

Comparison of modified Sequential Organ Failure Assessment (mSOFA) score with Sequential Organ Failure Assessment (SOFA) score to predict mortality in critically ill patients

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Abstract:

Background: Most of the currently used scoring systems can effectively predict mortality in critically ill patients, however, most of these scores are time-consuming to calculate and require laboratory parameters that are not readily available, limiting feasibility in low- and middle-income countries (LMICs).

Objectives: To compare modified Sequential Organ Failure Assessment (mSOFA) and Sequential Organ Failure Assessment (SOFA) scores to predict mortality among the critically ill patients.

Design: Prospective, observational, single centre cohort study.

Method: Patients surviving more than 48 hours in the Intensive Care Unit (ICU) of Tribhuvan University Teaching Hospital, Kathmandu, Nepal were enrolled in the study. Data were collected prospectively. SOFA and mSOFA scores were calculated at the time of admission and after 48 hours of stay in ICU. Patients were followed up until ICU discharge to document their survival status. Area under the receiver operating characteristic (ROC) curve was used to compare the two scores.

Results: Our study enrolled 100 critically ill patients during the study period with the mean age of 46 years ($SD=17$) and 43% male patients. Out of 100 patients, 37 died during the study period. The day 1, day 3, mean, delta, maximum, and total SOFA score were higher in non-survivors than in survivors. Similarly, the day 1, day 3, mean, delta, maximum and total mSOFA score was higher in non-survivors compared to the survivors. We found that the day 1 SOFA score predicted mortality better than the day 1 mSOFA score with an area under curve (AUC) of 0.79 (95% CI, 0.70-0.88) and 0.73 (95% CI, 0.64-0.83) respectively. While, day 3 SOFA and mSOFA scores performed equally well in predicting the mortality with AUC of 0.91 (95% CI, 0.85-0.96) and 0.92 (95% CI, 0.88-0.97) respectively.

Conclusions: Performance of mSOFA score was comparable to SOFA score for prediction of ICU mortality, when calculated at day 3 of admission. The mSOFA score can be an effective and feasible tool to predict outcome in places with resource limitations and during pandemics.

Keywords: ICU, modified SOFA score, mortality prediction, SOFA score.

Introduction:

In low- and middle-income countries (LMICs), where tertiary level hospitals are limited and intensive care facilities are

sparse, it is crucial to appropriately allocate resources with proper patient selection.¹ Due to limited resources, it is important to prognosticate the outcome early on, to provide the best care and consolidate resources for patients who are likely to survive.² Currently, many clinical scoring systems can measure the severity of the disease in critically ill patients, however, most of these scores are time-consuming to calculate and require parameters that are not readily available.³

The scoring system in critical care started in 1991 with the development of Severe Inflammatory Response Syndrome (SIRS) criteria for rapid bedside identification of sepsis.⁴ Within next 20 years, various complex clinical outcome prediction models were developed. A few of them being the Acute Physiology and Chronic Health Evaluation Score (APACHE), the Mortality Probability Model III (MPM3), and the Mortality in Emergency Department Sepsis score (MEDS). However, these scoring systems are complex and perform variably to predict outcome.³

Simpler models like the Sequential Organ Failure Assessment (SOFA) score have been developed and has been validated across a range of healthcare settings and environments.⁵ SOFA

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score evaluates respiratory, cardiovascular, hepatic, coagulation, renal and neurological systems each scored from 0 to 4 with an increasing score reflecting worsening organ dysfunction.^{5,6} The requirement for arterial and venous blood specimens to obtain various parameters for calculation of SOFA score may render it impractical in places of constrained resources and during pandemics.

Grissom et al. proposed and published a simplified version of the SOFA score known as the modified SOFA (mSOFA) score. When compared to SOFA score, mSOFA score can be effective, cheap, reliable, and non-time consuming in resource-limited settings.⁷ It was originally developed for a fast screening method during the Avian Influenza outbreak. The mSOFA score eliminates the platelet count, replaces partial pressure of arterial oxygen (PaO₂) with arterial oxygen saturation measured by a pulse oximeter (SpO₂), and replaces serum bilirubin with clinical assessment of scleral icterus or jaundice. The only laboratory value required for the mSOFA is serum creatinine to assess its ability to predict mortality. At our urban tertiary teaching hospital staff recorded patients with probable sepsis in the ED Information System (EDIS).⁷⁻⁹ Therefore, in this study, we prospectively studied the application of an mSOFA score, to assess its ability to predict mortality.

