Global Health & Medicine. 2023; 5(4):223-228.

ORIGINAL ARTICLE

DOI: 10.35772/ghm.2023.01008

The reverse shock index multiplied by the Glasgow Coma Scale score can predict the need for initial resuscitation in patients suspected of sepsis

Wataru Matsuda*, Akio Kimura, Tatsuki Uemura

Department of Emergency Medicine and Critical Care, Center Hospital of the National Center for Global Health and Medicine, Tokyo, Japan.

Abstract: For patients suspected of sepsis, early recognition of the need for initial resuscitation is key in management. This study evaluated the ability of a modified shock index — the reverse shock index multiplied by the Glasgow Coma Scale score (rSIG) — to predict the need for initial resuscitation in patients with sepsis. This retrospective study involved adults with infection who were admitted to a Japanese tertiary care hospital from an emergency department between January and November 2020. The rSIG, modified Early Warning Score (MEWS), quick Sequential Organ Failure Assessment (qSOFA), and original shock index (SI) values were recorded using initial vital signs. The primary outcome was the area under the receiver-operating characteristic curve (AUROC) for the composite outcome consisting of vasopressor use, mechanical ventilation, and 72-h mortality. Secondary outcomes were the AUROCs for each component of the primary outcome and 28-day mortality. As a result, the primary outcome was met by 67 of the 724 patients (9%). The AUROC was significantly higher for the rSIG than for the other tools (rSIG 0.84 [0.78 – 0.88]; MEWS 0.78 [0.71 – 0.84]; qSOFA 0.72 [0.65 – 0.79]; SI 0.80 [0.74 – 0.85]). Compared with MEWS and qSOFA, the rSIG also had a higher AUROC for vasopressor use and mechanical ventilation, but not for 72-h mortality or in-hospital mortality. The rSIG could be a simple and reliable predictor of the need for initial resuscitation in patients suspected of sepsis.

***Keywords*:** shock index, sepsis, early warning score, emergency department, resuscitation, triage

Introduction

Early recognition is key in the management of sepsis because initial resuscitation for sepsis or septic shock, namely, a sepsis bundle, should be recommended to start immediately. Japanese clinical practice guidelines recommend initial assessment based on vital signs when sepsis is suspected (*1*). However, although vital signs can be measured quickly, it remains unclear how they should be evaluated when used to determine the need for early resuscitation.

Because qSOFA — a simply predictive tools for sepsis using vital signs — have low sensitivity, international guidelines recommend using an early warning method when screening for sepsis, such as the modified Early Warning Score (MEWS) (*2*). However, the MEWS is time-consuming and difficult to implement unless trained medical staff and well-equipped facilities are available. Furthermore, although the MEWS is a good predictor of in-hospital mortality (*3-5*), admission to an intensive care unit (ICU) (*4,5*), and a diagnosis of sepsis (*6,7*), it is unclear whether it is a good predictor of the need for initial resuscitation.

Adherence to the sepsis bundle is low worldwide (*8-19*) because it requires significant medical resources to achieve adherence. Achieving a bundle in all patients with sepsis places a high burden on medical staff, so it makes sense to prioritize high-risk sepsis patients for initial resuscitation.

The shock index (SI) or a modified SI has also been used for the initial assessment of sepsis (*20-24*). The SI is considered useful for identifying patients with sepsis who require initial resuscitation because it is a hemodynamic assessment. Among the modified SIs in use, a simple modified SI developed for trauma patients, the reverse shock index multiplied by the Glasgow Coma Scale score (rSIG), has been reported to be superior to conventional scoring systems in predicting short-term mortality (*25-31*), need for massive transfusion (*28,32*), and need for early intervention (*28,33,34*). Despite its simplicity, we hypothesized that the rSIG would be better than conventional tools for identifying patients with sepsis who require intensive organ support in the early phase. Therefore, in this study, we evaluated whether the rSIG would be a better predictor of the need for vasopressor use, the need for mechanical ventilation, or of death within the initial 72 h after triage when compared with the MEWS, quick Sequential Organ Failure Assessment (qSOFA), and SI.

