



Shock index and modified shock index as triage screening tools for sepsis

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ABSTRACT

Background: Fever is one of the common conditions encountered in the emergency department, which related to a spectrum of diseases severity. Identifying sepsis patients from uncomplicated febrile patients is challenging in the emergency triage areas and pre-hospital settings.

Objectives: Assess the triage shock index (SI) and modified shock index (MSI) in febrile patients as predictors for sepsis and sepsis-related outcomes.

Design: A retrospective cohort study.

Setting: Patients presented to the Emergency Department of King Khalid University Hospital.

Patients and methods: The analysis included all febrile adult patients triaged with a temperature of 38 °C or more from January 2016 to December 2017. Based on triage vital sign we calculate the SI with cut-off levels of ≥ 0.7 and ≥ 1 and MSI with cut-off levels of ≥ 1 and ≥ 1.3 . We report the Relative Risk, Sensitivity, Specificity, Positive and Negative Predictive Values of the predictors.

Main outcome measures: Sepsis and sepsis-related outcomes such as hyperlactatemia, ICU admission, and 28 days mortality.

Sample size: 274 patients.

Results: 274 patients met our inclusion/exclusion criteria. Of the 274 patients, 252 patient (92%) were septic, 62 patients (22%) had hyperlactatemia, 20 patients admitted to the ICU, and 5 patient died within 28 days. An MSI of ≥ 1 had a sensitivity of 90% for sepsis predication, 85% for ICU admission and 100% for 28 days mortality. MSI of ≥ 1.3 showed a specificity (59%–100%) for all the outcomes of interest. Non-significant statistical trends of greater accuracy of MSI over SI.

Conclusion: MSI and SI were found to be promising predictors in triaging febrile patients. However no single cut-off values of MSI or SI were found to have an optimal accuracy for prediction of sepsis and sepsis-related outcomes. Further studies are required to assess the incorporation of MSI in a multi-item scaling system for the prediction of sepsis and its related outcomes.

Limitations: Small single center study and the results may not be generalizable.

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Introduction

Sepsis and septic shock are medical emergencies that require immediate recognition and management. A retrospective study of an international database reported the worldwide incidence of sepsis as 437 per 100,000 persons for the years between 1995 and 2015 [1]. The incidence of the disease is rising [2,3], and mortality

is correlated with the severity of the disease [4]. Several studies confirmed that early recognition and treatment of sepsis can avert progression of the disease and decrease the associated morbidity and mortality as well as the financial costs [5–7]. According to the Surviving Sepsis Campaign 2018, the 1st hour for the identification and starting the management for sepsis starts from the patient's arrival at triage [8].

Fever is a common finding in Emergency Departments' (EDs) triage and is caused by a broad spectrum of diseases. It is the first clue for sepsis as found in 55–76% of septic patients [9,10]. However, identifying patients with sepsis from those with uncomplicated febrile illnesses is not clinically straightforward, as the

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signs of sepsis can be subtle, nonspecific, and easily missed in dynamic areas such as ED triage or pre-hospital settings [11–13]. Therefore, in order to improve the assessment of febrile patients presenting to EDs we need simple screening parameters to optimize the triaging process, improve risk stratification and contribute to the early identification of severely ill patients in a shorter time.

Few triage tools have been studied to predict and risk stratify the suspected patient with sepsis in the ED triage. A commonly referred tool is the qSOFA (Quick Sepsis Related Organ Failure Assessment), which had a great prognostication power revealed from Critical Care literature. However, when qSOFA was assessed in ED triage it was found to have poor sensitivity in predicting sepsis-related adverse outcomes [14–18]. National Early Warning Score (NEWS) is another scoring system that was found to be more accurate as a predictor of severe sepsis or septic shock with sensitivity of 92.6% and a specificity of 77% [19,20]. However, NEWS is composed of seven variables, and each variable is categorized into three to seven subdivisions each scored from 0 to 3 based on specific values. The complexity of the NEWS scoring system may limit the practicality of its use in dynamic areas such as ED triage or pre-hospital sitting. Furthermore, both qSOFA and NEWS were calculated based on Glasgow Coma Scale (GCS), which limits its utility to those with intellectual disability, dementia or with altered mental status.

