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Reverse shock index multiplied by Glasgow coma scale as a predictor of massive transfusion in trauma

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ABSTRACT

Background and purpose: Previous studies have identified that the reverse shock index multiplied by the Glasgow Coma Scale score (rSIG) is a good predictor of mortality in trauma patients. However, it is unknown if rSIG has utility as a predictor for massive transfusion (MT) in trauma patients. The present study evaluated the ability of rSIG to predict MT in trauma patients.

Methods: This was a retrospective, observational study performed at a level 1 trauma center. Consecutive patients who presented to the trauma center emergency department between January 2016 and December 2018 were included. The predictive ability of rSIG for MT was assessed as our primary outcome measure. Our secondary outcome measures were the predictive ability of rSIG for coagulopathy, in-hospital mortality, and 24-h mortality. We compared the prognostic performance of rSIG with the shock index, age shock index, and quick Sequential Organ Failure Assessment.

Results: In total, 1627 patients were included and 117 (7.2%) patients received MT. rSIG showed the highest area under the receiver operating characteristic (AUROC) curve (0.842; 95% confidence interval [CI], 0.806–0.878) for predicting MT. rSIG also showed the highest AUROC for predicting coagulopathy (0.769; 95% CI, 0.728–0.809), in-hospital mortality (AUROC 0.812; 95% CI, 0.772–0.852), and 24-h mortality (AUROC 0.826; 95% CI, 0.789–0.864). The sensitivity of rSIG for MT was 0.79, and the specificity of rSIG for MT was 0.77. All tools had a high negative predictive value and low positive predictive value.

Conclusion: rSIG is a useful, rapid, and accurate predictor for MT, coagulopathy, in-hospital mortality, and 24- h mortality in trauma patients.

1. Introduction

Injury is the sixth most common cause of death in the world and is also the leading cause of death in people under the age of 40 years. About 50% of deaths within 24 h after trauma are due to hemorrhage, which is the biggest avoidable cause of death in severe trauma patients [1,2]. Massive transfusion protocols (MTPs) for severe bleeding have been shown to improve outcomes; however, early identification of patients with massive hemorrhage is crucial [3]. Many studies have been reported for the prediction of massive transfusion (MT) in severe trauma patients [4,5].

Shock index (SI) is one of the tools for assessing severity in trauma patients. It was introduced by Allower and Burri in 1967 and is defined as the ratio of heart rate (HR) to systolic blood pressure (SBP) [6]. Since

Abbreviations: ATC, acute traumatic coagulopathy; AUROC, area under receiver operating characteristic; GCS, Glasgow coma scale; HR, heart rate; ISS, injury severity score; MT, massive transfusion; MTP, massive transfusion protocol; qSOFA, quick Sequential Organ Failure Assessment; ROC, receiver operating characteristic; rSIG, reverse shock index multiplied by Glasgow coma scale; SBP, systolic blood pressure; SI, shock index; SIA, age shock index.

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SI is calculated from HR and SBP values, it can be obtained easily at the bedside of the patient and can evaluate the shock state more accurately than the HR and SBP alone [7-9]. Owing to its ease and accurate prediction, many studies have identified the usefulness of SI for predicting mortality and MT in trauma patients [10-13]. Further, various derivatives of SI, such as the modified shock index and age shock index (SIA), have been introduced to improve the accuracy of SI [14,15].

Recently, Akio et al. developed the reverse shock index multiplied by the Glasgow Coma Scale (GCS) score (rSIG), which is calculated by multiplying the GCS with a ratio of SBP to HR [16]. They found that rSIG was a better predictor of in-hospital mortality and 24-h blood transfusion than SI and SIA. Two subsequent studies have also demonstrated that rSIG is a good predictor of mortality in trauma patients [17,18]. However, rSIG has never been used to predict MT in trauma patients. Therefore, the present study assessed the ability of rSIG to predict MT in trauma patients. Additionally, we assessed the ability of rSIG to predict in-hospital mortality, 24-h mortality, and coagulopathy, and compared the prognostic performance of rSIG with SI, SIA, and quick Sequential Organ Failure Assessment (qSOFA). We hypothesized that rSIG would have a good ability to predict MT and would be a better predictor than SI, SIA, and qSOFA.