Materials and Methods

Ethical approval and informed consent

The study was approved by the ethics committee at our hospital (approval number: NCGM-S-004384-00) and followed the principles of the Declaration of Helsinki. Informed consent was obtained using the opt-out method *via* the hospital website.

Study design and settings

This retrospective single-center study was performed at an urban tertiary care hospital in Japan. About 20,000 patients visit its emergency department each year, and more than half arrive by ambulance. This study included patients admitted to the hospital for infections from the emergency department. All patients with infection were evaluated for sepsis and initially treated in accordance with national and international guidelines by emergency physicians. Exclusion criteria were transfer from another hospital, less than 18 years of age, a definitive diagnosis of COVID-19, and missing data for vital signs at triage.

Data collection

Information was collected on age, sex, site of infection, vital signs, initial Sequential Organ Failure Assessment (SOFA) score, and 28-day and in-hospital mortality. Vital signs included the first values recorded in the hospital. The SOFA score was assessed at the time of admission to the ICU or a ward.

The primary outcome was the area under the receiver-operating characteristic curve (AUROC) for the composite events consisting of vasopressor use, mechanical ventilation, and 72-h mortality. Secondary outcomes were each component of the composite events of primary outcome and 28-day mortality.

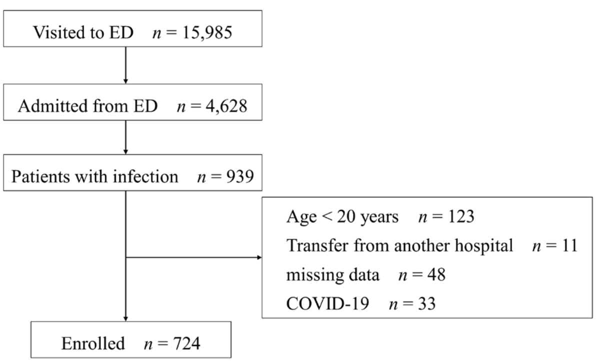


Figure 1. Flow of participants through the study. ED, emergency department

Statistical analysis

Categorical variables were examined using Fisher's exact test and continuous variables using the Mann–Whitney *U* test. Receiver-operating characteristic curves (ROC) were generated to visualize the impact of shifting the positive cutoff value on true-positive (sensitivity) and false-positive (1 − specificity) rates. The AUROCs were compared using the technique described by DeLong *et al.* (*35*). Statistical significance was set at $p < 0.05$ in all analyses. Sensitivity analyses were performed based on age < 80 years, without treatment limitation, and optimal cut-off values. The optimal cut-off values were defined by the value when the AUROC of each score was maximum. All statistical analyses was performed using R version 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria) and JMP Pro version 15 (SAS Institute Inc., Cary, NC). We were not able to impute missing data for vital signs because they were probably not random.

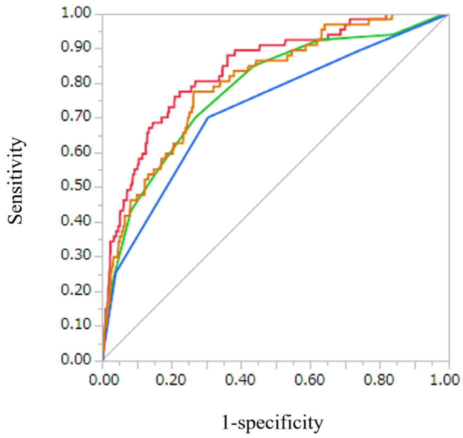
Results

A total of 724 patients were enrolled between January and November 2020 (Figure 1). Most patients were elderly and one third had a treatment limitation, such as a do-not-attempt resuscitation or intubation order (Table 1). Overall, 455 patients (63%) were diagnosed with sepsis