The shock index (SI) is a bedside assessment tool calculated by dividing heart rate (HR) over systolic blood pressure (SBP) and the modified shock index (MSI) is calculated by dividing HR over mean arterial pressure (MAB). Two ED Observational Studies assessed the SI for suspected septic patients and revealed a promising result as a predictor of hyperlactatemia and mortality [21,22]. However, the sensitivity and specificity of the SI varied according to the cut-off, but is generally considered a suboptimal predictor. On the other hand, MAP is the recommended indicator to be followed for deciding fluid resuscitations and vasopressors titration as it is believed to be a better marker for organs perfusion than SBP or DBP alone [8,23]. Nevertheless, a retrospective cohort study of ICU septic patients found that elevated MSI was associated with myocardial dysfunction and mortality [24]. In addition, MSI was found to be superior to the SI in predicting mortality in ED studies [25,26]. Therefore, we hypothesized that MSI will be a greater prognostic tool that will help in risk-stratifying febrile patients and facilitate early identification of sepsis and sepsis-related outcomes.

The purpose of our study is to assess the utility of MSI and SI upon triaging febrile adults as a predictor for sepsis and sepsis-related outcomes including hyperlactatemia ≥ 2 mmol, as a marker of sepsis severity and a surrogate indicator for poor prognosis [27–29], and as predictor for ICU admission and 28 days mortality.

Materials and methods

Institutional review board (IRB) approval was obtained from the ethical research committee at King Khalid University Hospital, King Saud University. All measures were taken to preserve the integrity and privacy of data. We conducted a retrospective cohort study among all patients presenting to the ED of King Khalid University Hospital from January 2016 to December 2017. It is an Academic Tertiary Center with 800-beds and more than 135,000 ED visits annually. Patients included were adults >18 years age, triaged with a temperature $\geq 38^\circ\text{C}$. We excluded immunocompromised patients, end-stage malignancies, patients with pacemakers, trauma cases, or non-infectious cause of hyperthermia (e.g. thyrotoxicosis, heat stroke).

Data were retrieved from the electronic filing system according to the inclusion criteria. We identified 2454 visits matching our primary inclusion criteria. We only considered the first visits within the study period for the analysis and any repeated visits were

removed after identified by the medical record number. Many cases were discharged as low triage categories and were not included in the study. The trained reviewers abstracted the data and filled our standardized online data collection sheet (*Google Sheets*). Data collection process was monitored by the primary investigator. Then the results went for a cross-review for quality assurance and the discrepancies were around 5% and resolved by a third independent reviewer. Eventually, the total number of eligible patients meeting the inclusion/exclusion criteria was 274; and those were analyzed in the study.

From the triage nurse notes the SBP, DBP and MAP readings were documented based on the direct measurement by the automated oscillometric sphygmomanometer, temperatures were measured by oral or axillary digital thermometer and HR by pulse oximeter readings. After completing the data collection process, the MSI was then calculated by dividing HR over mean arterial pressure (MAB) and cut-off levels ≥ 1 and ≥ 1.3 were used, based on previous studies, that recognized this level as a discriminating point between high and low readings [24–26]. The SI was also calculated by dividing HR over SBP and cutoff values of ≥ 0.7 and ≥ 1 were chosen based on previous sepsis studies as well [21].

The outcomes of interest are diagnoses of sepsis, hyperlactatemia, ICU admission and 28 days mortality. Sepsis was defined as confirmed or suspected infection together with two or more SIRS criteria (temperature $>38.0^\circ\text{C}$, tachycardia >90 bpm, tachypnea >20 breaths/minute or $\text{PCO}_2 < 32$ mm Hg, leukocytosis $> 12 \times 10^9/\text{l}$ or leucopenia $< 4 \times 10^9/\text{l}$ or Bands $>10\%$) [30]. Hyperlactatemia is defined as serum lactate ≥ 2.0 mmol/l as found to be an objective surrogate for sepsis severity and worse prognosis [27–29]. For SIRS criteria and lactate level, the initial ED laboratory results were considered for the analysis.

