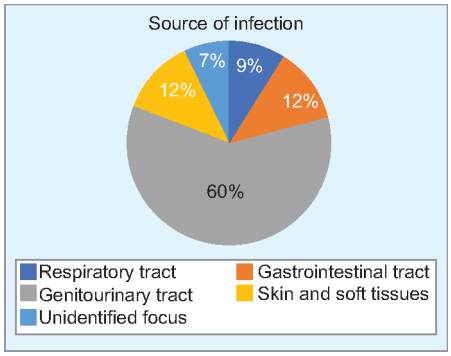

Fig. 2: Pie Chart illustrating the distribution of the source of infection in our patients

Table 1: Clinical characteristics of the patients in our study

Parameters		*Mean ± SD*	*Median*	*Minimum, maximum values*	*Total (n = 140) n (%)*	*Mortality n (%)*	*p-value (Chi-square test)*
Age		60.27 ± 15.73	63.5	18, 86	–	–	
Sex	Males		–		66 (47.14%)	–	
	Females				74 (52.86%)		
Day of illness on presentation		6.34 ± 4.49	5	1, 21	–	–	
Length of hospital stay among survivors (*n* = 100)		7.76 ± 5.17	7	2, 32	–	–	
Hypotension		–	–	–	64 (45.7%)	31 (48.4%)	<0.0001
Treatment with a vasopressor		–	–	–	54 (38.6%)	26 (48.1%)	<0.0001
Needed ventilatory support (in the first 2 days)		–	–	–	39 (27.9%)	23 (59%)	<0.0001

Table 2: ROC curve characteristics for various scores calculated on admission in predicting sepsis-induced organ dysfunction

Score (on admission)	*Area under ROC curve*	*95% CI for AUC*	*p-value for AUC*	*Criterion*	*Sensitivity (%)*	*Specificity (%)*
SIRS	0.604	0.518–0.685	0.0678	>2	67.27	56.67
qSOFA	0.727	0.646–0.799	<0.0001	>1	64.55	80.00
SOFA	0.938	0.885–0.972	<0.0001	>2	84.55	86.67
NEWS2	0.778	0.700–0.844	<0.0001	>9	46.36	100.00

Table 3: ROC curves comparison for various scores calculated on admission in predicting sepsis-induced organ dysfunction

Score comparisons	*AUC comparisons*			*p-value*
	Difference between AUC	*Standard error*	*95% CI for difference*	
NEWS2 vs SOFA	0.160	0.0361	0.0892–0.231	$p < 0.0001$
NEWS2 vs qSOFA	0.0509	0.0366	−0.0208–0.123	$p = 0.1638$
SOFA vs qSOFA	0.211	0.0426	0.127–0.294	$p < 0.0001$

Table 4: ROC curve characteristics for various scores in sepsis mortality prediction

Score	*Area under ROC curve*	*95% CI for AUC*	*p-value for AUC*	*Criterion*	*Sensitivity (%)*	*Specificity (%)*
SIRS	0.583	0.497–0.666	0.078	>2	72.50	42.00
qSOFA on admission	0.767	0.689–0.835	<0.0001	>1	85.00	57.00
qSOFA on day 2	0.916	0.858–0.956	<0.0001	>1	92.50	78.00
SOFA	0.777	0.699–0.843	<0.0001	>7	65.00	79.00
NEWS2 on admission	0.814	0.740–0.875	<0.0001	>10	67.50	83.00
NEWS2 on day 2	0.935	0.880–0.969	<0.0001	>9	82.50	92.00