Table 1. Patient characteristics

Variable	n = 724
Age, years, median [IQR]	81 [71, 88]
Male, n (%)	376 (52)
Vital signs	
Systolic blood pressure, mmHg, median [IQR]	131 [111, 150]
Heart rate, beats/min, median [IQR]	96 [82, 111]
Glasgow Coma Scale score, median [IQR]	15 [13, 15]
Respiratory rate, beats/min, median [IQR]	20 [18, 24]
Body temperature, °C, median [IQR]	37.7 [36.9, 38.6]
Initial SOFA score, median [IQR]	3 [1, 4]
Main sites of infection, n (%)	
Respiratory	322 (44)
Urinary	161 (22)
Abdomen	133 (18)
Soft tissue	49 (7)
Other	59 (8)
Sepsis, n (%)	455 (63)
Septic shock, n (%)	33 (5)
Treatment limitation, n (%)	256 (35)
Composite outcome	
Any, n (%)	67 (9)
Vasopressor use within 72 h, n (%)	44 (6)
Mechanical ventilation within 72 h, n (%)	31 (4)
Death within 72 h, n (%)	22 (3)
Death at day 28, n (%)	61 (8)
In-hospital death, n (%)	85 (12)

*Categorical variables were analyzed by Fisher's exact test and continuous variables by the Mann–Whitney *U* test. Sepsis and septic shock were diagnosed based on the Sepsis-3 definitions. SOFA, Sequential Organ Failure Assessment.



	AUROC	Lower 95%	Upper 95%
rSIG	0.84	0.78	0.88
MEWS	0.78	0.71	0.84
qSOFA	0.72	0.65	0.79
SI	0.80	0.74	0.85

	Chi square	*p* value
rSIG *vs.* MEWS	5.95	0.015
rSIG *vs.* qSOFA	0.17	< 0.001
rSIG *vs.* SI	5.33	0.021

Figure 2. Comparisons of receiver operating characteristic (ROC) curves for the composite outcome consisting of vasopressor use, mechanical ventilation, and 72-h mortality. rSIG, reverse shock index multiplied by Glasgow Coma Scale score; MEWS, modified Early Warning Score; qSOFA, quick Sequential Organ Failure Assessment; SI, shock index; AUROC, area under ROC. Red, green, blue and yellow lines indicate rSIG, MEWS, qSOFA and SI respectively.

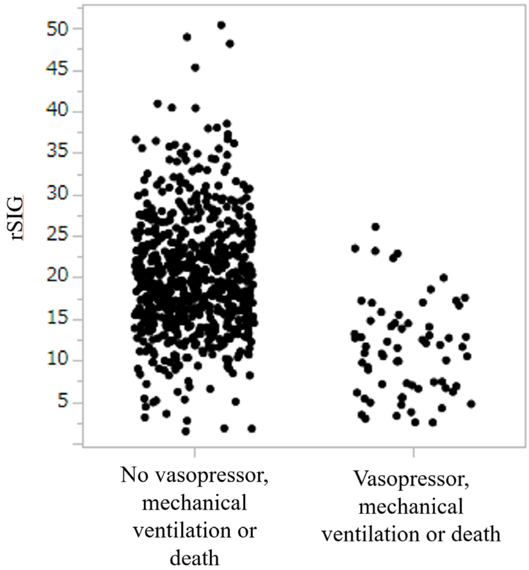


Figure 3. Distribution of rSIG values according to whether or not the composite events of primary outcome was met. rSIG, reverse shock index multiplied by the Glasgow Coma Scale score. The composite events included vasopressor use, mechanical ventilation, and 72-h death.

Table 2. Results of sensitivity analyses

Variable	AUROC	95% CI	*p* value
Age < 80 years, *n* = 319			
rSIG	0.87	0.79 – 0.92	
vs. MEWS	0.75	0.66 – 0.83	0.005
vs. qSOFA	0.75	0.66 – 0.83	< 0.001
vs. SI	0.79	0.69 – 0.86	0.008
Without treatment limitation, *n* = 468			
rSIG	0.86	0.79 – 0.91	
vs. MEWS	0.77	0.68 – 0.84	0.003
vs. qSOFA	0.73	0.65 – 0.81	< 0.001
vs. SI	0.81	0.73 – 0.86	0.004
Optimal cut-off value*			
rSIG ≤ 15	0.77	0.72 – 0.82	
vs. MEWS ≥ 5	0.72	0.66 – 0.77	0.028
vs. qSOFA ≥ 2	0.70	0.64 – 0.75	0.013
vs. SI ≤ 0.9	0.71	0.65 – 0.77	0.027