2. Methods

2.1. Study design and setting

This study is a retrospective, single-center study performed at a trauma center of a 1400-bed, university affiliated hospital. Our trauma center acts as a level I regional trauma center, is responsible for approximately 7 million people, and is one of the biggest trauma centers in the country. Almost 1000 trauma patients with an injury severity score (ISS) >15 are treated annually. This study was approved by the *Institutional Review Board of our hospital* (*IRB* 2006–005-091). Requirement of informed consent was waived because the data were analyzed anonymously and retrospectively.

2.2. Study population

This study enrolled patients from the independent trauma center emergency department (ED) at our hospital, which is separate from the general ED. The admission criteria for the trauma center ED are based on the “Guidelines for field triage of injured patients – steps one and two” [19], but admission is ultimately determined by the emergency physician. If the patient did not meet the field triage criteria, but the emergency physician's judgment indicated severe trauma, the patient was admitted to the trauma center ED. The consecutive patients who presented to the trauma center ED between January 2016 and December 2018 were included in the study. Exclusion criteria were as follows: (a) age < 16 years, (b) transferred from other hospitals, (c) cardiac arrest when presented to the ED, and (d) missing values for SBP, HR, respiratory rate (RR), and GCS.

2.3. Data collection and variables

The data were obtained from the Korean Trauma Data Bank (KTDB) and the electronic medical records. The KTDB was instituted by the Ministry of Health and Welfare of Korea in 2013, to accumulate comprehensive data about trauma patients [20]. The following data were retrieved from the database: age, sex, vital signs (SBP, DBP, HR, RR) at ED presentation, GCS at ED presentation, packed red blood cells transfused within the first 4 and 24 h of admission in ED, ISS, MT, in-hospital mortality, and 24-h mortality. The following laboratory data obtained at ED presentation were also collected: prothrombin time international normalized ratio (PT INR), activated partial thromboplastin time (aPTT), hemoglobin level, platelet count, and lactate level. We calculated SI, SIA, and rSIG using the following formulae:

$$SI = HR/SBP$$

$$SIA = SI * age$$

$$rSIG = (SBP/HR) * GCS$$

qSOFA score was calculated as the sum of 1 point each for SBP ≤100 mmHg, GCS ≤14, and RR ≥22 breaths/min.

2.4. Outcome measures

The primary outcome was MT, defined as the transfusion of 10 or more units of packed red blood cells within 24 h of presentation to the trauma center ED [21]. The secondary outcomes were in-hospital mortality, 24-h mortality, and coagulopathy. Coagulopathy was defined as PT INR >1.2 [22-24].

2.5. Statistical analyses

Continuous variables with a normal distribution are described by the mean ± standard deviation, while those with an abnormal distribution are described by the median and interquartile range. Categorical variables are reported as the frequency (percentage). The continuous variables were compared using the Wilcoxon rank-sum test and categorical variables using Fisher's exact test. A receiver operating characteristic (ROC) curve analysis was carried out and the area under the ROC curve (AUROC) was calculated to assess the prognostic ability of SI, SIA, qSOFA, and rSIG in severe trauma patients. The AUROCs were compared using Delong's method [25]. Further, 95% confidence intervals (CIs) were computed with 2000 stratified bootstrap replicates. Statistical analyses were performed using the software R (http://cran.r-project.org), version 4.0.0 with additional packages (tableone, pROC, and plotROC). All tests were two-sided, and *p*-values less than 0.05 were considered statistically significant.

3. Results

3.1. Patients' characteristics

In total, 3927 patients presented to the trauma center ED between January 2016 and December 2018. Based on the exclusion criteria, 2300 patients were excluded from the study. The criteria for exclusion and the respective numbers were as follows: age < 16 years (n = 144), transferred from other hospitals (n = 1886), cardiac arrest when presented to the ED (n = 218), and missing values (n = 41). Finally, 1627 patients were included in this study (Fig. 1).

Among all patients, 1259 (77.4%) were men. The median age was 53 (range, 37–63) years, and the median ISS was 17 (range, 10–26). In total, 117 (7.2%) patients received MT. In-hospital mortality and 24-h mortality was 137 (8.4%) and 128 (7.9%), respectively. Coagulopathy was observed in 179 (11.5%) patients.