Table 5: ROC curves comparison for various scores in sepsis mortality prediction

Score comparisons	*AUC comparisons*			*p-value*
	Difference between AUC	*Standard error*	*95% CI for difference*	
NEWS2 on admission vs NEWS2 on day 2	0.120	0.0321	0.0575–0.183	$p = 0.0002$
NEWS2 on admission vs SOFA	0.0375	0.0316	−0.0244–0.0994	$p = 0.2352$
NEWS2 on admission vs qSOFA on admission	0.0469	0.0275	−0.00694–0.101	$p = 0.0878$
NEWS2 on admission vs qSOFA on day 2	0.102	0.0365	0.0306–0.174	$p = 0.0051$
NEWS2 on day 2 vs SOFA	0.158	0.0376	0.0843–0.231	$p < 0.0001$
NEWS2 on day 2 vs qSOFA on admission	0.167	0.0371	0.0944–0.240	$p < 0.0001$
NEWS2 on day 2 vs qSOFA on day 2	0.0183	0.0166	−0.0143–0.0508	$p = 0.2720$
SOFA vs qSOFA on admission	0.00938	0.0385	−0.0660–0.0848	$p = 0.8074$
SOFA vs qSOFA on day 2	0.140	0.0382	0.0648–0.214	$p = 0.0003$
qSOFA on admission vs qSOFA on day 2	0.149	0.0343	0.0818–0.216	$p < 0.0001$

qSOFA scores on admission were 7.5, 5, and 2, respectively, while the median NEWS2 and qSOFA scores on day 2 were 5.5 and 1, respectively. NEWS2 ≥11 had a mortality rate of 61.4%, SOFA ≥15 had a mortality rate of 75%, and qSOFA of 3 had a mortality rate of 59.4%.

Out of 140 patients, 110 (78.6%) had sepsis-induced organ dysfunction. The SOFA score had the highest AUC (Table 2 and Fig. 3) for identifying sepsis-induced organ dysfunction compared to NEWS2 and qSOFA, and the difference was statistically significant ($p < 0.0001$) (Table 3). Apart from the SOFA score, NEWS2 had a higher AUC than qSOFA, but the difference between the two was not statistically significant.

The NEWS2 score on day 2, followed by the qSOFA score on day 2, had the highest AUC (Table 4 and Fig. 4) for predicting in-hospital sepsis mortality. However, the difference between their AUCs did not reach statistical significance ($p = 0.2720$) as shown in Table 5. Among the admission scores, NEWS2 was better than SOFA and qSOFA; however, the differences in AUCs between the scores were not statistically significant.

Out of 100 survivors, 58% ($n = 58$) had an LOHS of >5 days. The NEWS2 score on day 2, followed by the qSOFA score on day 2, had the highest AUC (Table 6 and Fig. 5) for predicting an LOHS of >5 days among survivors. However, the difference between their AUCs did not reach statistical significance ($p = 0.1015$) as shown in Table 7. Among the admission scores, SOFA demonstrated the highest AUC, and the difference between SOFA and qSOFA was statistically significant.

The number of comorbidities showed a significantly higher AUC for predicting mortality compared to age and DOI at admission ($p = 0.0002$) (Table 8 and Fig. 6).

Table 6: ROC curve characteristics for various scores in prediction of LOHS > 5 days among survivors

Score	*Area under ROC curve*	*95% CI for AUC*	*p-value for AUC*	*Criterion*	*Sensitivity (%)*	*Specificity (%)*
NEWS2 on admission	0.635	0.533–0.729	0.0149	>9	32.76	90.48
NEWS2 on day 2	0.757	0.661–0.838	<0.0001	>2	86.21	54.76
SOFA	0.675	0.574–0.765	0.0014	>2	72.41	57.14
qSOFA on admission	0.563	0.461–0.662	0.2455	>1	50.00	66.67
qSOFA on day 2	0.705	0.605–0.792	<0.0001	>0	84.48	47.62
SIRS	0.556	0.453–0.656	0.2798	>2	62.07	47.62

Table 7: ROC curves comparison for various scores in the prediction of LOHS > 5 days among survivors