*Optimal cut-off values were defined by the value when each AUROC was maximum. rSIG, reverse shock index multiplied by Glasgow Coma Scale score; MEWS, modified Early Warning Score; qSOFA, quick Sequential Organ Failure Assessment; SI, shock index.

and 33 (5%) with septic shock according to the SEPSIS-3 criteria. In total, 67 patients (9%) required treatment with a vasopressor or mechanical ventilation or died within 72 h of triage.

Primary outcome

In terms of the primary outcome, the AUROCs for the rSIG, MEWS, qSOFA, and SI were 0.84 (0.78 – 0.88), 0.78 (0.71 – 0.84), 0.72 (0.65 – 0.79), and 0.80 (0.74 – 0.85), respectively (Figure 2). The AUROC for the rSIG was significantly higher than that of MEWS (p = 0.015), qSOFA (p < 0.001) and SI (p = 0.021). Figure 3 shows the distribution of rSIG values according to whether or not the composite events of primary outcome were met.

Table 2 showed the results of the sensitivity analyses. In subgroups of patients with age < 80 years (n = 319) and patients without treatment limitation (n = 468), The AUROC for the rSIG was significantly higher than that of the other tools.

The optimal rSIG, MEWS, qSOFA, and SI cut-off values were 14.8, 5, 2, and 0.87, respectively. Sensitivity and specificity of rSIG ≤ 15 were 0.78 and 0.77, respectively. When individual optimal cutoff values were used, the AUROCs for the rSIG ≤ 15, MEWS ≥ 5, qSOFA ≥ 2 and SI ≤ 0.9 were 0.77 (0.72 – 0.82), 0.72 (0.66 – 0.77), 0.70 (0.64 – 0.75), and 0.71 (0.65 – 0.77), respectively (Table 2). The AUROC for the rSIG was significantly higher than that of MEWS (p = 0.028), qSOFA (p = 0.013) and SI (p = 0.027).

Secondary outcomes

Table 3. Results for secondary outcomes

Variable	AUROC	95% CI	*p* value
Vasopressor use within 72 h			
rSIG	0.85	0.78 – 0.90	
vs. MEWS	0.78	0.70 – 0.84	0.017
vs. qSOFA	0.73	0.64 – 0.81	< 0.001
vs. SI	0.83	0.76 – 0.88	0.26
Mechanical ventilation within 72 h			
rSIG	0.82	0.73 – 0.88	
vs. MEWS	0.74	0.65 – 0.82	0.052
vs. qSOFA	0.67	0.58 – 0.74	< 0.001
vs. SI	0.77	0.68 – 0.84	0.07
Death at 72 h			
rSIG	0.86	0.76 – 0.93	
vs. MEWS	0.86	0.77 – 0.91	0.87
vs. qSOFA	0.86	0.78 – 0.91	0.88
vs. SI	0.82	0.70 – 0.90	0.11
Death at 28 d			
rSIG	0.75	0.68 – 0.81	
vs. MEWS	0.71	0.64 – 0.77	0.07
vs. qSOFA	0.71	0.63 – 0.78	0.13
vs. SI	0.72	0.65 – 0.78	0.06

rSIG, reverse shock index multiplied by Glasgow Coma Scale score; MEWS, modified Early Warning Score; qSOFA, quick Sequential Organ Failure Assessment; SI, shock index.