Material and Methods:

We hypothesized that the mSOFA and SOFA scores calculated among the critically ill patients in the intensive care unit are similar in predicting mortality. Written informed consent was obtained from all the patients or their legal surrogates before enrollment. Patients surviving more than 48 hours in the ICU of Tribhuvan University Teaching Hospital, Kathmandu from June 2012 to December 2012 were enrolled in the study. SOFA and mSOFA scores were calculated at the time of admission and after 48 hours of stay in ICU. Consecutive

patients 16 years and older, admitted to ICU were included in this study. Patients who died within 48 hours of admission and patients who were taken away from ICU against medical advice were excluded from the study.

Data were prospectively collected by trained ICU medical officers or resident doctors. A standard Microsoft Excel data collection form was used. The SOFA score in our study was calculated as per Table 1 and the mSOFA was calculated as per Table 2. The scores were calculated at the time of admission and on third day of admission. Patients were followed up until ICU discharge to document their survival status. We calculated day 1, day 3, mean, maximum, delta, and total SOFA score and mSOFA score among survivors and non-survivors. Mean score was calculated as the mean of the day 1 and day 3 scores. Of the scores at day 1 and day 3, whichever was higher, that value was considered as maximum score. Delta score was calculated as the difference between day 3 and day 1 scores. The positive value indicating increasing score and the negative value indicating the decreasing score. Total score was calculated as the sum of day 1 and day 3 scores.

All study data were collected in Microsoft Excel and analyzed using SPSS 21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.). Continuous data were reported as mean and standard deviation (SD). Categorical data were reported as frequency and percentage. We compared mSOFA score mortality prediction to the SOFA score by areas under the receiver operating characteristic (ROC) curve. ROC curves were also used to calculate the cut-off values, sensitivity, specificity, overall correctness, and positive and negative predictive values. The best Youden index (sensitivity + specificity - 1) was used to determine the best cut-off point. For all statistical analyses, significance was accepted at $P < 0.05$.

Table-1: Sequential Organ Failure Assessment (SOFA) Score.⁵

Organ System/Score	0	1	2	3	4
Respiratory (PaO ₂ /FiO ₂ , mmHg)	>400	≤400	≤300	≤200	≤100
Coagulation (Platelets x10 ³ /μL)	>150	≤150	≤100	≤50	≤20
Hepatobiliary (Bilirubin, mg/dL)	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular (hypotension)	No hypotension	MAP <70 mm Hg	Dopamine ≤5 μg/kg/min or Dobutamine any dose	Dopamine >5 μg/kg/min Epinephrine ≤0.1 μg/kg/min Norepinephrine ≤0.1 μg/kg/min	Dopamine >15 μg/kg/min Epinephrine >0.1 μg/kg/min Norepinephrine >0.1 μg/kg/min
Central nervous system (Glasgow Coma Scale)	15	13-14	10-12	6-9	<6
Renal (Creatinine mg/dL or urine output mL/day)	<1.2	1.2-1.9	2.0-3.4	3.5-4.9 or urine <500 mL/day	>5.0 or urine <200 mL/day

Table-2: Modified Sequential Organ Failure Assessment (mSOFA) Score.⁷

Organ System	0	1	2	3	4
Respiratory (SpO2/FiO2)	>400	≤400	≤315	≤235	≤150
Hepatobiliary	No scleral icterus		Scleral icterus		
Cardiovascular (hypotension)	No hypotension	MAP <70 mm Hg	Dopamine ≤5 µg/kg/min or Dobutamine any dose	Dopamine >5 µg/kg/min Epinephrine ≤0.1 µg/kg/min or Norepinephrine ≤0.1 µg/kg/min	Dopamine >15 µg/kg/min Epinephrine >0.1 µg/kg/min Norepinephrine >0.1 µg/kg/min
Central nervous system (Glasgow Coma Scale)					
Coma Scale)	15	13-14	10-12	6-9	<6
Renal (Creatinine mg/dL)	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	>5.0

Result:

A total of 100 eligible patients were enrolled during the study period. The mean age of patients was 46 years (SD=17) and 43% of patients were male. Out of 100 patients, 37 died during the study period. The day 1, day 3, mean, delta, maximum, and total SOFA score (SD) were found to be 10.18 (3.58), 11.24 (3.78), 10.66 (3.44), 1.05 (2.28), 11.62 (3.71), and 21.43 (7.01) among non-survivors which were higher

than the survivors. Similarly, the day 1, day 3, mean, delta, maximum and total mSOFA score (SD) was found to be 9.00 (2.75), 10.24 (3.04), 9.62 (2.68), 1.24 (2.22), 10.54 (3.06), and 19.24 (5.36) among non-survivors which were higher than the survivors (Table 3).

Table 3: The mean and standard deviation of day 1, day 3, mean, delta, maximum and total SOFA, and mSOFA score among survivors and non-survivors.