Data were analyzed by using Statistical Package for Social Studies (SPSS 22; IBM Corp., New York, NY, USA). Continuous variables were expressed as mean \pm standard deviation and categorical variables were expressed as percentages. The t-test was used for continuous variables and Chi square test was used for categorical variables. Sensitivity, Specificity, Positive predictive value (PPV), Negative predictive value (NPV), likelihood ratio and Area under the curve (AUC) were used to assess the performance of the predictors. A p-value <0.05 was considered statistically significant.

Results

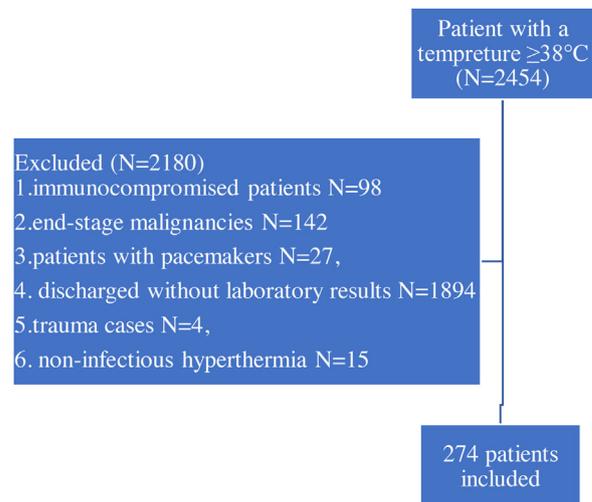
During the research period, 2454 patients triaged with temperature $\geq 38^\circ$ and 2180 patient were excluded as illustrated in (Fig. 1). Of the 274 included patients, the mean age was 48 years and 50% of them were males. Tables 1 and 2 demonstrate the sample characteristics and the outcomes per predictor.

Table 1 revealed the major comorbidities were Cardiac (Ischemic Heart Diseases or Heart Failure) in 47%, Diabetes in 35%, Hypertension in 31% and Chronic Renal Failure in 9% of cases. In our sample 252 of the patients (91.9%) were having sepsis and 67 patients (24.4%) developed hypercalcemia more than 2.0 mmol/l. A total of 38 patients (13.9%) were high-acuity with Canadian Triage Acuity Scores of 1–2 and triaged directly to resuscitation area. 161 patients (59.4%) of the total patients were admitted to the hospital, with 7.3% admitted to the ICU and five patients (1.8%) died within 28 days.