Table 3 shows the secondary outcomes. The AUROC for vasopressor use within 72 h was significantly higher for the rSIG (0.85 [0.78 – 0.90]) than for the MEWS (0.78 [0.70 – 0.84], $p = 0.017$) or qSOFA (0.73 [0.64 – 0.81], $p < 0.001$) but not for the SI (0.83 [0.76 – 0.88], $p = 0.26$). The AUROC for mechanical ventilation within 72 h was significantly higher for the rSIG (0.82 [0.73 – 0.88]) than for the qSOFA (0.67 [0.58 – 0.74], $p < 0.001$) but not for the MEWS (0.74 [0.65 – 0.82], $p = 0.052$) or SI (0.77 [0.68 – 0.84], $p = 0.07$). There was no significant difference in the AUROCs for 72-h or 28-day mortality between rSIG and the other tools (72-h mortality: rSIG 0.86 (0.76 – 0.93), MEWS 0.86 (0.77 – 0.91), qSOFA 0.86 (0.78 – 0.91), SI 0.82 (0.70 – 0.90), 28-day mortality: rSIG 0.75 (0.68 – 0.81), MEWS 0.71 (0.64 – 0.77), qSOFA 0.71 (0.63 – 0.78), SI 0.72 (0.65 – 0.78)).

Discussion

In this study, the rSIG was superior in predicting the need for intensive organ support and death in the early phase in patients with infection compared with the MEWS, qSOFA, and SI. Furthermore, the performance of the rSIG was similar to or better than the qSOFA and MEWS in terms of vasopressor use, mechanical ventilation and short-term mortality. Although the rSIG has been used mainly for trauma, the results of this study suggest that it may also be useful for patients with infection. The optimal rSIG cut-off value reported for trauma patients ranges from 9.5 to 14.8 (*26-28,32*), which is similar to that in our study. Considering that vital signs are not disease-specific parameters, we believe that our result is reasonable.

Interestingly, the rSIG was found to have a higher AUROC for need of mechanical ventilation, even without inclusion of the respiratory rate which is usually an important parameter in the clinical assessment. The respiratory rate is often difficult to measure accurately (*36,37*), therefore , it was suitable to be a factor in inadequate assessment. Body temperature can also lead to misjudgments: sepsis with fever has been shown to have a better outcome than sepsis without fever (*38*), in contrast with the MEWS, which scores higher for hyperthermia. Not including the respiratory rate and body temperature measurements in the rSIG may have contributed to its high predictive performance.

Japan is an aging society and most of our patients were elderly. Interpretation of vital signs is complicated in the elderly for several reasons, including underlying medical conditions and use of antihypertensive medications. For example, it has been reported that the relationship between vital signs and outcome in patients with sepsis differs between the elderly and non-elderly (*39*). Therefore, we performed a sensitivity analysis by subgroup, namely, for age < 80 years and presence of treatment limitations. The results were similar to the analysis of all patients, which increases the generalizability of our findings.

Given that the rSIG was significantly more predictive of vasopressor use than the MEWS or qSOFA, it may be better at predicting the need for initial resuscitation. Triggering initial resuscitation based on the rSIG value could lead to earlier management (*e.g.*, antibiotic therapy, use of a vasopressor, or admission to the ICU). Although a matter of controversy in patients without shock, there is some evidence suggesting that every 1-h delay in administration of antibiotics increases the likelihood of mortality in patients with shock (*40-42*). Yet, adherence to the sepsis bundle is particularly low in patients with septic shock because of the time required to perform procedures such as intubation or insertion of a central venous catheter. Therefore, early recognition is particularly important in patients with septic shock.

This study has some limitations. First, screening was performed according to the final diagnosis because the study was retrospective in nature. Therefore, we were unable to include patients who were suspected of having an infection at triage but were ultimately determined to be free of infection. Second, we excluded patients with COVID-19 because the pattern of organ failure in COVID-19 may differ from that in conventional sepsis. Also, owing to local circumstances, it was not possible to enroll a sufficient number of patients with COVID-19 to be able to evaluate the triage tool in this cohort. However, international sepsis guidelines have been published for conventional sepsis and sepsis in patients with COVID-19 (*2,43*). Based on the above, we consider it appropriate to distinguish between conventional sepsis and COVID-19 at this time. Third, we included only hospitalized patients because we were unable to investigate outcomes in patients who did not require hospitalization.