Outcome		SOFA1	SOFA3	Mean	Delta SOFA	mSOFA1 SOFA	mSOFA3	Mean	Delta mSOFA	mSOFA
Survivors	Mean	6.46	4.80	5.63	-1.65	6.38	4.17	5.27	-2.20	
	SD	2.75	2.91	2.62	2.17	2.85	2.75	2.60	2.10	
Non-survivors	Mean	10.18	11.24	10.60	1.05	9.00	10.24	9.62	1.24	1.24
	SD	3.58	3.78	3.44	2.28	2.75	3.04	2.68	2.22	

Using the ROC curve, we found that the day 1 SOFA score predicted mortality better than the day 1 mSOFA score with an AUC of 0.79 (95% CI, 0.70-0.88) and 0.73 (95% CI, 0.64-0.83) respectively (Figure 1). While, day 3 SOFA and mSOFA scores performed equally well in predicting the mortality with AUC of 0.91 (95% CI, 0.85-0.96) and 0.92 (95% CI, 0.88-0.97) respectively (Figure 2).

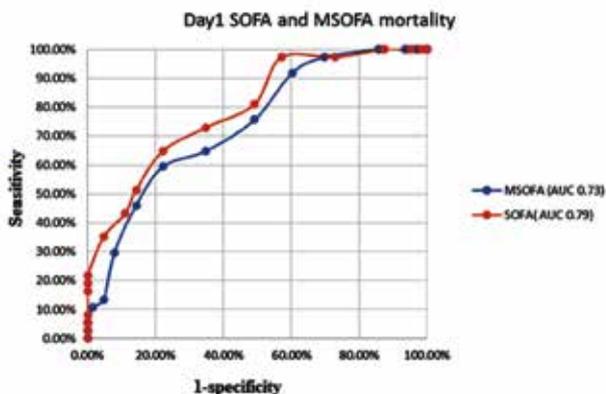


Figure-1: Receiver operating characteristics curve for day 1 SOFA and mSOFA score and prediction of mortality

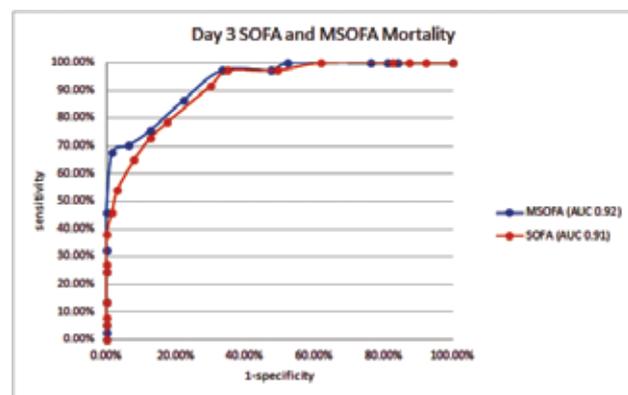


Figure-2: Receiver operating characteristics curve for day 3 SOFA and mSOFA score and prediction of mortality

The area under the ROC curve of sub-variables of SOFA score and of mSOFA score is expressed in Table 4. The outcome predicted by both the models is fair to excellent.

Table-4: Area under Receiver Operating Characteristics for SOFA and mSOFA score.

Sub-variables	AUC SOFA	AUC MSOFA
Day 1	0.79	0.73
Day 3	0.91	0.92
Mean	0.87	0.87
Maximum	0.85	0.83
Total	0.87	0.87
Delta	0.81	0.89

By plotting the area under the ROC curve, the cut-off value for the different models was identified. The cut-off value is the number for that scoring system, above which the mortality prediction is highest and this value corresponds to the highest Youden index (sensitivity + specificity -1). The cut-off values and Youden index along with the sensitivity and specificity of different score models are expressed in Table 5.

Table 5: Cut-off values, sensitivity, and specificity of different score models predicting the mortality

Score models	SOFA				mSOFA			
	Cut off value	Sensitivity	Specificity	Youden index	Cut off value	Sensitivity	Specificity	Youden index
Day 1	≥ 8	93.00	50.80	0.438	≥ 9	59.46	77.78	0.372
Day 3	≥ 9	73.00	77.80	0.508	≥ 10	67.57	98.41	0.660
Mean	≥ 8	78.38	79.37	0.578	≥ 9	67.57	90.48	0.580
Maximum	≥ 9	81.08	74.60	0.557	≥ 10	70.27	85.71	0.560
Total	≥ 17	70.27	85.71	0.560	≥ 18	67.57	90.48	0.580
Delta	≥ 0	81.08	68.25	0.493	≥ 1	72.97	95.24	0.682

Discussion:

In low- and middle-income countries (LMICs), it is crucial to prognosticate the outcome early on, to provide the best care and consolidate resources for patients who are likely to survive. The scoring system in critical care started in 1991 with the development of Severe Inflammatory Response Syndrome (SIRS) criteria for rapid bedside identification of sepsis. Within next 20 years, various complex clinical outcome prediction models were developed. A few of them being the Acute Physiology and Chronic Health Evaluation Score (APACHE), the Mortality Probability Model III (MPM3), and the Mortality in Emergency Department Sepsis score (MEDS). However, these scoring systems are complex and perform variably to predict outcome.³

A simpler scoring system, the SOFA score had been used for a long time as a tool to measure organ dysfunction and to predict mortality in critically ill patients. However, it also requires multiple laboratory values derived from arterial and venous blood and seems impractical in places with constrained resources and during pandemics. mSOFA score is likely more feasible to implement in resource-limited settings compared to SOFA score.