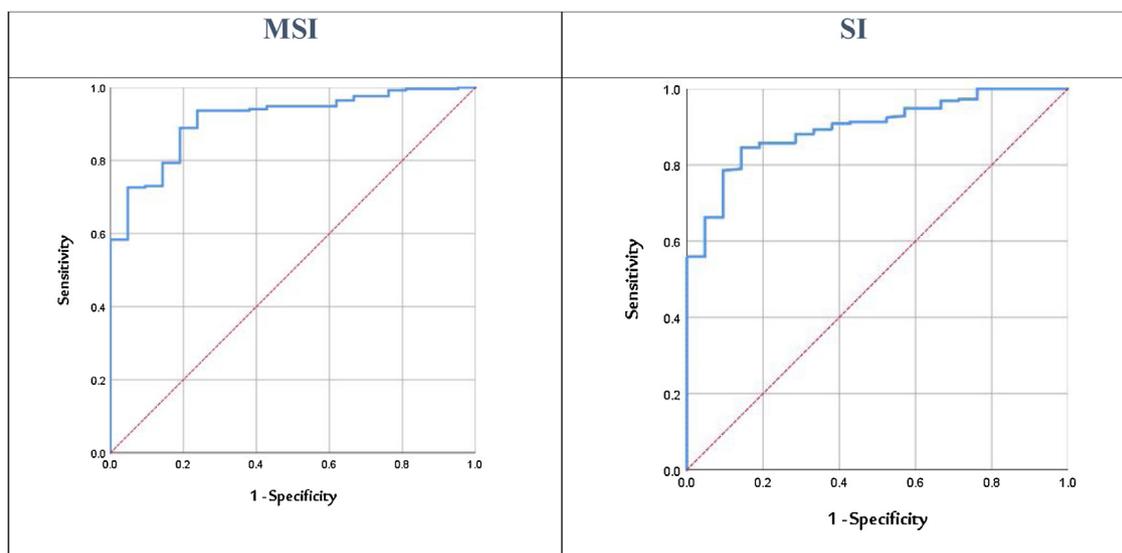
Table 2 revealed that patients with $\text{MSI} \geq 1$ were at least five times more likely to have sepsis hyperlactatemia, ICU admission, and mortality than those with a MSI of less than one. However, 84% of our samples had $\text{MSI} \geq 1$. Patient with $\text{SI} \geq 0.7$ were three time more likely to have sepsis hyperlactatemia, ICU admission, and mortality than those with an SI of less than 0.7, and around 80% of the samples had an SI greater than or equal to one.

Table 1
Patient characteristics.

Patient characteristic	Total patients (274)	
	Number	%
Age (mean, SD)	48.35	20.78
Male	137	50.00
Female	137	50.00
Cardiac disease	47	17.15
Diabetes mellitus (DM)	96	35.04
Hypertension (HTN)	85	31.02
Chronic renal failure	25	9.12
Serum Creatinine (mean, SD)	116.56	126.18
Hyperthyroidism	2	0.73
Hypothyroidism	26	9.49
On Beta-blocker medication	29	10.58
On Ca-channel blocker medication	13	4.74
Canadian triage and acuity scale of 1 or 2	38	13.9
Temperature (mean, SD)	38.69	0.53
Systolic blood pressure (mean, SD)	123.88	20.83
Diastolic blood pressure (mean, SD)	67.44	13.78
Mean arterial blood pressure (mean, SD)	86.07	13.47
Heart rate (mean, SD)	107.26	19.04
Respiratory rate (mean, SD)	20.62	3.24
SI (mean, SD)	0.90	0.25
Lactate (mean, SD)	1.72	1.58
White blood cells > 12,000 or < 4000	119	43.43
Hospital admission	161	59.4
ICU admission	20	7.3
28 day mortality	5	1.8
Source of the infection		
Lower respiratory tract infection	72	26.9
Upper respiratory tract infection	44	16.4
Urinary tract infections	43	16
Skin and soft tissue	16	6
Central nervous system infections	5	1.8
Others	88	32.8

**Fig. 1.** Study flow chart.**Table 2**
Frequency of outcomes per predictor.

Predictor		Sepsis N=252	Lactate ≥ 2 N=62	ICU N=20	Mortality N=5
MSI ≥ 1	Yes 232 (84.7%)	227 (83.2%)	52 (19.0%)	17 (6.3%)	5 (1.8%)
	No 42 (15.3)	25 (9.2%)	10 (3.6%)	3 (1.1%)	0 (0.0%)
MSI ≥ 1.3	Yes 112 (40.9%)	112 (59.0%)	31 (11.3%)	10 (3.7%)	4 (1.5%)
	No 162 (59.1%)	140 (51.3%)	31 (11.3%)	10 (3.7%)	1 (0.4%)
SI ≥ 0.7	Yes 219 (799)	215 (78.5%)	48 (17.3%)	15 (5.5%)	5 (1.8%)
	No 55 (20.1)	37 (13.5%)	14 (5.1%)	5 (1.9%)	0 (0.0%)
SI ≥ 1	Yes 84 (30.7%)	84 (30.1%)	26 (9.5%)	6 (2.2%)	1 (0.4%)
	No 190 (69.3)	168 (61.3%)	36 (13.7%)	14 (5.2%)	4 (1.5%)