Conclusions

The rSIG was a significantly better predictor of the need for a vasopressor, the need for mechanical ventilation, and death within 72 h of triage in patients with infection at an emergency department. The rSIG could be a simple and reliable predictor of the need for initial resuscitation in patients with sepsis.

Funding: This work was supported in part by a Grant-in-Aid for Research from the National Center for Global Health and Medicine (20A3002).

Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. Egi M, Ogura H, Yatabe T, *et al.* The Japanese Clinical Practice Guidelines for Management of Sepsis and Septic Shock 2020 (J-SSCG 2020). J Intensive Care. 2021; 9:53.
2. Evans L, Rhodes A, Alhazzani W, *et al.* Surviving sepsis campaign: International guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021; 47:1181-247.
3. Churpek MM, Snyder A, Han X, Sokol S, Pettit N, Howell MD, Edelson DP. Quick sepsis-related organ failure assessment, systemic inflammatory response syndrome, and early warning scores for detecting clinical deterioration in infected patients outside the intensive care unit. Am J Respir Crit Care Med. 2017; 195:906-911.
4. Usul E, Korkut S, Kayipmaz AE, Halici A, Kavalci C. The role of the quick sequential organ failure assessment score (qSOFA) and modified early warning score (MEWS) in the pre-hospitalization prediction of sepsis prognosis. Am J Emerg Med. 2021; 41:158-162.
5. Sabir L, Ramlakhan S, Goodacre S. Comparison of qSOFA and Hospital Early Warning Scores for prognosis in suspected sepsis in emergency department patients: A systematic review. Emerg Med J. 2022; 39:284-294.
6. Wattanasit P, Khwannimit B. Comparison of the accuracy of early warning scores with qSOFA and SIRS for predicting sepsis in the emergency department. Am J Emerg Med. 2021; 46:284-288.
7. McGrath SP, Perreard I, MacKenzie T, Calderwood M. Improvement of sepsis identification through multi-year comparison of sepsis and early warning scores. Am J Emerg Med. 2022; 51:239-247.
8. Townsend SR, Phillips GS, Duseja R, Tefera L, Cruikshank D, Dickerson R, Nguyen HB, Schorr CA, Levy MM, Dellinger RP, Conway WA, Browner WS, Rivers EP. Effects of compliance with the early management bundle (SEP-1) on mortality changes among Medicare beneficiaries with sepsis: A propensity score matched cohort study. Chest. 2022; 161:392-406.
9. Umemura Y, Abe T, Ogura H, *et al*. Hour-1 bundle adherence was associated with reduction of in-hospital mortality among patients with sepsis in Japan. PLoS One. 2022; 17:e0263936.
10. Milano PK, Desai SA, Eiting EA, Hofmann EF, Lam CN, Menchine M. Sepsis bundle adherence is associated with improved survival in severe sepsis or septic shock. West J Emerg Med. 2018; 19:774-781.
11. Ranzani OT, Monteiro MB, Besen B, Azevedo LCP. Association of sepsis diagnosis at daytime and on weekdays with compliance with the 3-hour sepsis treatment bundles. A multicenter cohort study. Ann Am Thorac Soc. 2020; 17:980-987.