Score comparisons	*AUC comparisons*			*p-value*
	Difference between AUC	*Standard error*	*95% CI for difference*	
NEWS2 on admission vs NEWS2 on day 2	0.123	0.0569	0.0110–0.234	$p = 0.0313$
NEWS2 on admission vs SOFA	0.0398	0.0517	−0.0615–0.141	$p = 0.4411$
NEWS2 on admission vs qSOFA on admission	0.0714	0.0390	−0.00498–0.148	$p = 0.0669$
NEWS2 on admission vs qSOFA on day 2	0.0700	0.0610	−0.0495–0.189	$p = 0.2509$
NEWS2 on day 2 vs SOFA	0.0827	0.0649	−0.0445–0.210	$p = 0.2024$
NEWS2 on day 2 vs qSOFA on admission	0.194	0.0634	0.0698–0.318	$p = 0.0022$
NEWS2 on day 2 vs qSOFA on day 2	0.0525	0.0321	−0.0103–0.115	$p = 0.1015$
SOFA vs qSOFA on admission	0.111	0.0530	0.00733–0.215	$p = 0.0359$
SOFA vs qSOFA on day 2	0.0302	0.0635	−0.0943–0.155	$p = 0.6346$
qSOFA on admission vs qSOFA on day 2	0.141	0.0623	0.0193–0.264	$p = 0.0232$

Table 8: ROC curve characteristics of various parameters in sepsis mortality prediction

Parameter	*Area under ROC curve*	*95% CI for AUC*	*p-value for AUC*	*Criterion*	*Sensitivity (%)*	*Specificity (%)*
Age	0.560	0.473–0.643	0.2480	>39	100	14
No. of comorbidities	0.687	0.604–0.763	0.0002	>2	55	76
DOI on admission	0.592	0.506–0.674	0.0745	>4	65	54

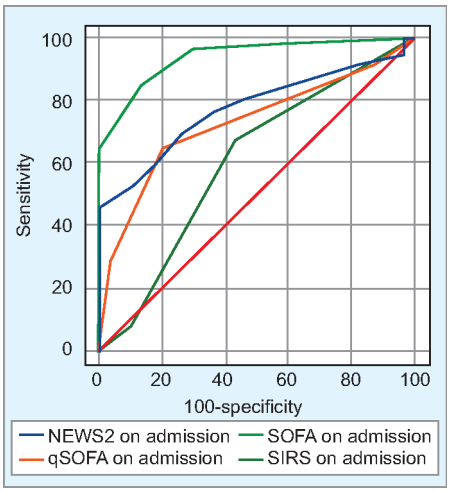

Fig. 3: Comparison of ROC curves with AUCs for NEWS2, SOFA, qSOFA, and SIRS scores calculated on admission in detecting sepsis-induced organ dysfunction

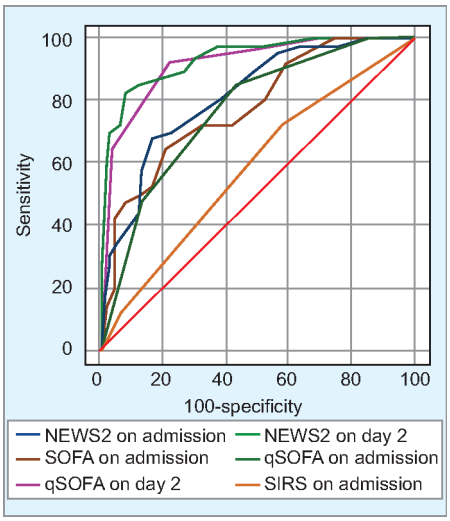

Fig. 4: Comparison of ROC curves with AUCs for NEWS2, SOFA, qSOFA, and SIRS scores calculated on admission, and NEWS2 and qSOFA scores calculated on day 2 in predicting the mortality of our patients