**Fig. 2.** ROC curve for prediction of sepsis.**Table 3**
Performance predictors for sepsis.

Performance predictor	MSI ≥ 1	MSI ≥ 1.3	SI ≥ 0.7	SI ≥ 1
Relative Risk (95%CI)	1.64 (1.28–2.11)	1.16 (1.08–1.23)	1.46 (1.21–1.76)	1.13 (1.07–1.19)
Positive predictive value	97.8%	100%	98.2%	100%
Negative predictive value	39%	13%	31.5%	11.1%
Sensitivity	90.1%	44.4%	85.3%	33.3%
Specificity	76.2%	100%	81%	100%
AUC (95%CI)	0.913 (0.862–0.963)		0.897 (0.844–0.950)	

Table 4

Performance of predictor for hyperlactatemia.

Predictor	MSI ≥ 1	MSI ≥ 1.3	SI ≥ 0.7	SI ≥ 1
Relative Risk (95%CI)	0.94(0.52–1.70)	1.45(0.94–2.24)	0.86 (0.51–1.44)	1.63 (1.06–2.52)
Positive predictive value	22.4%	27.7%	21.9%	31%
Negative predictive value	76.2%	80.9%	74.5%	81.1%
Sensitivity	83.9%	50%	77.4%	41.9%
Specificity	15.1%	61.8%	19.3%	72.6%
AUC (95%CI)	0.579 (0.487–0.670)		0.564 (0.473–0.655)	

Table 5

Performance predictors for ICU admission.

Performance predictor	MSI ≥ 1	MSI ≥ 1.3	SI ≥ 0.7	SI ≥ 1
Relative Risk (95%CI)	1.03 (0.3144–3.3471)	1.45 (0.62–3.36)	0.75(0.29–1.98)	0.97 (0.39–2.44)
Positive predictive value	7.4%	8.9%	6.9%	7.1%
Negative predictive value	92.7%	93.7%	90.7%	92.5%
Sensitivity	85%	50%	75%	30%
Specificity	15.1%	59.4%	19.5%	68.9%
AUC (95%CI)	0.524 (0.378–0.669)		0.477 (0.338–0.616)	

Table 6

Performance predictors for 28 days mortality.

Performance predictor	MSI ≥ 1	MSI ≥ 1.3	SI ≥ 0.7	SI ≥ 1
Relative Risk (95%CI)	2.03 (0.11–36.05)	5.79 (0.65–51.08)	0.15 (0.05–0.42)	0.57 (0.06–4.98)
Positive predictive value	2.2%	3.6%	2.3%	1.2%
Negative predictive value	100%	99.4%	100%	97.9%
Sensitivity	100%	80%	100%	20%
Specificity	15.7%	59.7%	20.5%	69%
AUC (95%CI)	0.750 (0.233–0.867)		0.614 (0.466–0.762)	

Table 3 revealed that both MSI and SI were associated with sepsis and the most sensitive predictor was MSI ≥ 1 (90.1%) with a specificity of 76.2% and positive predictive value of 97.8%. Both MSI ≥ 1.3 , and SI ≥ 1 were specific for prediction of sepsis, but MSI was more accurate in term of sensitivity. Fig. 2 demonstrate the ROC curve of MSI and SI for prediction of sepsis.

Table 4 demonstrated that only cases with MSI ≥ 1.3 and SI ≥ 1 were associated with hyperlactatemia as the relative risks were 1.45 and 1.63, respectively. MSI ≥ 1.3 were most sensitive predictor whereas SI ≥ 1 were most specific and both have a positive predictive value of around 81%. there were no association between in the lower cut-off values of MSI ≥ 1 and SI ≥ 0.7 with hyperlactatemia.