12. Machado FR, Ferreira EM, Schippers P, *et al*. Implementation of sepsis bundles in public hospitals in Brazil: A prospective study with heterogeneous results. Crit Care. 2017; 21:268.
13. Sonis JD, Benzer TI, Black L, Filbin MR, Hayes BD, Hibbert KA, Kraus C, Raja AS, Temin E, Vareschi M, White BA, Wilcox SR, Aaronson EL. Utilization of a multidisciplinary emergency department sepsis huddle to reduce time to antibiotics and improve SEP-1 compliance. Am J Emerg Med. 2020; 38:2400-2404.
14. Hu B, Xiang H, Dong Y, Portner E, Peng Z, Kashani K. Timeline of sepsis bundle component completion and its association with septic shock outcomes. J Crit Care. 2020; 60:143-151.
15. Baghdadi JD, Brook RH, Uslan DZ, Needleman J, Bell DS, Cunningham WE, Wong MD. Association of a care bundle for early sepsis management with mortality among patients with hospital-onset or community-onset sepsis. JAMA Intern Med. 2020; 180:707-716.
16. Prachanukool T, Sanguanwit P, Thodamrong F, Suttapanit K. The 28-day mortality outcome of the complete hour-1 sepsis bundle in the emergency department. Shock. 2021; 56:969-974.
17. Wang L, Ma X, He H, Su L, Guo Y, Shan G, Wang Y, Zhou X, Liu D, Long Y; China National Critical Care Quality Control Center Group. Compliance with the Surviving Sepsis Campaign guideline 1-hour bundle for septic shock in China in 2018. Ann Transl Med. 2021; 9:278.
18. Bahar İ, Oksuz H, Şenoğlu N, Demirkiran H, Aydoğan M, Tomak Y, Çömez M, Bayrakçı S, Gönüllü E, Berktaş M. Compliance with the surviving sepsis campaign bundle: A multicenter study from Turkey. Cureus. 2021; 13:e14989.
19. You JS, Park YS, Chung SP, *et al.* Relationship between time of emergency department admission and adherence to the Surviving Sepsis Campaign bundle in patients with septic shock. Crit Care. 2022; 26:43.
20. Berger T, Green J, Horeczko T, Hagar Y, Garg N, Suarez A, Panacek E, Shapiro N. Shock index and early recognition of sepsis in the emergency department: pilot study. West J Emerg Med. 2013; 14:168-174.
21. Althunayyan SM, Alsofayan YM, Khan AA. Shock index and modified shock index as triage screening tools for sepsis. J Infect Public Health. 2019; 12:822-826.
22. Middleton DJ, Smith TO, Bedford R, Neilly M, Myint PK. Shock index predicts outcome in patients with suspected sepsis or community-acquired pneumonia: A systematic review. J Clin Med. 2019; 8:1144.
23. Jouffroy R, Pierre Tourtier J, Gueye P, Bloch-Laine E, Bounes V, Debaty G, Boularan J, Carli P, Vivien B. Prehospital shock index to assess 28-day mortality for septic shock. Am J Emerg Med. 2020; 38:1352-1356.
24. Jouffroy R, Gilbert B, Thomas L, Bloch-Laine E, Ecollan P, Boularan J, Bounes V, Vivien B, Gueye PN. Association between prehospital shock index variation and 28-day