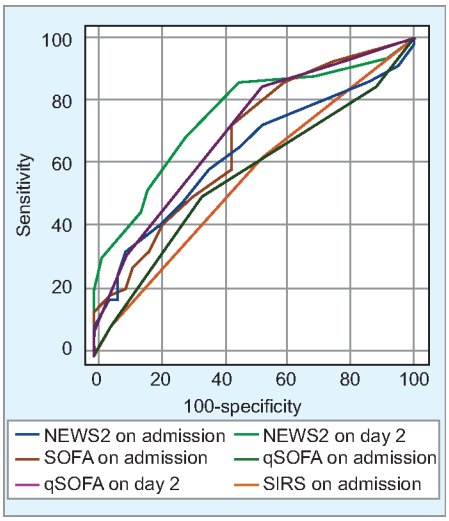

Fig. 5: Comparison of ROC curves with AUCs for NEWS2, SOFA, qSOFA, and SIRS scores calculated on admission, and NEWS2 and qSOFA scores calculated on day 2 in the prediction of LOHS > 5 days among survivors

Discussion

We enrolled 140 patients based on our inclusion and exclusion criteria. Our study population had a mean age of 60.27 ± 15.73 years and a median age of 63.5 years. This was similar to other sepsis studies,[8–12] in which the mean age has been reported to range

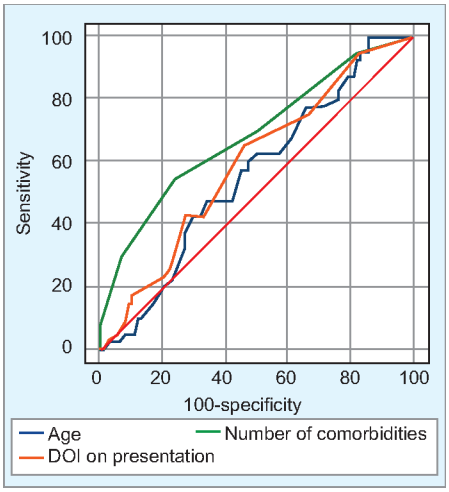

Fig. 6: Comparison of ROC curves with AUCs for age, number of comorbidities, and DOI on presentation in predicting mortality

between 60 and 65 years. The in-hospital mortality rate was 28.6% (n = 40). Mortality rates in other sepsis studies have ranged from 24 to 67%.[13–17]

A total of 110 patients (78.6%) had sepsis-induced organ dysfunction. The SOFA score (0.938) had the highest AUC in identifying sepsis-induced organ dysfunction, followed by NEWS2 and qSOFA scores. NEWS2 on admission >9 had the highest specificity, and SOFA >2 had the highest sensitivity in significantly predicting sepsis-induced organ dysfunction. The differences between the AUCs of SOFA and NEWS2, and SOFA and qSOFA, were statistically significant. However, the AUC difference between NEWS2 and qSOFA was not statistically significant. Mellhammar et al.,[18] in their 2019 study, reported that NEWS2 was significantly better than qSOFA in detecting sepsis-induced organ dysfunction. The superior performance of the SOFA score in detecting sepsis-induced organ dysfunction compared to NEWS2 and qSOFA could be due to the similarity between the SOFA score criteria and the definition of sepsis-induced organ dysfunction.

Several studies[18–25] are available comparing various scores in predicting in-hospital sepsis mortality. However, we could not find a study that compared NEWS2, SOFA, and qSOFA for sepsis mortality prediction. A study conducted by Asmarawati et al.[26] included NEWS2, SOFA, qSOFA, and the acute physiology and chronic health evaluation II (APACHE II) scores for predicting mortality; however, it was performed in COVID-19 patients. The study found that the initial NEWS2 had a higher AUC in predicting mortality compared to the other scores. A study conducted by Bhattacharya et al.,[13] which included 122 sepsis patients to determine the efficacies of SIRS, SOFA, and qSOFA scores for predicting sepsis mortality, concluded that both SOFA and qSOFA were superior to SIRS. However, their analysis did not include NEWS2, which was incorporated in our study.