Table 5 revealed that MSI was associated with ICU admission. Values of MSI ≥ 1 were 85% sensitive with 92.7% negative predictive value but with low specificity (15.1%) whereas MSI ≥ 1.3 were 50% sensitive and 59.4% specific. SI was not associated with ICU admission

Table 6 revealed that only MSI can predict the 28 days mortality. MSI ≥ 1.3 were 80%, 59% specific and 99.4% negative predictive value.

Generally, there were trends of greater accuracy of MSI over SI in the prediction of sepsis and sepsis-related outcomes but not a statistically significant difference, as there were clear overlaps in the wide confidence intervals of AUCs and Relative Risk of SI and MSI.

Discussion

To the best of our knowledge, this is the first study to assess the relationship between triage MSI and sepsis or sepsis-related outcomes. Our findings indicate that an MSI of ≥ 1.3 was associated with all the outcomes of interest including sepsis, hyperlactatemia, ICU admission and 28 days mortality with a good specificity ranging from 59% to 100%. However, the MSI cut-off of ≥ 1 was more sensitive in the prediction of sepsis (90%), ICU admissions (85%) and mortality (100%), but was less specific towards, and cannot predict,

hyperlactatemia. An SI of ≥ 1 was associated with sepsis and hyperlactatemia but not with ICU admission or mortality. An SI of ≥ 0.7 was less sensitive than MSI ≥ 1 for the prediction of sepsis and not an accurate predictor for other outcomes.

Our findings were consistent with the previous studies, which revealed that MSI is a predictor of mortality [24,25,31]. In the context of SI, Burger et al. did a cohort study to assess it as a predictor for hyperlactatemia and 28 days mortality. Although they used triage vitals to calculate the SI, the sample set was limited to ED patients screened for sepsis and planned for admission. They found that SI of ≥ 1 is 48% sensitive and 81% specific which is roughly in accord with our findings. In addition, they demonstrated that SI is associated with 28 days mortality. Another observational study was done by Yussouf et al., to assess SI of ED patient and found SI of ≥ 1 is associated with mortality, which was not apparent in our study [21]. However, both studies targeted ED patients for admission whereas our study targeted all triaged patients. We believe that our sample represents a wider spectrum of severity and provide more applicability in the triage settings.

Despite our study having revealed that MSI is a promising predictor tool that could help in the risk stratification process of the febrile patients it is considered as the triage qSOFA to have a sub-optimal accuracy for the prediction of sepsis-related outcomes. This might indicate the need for further studies that incorporate MSI in a multi-item scaling system to provide the desired accuracy instead of relying on a single cut-off value. Nevertheless, further larger multicenter prospective studies are required to assess the MSI as a predictor of sepsis and sepsis-related outcomes.

We acknowledge that there are some limitations to our study. First, it is a single center retrospective study from a limited set of data that were available in the electronic medical records. The accuracy of the data remains subjective to the process of documentation. In addition, we recognized lab results that were based on a single set of initial laboratory results while sepsis development is more of a dynamic process. We did not use the updated definition of sepsis-3 because the study started while qSOFA was not yet validated nor

evaluated to be used in the Emergency Departments of developing countries. When we compare MSI to SI among the study outcomes, there were clear overlaps in the wide confidence intervals of AUCs and Relative Risk and we believed that our sample was not sufficiently large to demonstrate superior accuracy. Additionally, not every patient with sepsis presents with fever, and therefore this study is only applicable for patients presenting to ED with fever from suspected sepsis.

Conclusion

MSI of ≥ 1 was the most sensitive predictor of sepsis in febrile patients and $MSI \geq 1.3$ was the best predictor for sepsis-related outcomes including hyperlactatemia, ICU admission and 28 days mortality. However, no single cut-off values of MSI or SI were found to have an optimal accuracy for the prediction of sepsis-related outcomes. Further studies are required to assess the incorporation of MSI in a multi-item scaling system for the prediction of sepsis-related outcomes.

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Competing interests

None declared.

Ethical approval

Institutional review board (IRB) approval was obtained from the ethical research committee at King Khalid University Hospital, King Saud University (research project number E-17-2804).

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