mortality among patients with septic shock. BMC Emerg Med. 2022; 22:87.
25. Kimura A, Tanaka N. Reverse shock index multiplied by Glasgow Coma Scale score (rSIG) is a simple measure with high discriminant ability for mortality risk in trauma patients: an analysis of the Japan Trauma Data Bank. Crit Care. 2018; 22:87.
26. Wu SC, Rau CS, Kuo SCH, Chien PC, Hsieh HY, Hsieh CH. The reverse shock index multiplied by Glasgow Coma Scale Score (rSIG) and prediction of mortality outcome in adult trauma patients: a cross-sectional analysis based on registered trauma data. Int J Environ Res Public Health. 2018; 15:2346.
27. Chu WT, Liao CH, Lin CY, Chien CY, Lin CC, Chang KW, Chen JH, Chen WL, Huang CC, Lim CJ, Chung JY. Reverse shock index multiplied by Glasgow Coma Scale (rSIG) predicts mortality in severe trauma patients with head injury. Sci Rep. 2020; 10:2095.
28. Lammers D, Conner J, Marenco C, Morte K, Martin M, Eckert M, *et al*. Optimal prospective predictors of mortality in austere environments. J Surg Res. 2020; 255:297-303.
29. Lammers DT, Marenco CW, Do WS, Conner JR, Horton JD, Martin MJ, Escobar MA Jr, Bingham JR, Eckert MJ. Pediatric adjusted reverse shock index multiplied by Glasgow Coma Scale as a prospective predictor for mortality in pediatric trauma. J Trauma Acute Care Surg. 2021; 90:21-26.
30. Lammers DT, Marenco CW, Morte KR, Conner JR, Horton JD, Barlow M, Martin MJ, Bingham JR, Eckert MJ, Escobar MA Jr. Addition of neurological status to pediatric adjusted shock index to predict early mortality in trauma: A pediatric Trauma Quality Improvement Program analysis. J Trauma Acute Care Surg. 2021; 91:584-589.
31. Frieler S, Lefering R, Gerstmeyer J, Drotleff N, Schildhauer TA, Waydhas C, Hamsen U; TraumaRegister DGU. Keeping it simple: the value of mortality prediction after trauma with basic indices like the reverse shock index multiplied by Glasgow Coma Scale. Emerg Med J. 2022; 39:912-917.
32. Lee YT, Bae BK, Cho YM, Park SC, Jeon CH, Huh U, Lee DS, Ko SH, Ryu DM, Wang IJ. Reverse shock index multiplied by Glasgow coma scale as a predictor of massive transfusion in trauma. Am J Emerg Med. 2021; 46:404-409.
33. Reppucci ML, Acker SN, Cooper E, Meier M, Stevens J, Phillips R, Moulton SL, Bensard DD. Improved identification of severely injured pediatric trauma patients using reverse shock index multiplied by Glasgow Coma Scale. J Trauma Acute Care Surg. 2022; 92:69-73.
34. Reppucci ML, Stevens J, Cooper E, Nolan MM, Jujare S, Acker SN, Moulton SL, Bensard DD. Use of reverse shock index times Glasgow coma scale (rSIG) to determine need for transfer of pediatric trauma patients to higher levels of care. J Pediatr Surg. 2023; 58:320-324.
35. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: A nonparametric approach. Biometrics 1988; 44:837-845.
36. Philip KE, Pack E, Cambiano V, Rollmann H, Weil S, O'Beirne J. The accuracy of respiratory rate assessment by doctors in a London teaching hospital: A cross-sectional study. J Clin Monit Comput. 2015; 29:455-460.
37. Badawy J, Nguyen OK, Clark C, Halm EA, Makam AN. Is everyone really breathing 20 times a minute? Assessing epidemiology and variation in recorded respiratory rate in hospitalised adults. BMJ Qual Saf. 2017; 26:832-836.
38. Sundén-Cullberg J, Rylance R, Svefors J, Norrby-Teglund A, Björk J, Inghammar M. Fever in the emergency department predicts survival of patients with severe sepsis and septic shock admitted to the ICU. Crit Care Med. 2017; 45:591-599.
39. Shimazui T, Nakada TA, Walley KR, *et al.* Significance of body temperature in elderly patients with sepsis. Crit Care. 2020; 24:387.
40. Seymour CW, Gesten F, Prescott HC, Friedrich ME, Iwashyna TJ, Phillips GS, Lemeshow S, Osborn T, Terry KM, Levy MM. Time to treatment and mortality during mandated emergency care for sepsis. N Engl J Med. 2017; 376:2235-2244.
41. Liu VX, Fielding-Singh V, Greene JD, Baker JM, Iwashyna TJ, Bhattacharya J, Escobar GJ. The timing of early antibiotics and hospital mortality in sepsis. Am J Respir Crit Care Med. 2017; 196:856-863.
42. Im Y, Kang D, Ko RE, Lee YJ, Lim SY, Park S, Na SJ, Chung CR, Park MH, Oh DK, Lim CM, Suh GY; Korean Sepsis Alliance (KSA) investigators. Time-to-antibiotics and clinical outcomes in patients with sepsis and septic shock: A prospective nationwide multicenter cohort study. Crit Care. 2022; 26:19.
43. Alhazzani W, Møller MH, Arabi YM, *et al.* Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). Intensive Care Med. 2020; 46:854-887.

Received January 20, 2023; Revised May 30, 2023; Accepted July 21, 2023.

Released online in J-STAGE as advance publication July 28, 2023.

**Address correspondence to*:
Wataru Matsuda, Department of Emergency Medicine and Critical Care, Center Hospital of the National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku, Tokyo 162-8655, Japan.
E-mail: wmatsuda@hosp.ncgm.go.jp