In our study, NEWS2 on day 2 had the highest AUC (0.935) in predicting in-hospital mortality, followed by qSOFA on day 2 (0.916), NEWS2 on admission, SOFA, and qSOFA on admission. A NEWS2 score on day 2 >9 had the highest specificity, while a qSOFA score on day 2 >1 had the highest sensitivity for significantly predicting mortality. The AUCs of all these scores were statistically significant. Although NEWS2 on day 2 had a higher AUC compared to qSOFA on day 2, the difference between their AUCs was not statistically significant; thus, qSOFA on day 2 is not statistically inferior to NEWS2 on day 2. Additionally, the day 2 scores of NEWS2 and qSOFA were significantly better than the admission scores of NEWS2, SOFA, and qSOFA. Among the admission scores, NEWS2 was better than SOFA and qSOFA; however, the differences in AUC between the scores were not statistically significant. Myrstad et al.[20] in 2020 showed that the NEWS2 score on admission was superior to qSOFA and other risk scores for predicting in-hospital sepsis mortality.

We also compared the scores to predict an LOHS >5 days in survivors. Among the 100 survivors, 58 had a hospital stay exceeding 5 days, while 42 were hospitalized for 5 days or less. On comparing the scores, NEWS2 on day 2 had the highest AUC (0.757), followed by qSOFA on day 2 (0.705), SOFA, NEWS2 on admission, and qSOFA on admission. The AUCs of NEWS2 on admission, NEWS2 on day 2, SOFA, and qSOFA on day 2 were statistically significant. A NEWS2 score on admission >9 had the highest specificity, while a NEWS2 score on day 2 >2 had the highest sensitivity in significantly predicting an LOHS >5 days among survivors. Although NEWS2 on day 2 had a higher AUC compared to qSOFA on day 2, the difference between their AUCs was not statistically significant. NEWS2 assessed on day 2 performed significantly better than its admission scores as well as the admission qSOFA score. Similarly, the day 2 qSOFA score was significantly superior to the qSOFA score at admission. Among the admission scores, SOFA was better than NEWS2 and qSOFA, with SOFA being significantly better than qSOFA.

Prior studies have reported that 55.5–65% of patients with sepsis had preexisting comorbid conditions.[27–29] In our study population, 14.3% had no comorbidities, 30% had one comorbidity, 22.9% had two comorbidities, 19.3% had three comorbidities, 11.4% had four comorbidities, 1.4% had five comorbidities, and 0.7% had six comorbidities. Although not our primary objective, apart from sepsis scores, we also compared the number of comorbidities, DOI on admission, and age in predicting in-hospital sepsis mortality. We found that the number of comorbidities had the highest AUC (0.687) for predicting in-hospital sepsis mortality, and it was statistically significant.

Limitations

The limitations of our study are: (i) the SOFA score on day 2 was not included, as we do not routinely repeat blood tests on day 2 for all sepsis patients, and performing them for study purposes would increase the treatment cost for the patients; (ii) the superior performance of the SOFA score in identifying sepsis-induced organ dysfunction compared to NEWS2 and qSOFA scores could be due to the similarity between the SOFA score criteria and the definition of sepsis-induced organ dysfunction; (iii) our study has a limited sample size, and large-scale studies are needed to establish more definitive and reliable conclusions; and (iv) our study population did not represent the entire spectrum of sepsis foci.

Conclusions

To conclude, among the admission scores, NEWS2 was better than SOFA and qSOFA in predicting in-hospital sepsis mortality, although the differences in AUC between the scores were not statistically significant, while SOFA was better than qSOFA in predicting the LOHS of sepsis survivors. Overall, the day 2 scores of NEWS2 and qSOFA were better than the admission scores in predicting both in-hospital sepsis mortality and LOHS of sepsis survivors, with no statistically significant difference observed between the two. Compared to NEWS2 and SOFA, qSOFA remains a simpler and quicker tool to prognosticate sepsis patients on admission and day 2. The SOFA score was superior in identifying sepsis-induced organ dysfunction patients.

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