Our study has shown that mSOFA scoring can predict mortality similar to SOFA when calculated at day 1 and day 3 of ICU admission. We found that the day 1 SOFA score predicted mortality better than the day 1 mSOFA score, but day 3 SOFA and mSOFA scores performed equally well in predicting the mortality. The derived variables for both SOFA and mSOFA score like the mean score, maximum score, total score and delta score performed well to predict mortality in ICU. The results of our study were dissimilar to the study

done by Grissom et al, where day 1 SOFA and mSOFA scores performed well in predicting mortality with AUC of 0.83 (95% CI 0.81-0.85) and 0.84 (95% CI 0.82-0.85) respectively. However, on day 3, SOFA and mSOFA predicted mortality with an AUC of 0.78 and 0.79, respectively.⁷

In another study by Junger et al, an area under receiver operating characteristics curve for SOFA and mSOFA was found to be 0.92 (95% CI, 0.87-0.96) and 0.79 (95% CI, 0.73-0.85) at day 1 in contrast to 0.79 (95% CI, 0.70-0.88) and 0.73 (95% CI, 0.64-0.83) in our study.¹⁰ In a study by Raymond et al., the 30-day mortality was 22/88 (25%) for those with a positive mSOFA score and 3 out of 140 (2.1%) of those with a negative mSOFA score (OR 15.2, 95% CI [4.4, 52.7]; $P < 0.001$), which equated to a negative predictive value of 97.9% (95% exact CI 93.9-99.6%) to assess its ability to predict mortality. At our urban tertiary teaching hospital staff recorded patients with probable sepsis in the ED Information System (EDIS).⁸ In another study by Rahmatinejad et al, the estimated AUCs of SOFA and mSOFA models were 0.751 and 0.739, respectively which was not statistically different ($P = 0.186$).⁹ The variation in results of our study as compared to other studies can be due to variable case mix and variation in level of care of the ICUs.

In line with our study, a study by Sendagire et al. in a resource-limited setting of Uganda showed that non-survivors had higher initial (7.7 SD 3.8 vs. 5.5 SD 3.3; $p = 0.007$), mean (8.1 SD 3.9 vs 4.7 SD 2.6; $p < 0.001$) and highest mSOFA scores (9.4 SD 4.2 vs. 5.8 SD 3.2; $p < 0.001$), with an increase of 1.0 (SD 3.1) mSOFA on average after 48 h when compared to survivors ($p < 0.001$). The AUC curves for each mSOFA category was initial-0.68, mean-0.76, maximum-0.76, and delta -0.74 scores.¹¹

The predictive model are highly dependent on the context. In general, their accuracy will decrease over time, because current clinical practices reflect less and less of the practices used when creating models. They are also most useful in population and cases, similar to those used during model construction. Although some predictive models like APACHE IV tried to incorporate a wide range of patient, regional, and clinical differences, it did not specifically include resource-poor hospitals of LMICs.¹² Therefore, it is not surprising that these models perform poorly in our context. Our research shows that in LMICs, SOFA and mSOFA perform well in predicting ICU mortality. However, mSOFA is simpler and cheaper and may be a better choice. In our study, the mortality rate in the ICU was as high as 37%. In addition to the need for better predictive models, the high mortality rate in the ICU indicates the need for targeted interventions to improve the management of common diseases such as sepsis, respiratory failure, and stroke. The development and use of protocols for the most common and severe ICU diseases will be an important enhancement for intensive care in LMICs.^{13,14}

Our study has several limitations. First, it was a single-center study conducted in a mixed medical surgical ICU. Study was conducted in a limited number of patients. A multicentric study involving larger number of patients and a broader case mix would confer greater external validity and applicability. Second, we calculated the scores at day 1 and day 3. Serial evaluation of the scores throughout the ICU stay would have helped to correlate the disease progression or organ dysfunction during the ICU stay with the ICU outcome.

Conclusion:

In this study, performance of mSOFA score was comparable to SOFA score for prediction of ICU mortality, when calculated at day 3 of admission. Other derived scores like the mean, maximum, total and delta scores for both SOFA and mSOFA score performed well to predict outcome. The mSOFA score can be an effective and feasible tool to predict outcome in places with resource limitations and during pandemics.

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