3.2. Comparison of the MT group and non-MT group

We compared the characteristics of the patients in the MT group and non-MT group (Table 1). No significant difference was observed in age between the two groups (p = 0.142). The patients in the MT group had lower SBP (p < 0.001) and GCS (p < 0.001) compared to those in the non-MT group, while HR (p < 0.001) and RR (p < 0.001) were higher in patients of the MT group than those in the non-MT group. In laboratory tests, the level of lactate (p < 0.001) and PT INR (p < 0.001) were significantly higher in the patients of the MT group than those in the non-MT group. Furthermore, the patients of the MT group showed higher SI (1.24 [0.85–1.84] vs. 0.71 [0.57–0.93]), SIA (60.00 [43.57–88.35] vs. 34.41 [25.15–46.49]), and qSOFA (2.00

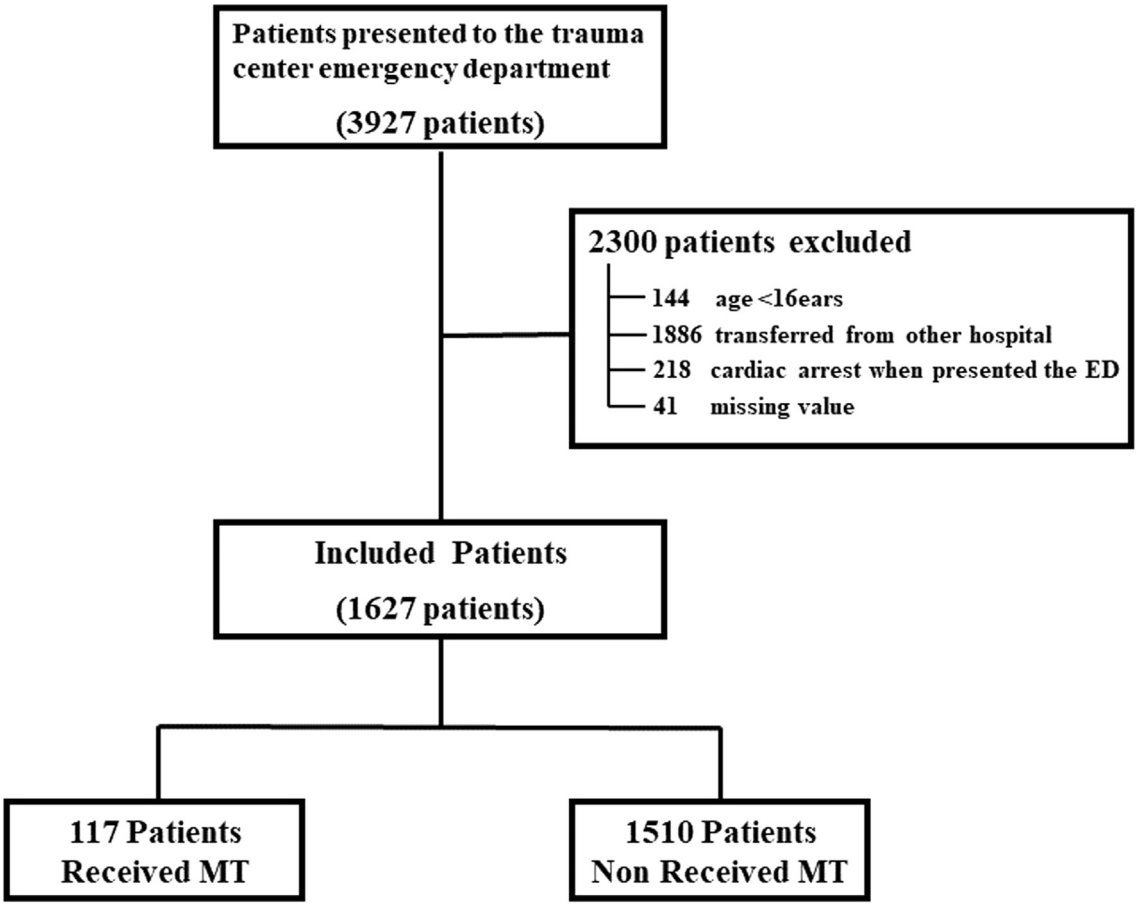

Fig. 1. Study flow diagram of trauma patients. ED, emergency department; MT, massive transfusion.

[2.00–3.00] vs. 1.00 [0.00–2.00]) than those in the non-MT group. The rSIG in the patients of the MT group was significantly lower than that in the non-MT group (6.47 [3.80–12.24] vs. 18.56 [12.92–24.14], $p < 0.001$). The proportion of patients with coagulopathy ($p < 0.001$), in-hospital mortality ($p < 0.001$), and 24-h mortality ($p < 0.001$) was significantly higher in the MT group than the non-MT group.

Table 1
Characteristics of included patients.

Variable	Total ($n = 1627$)	Non-massive transfusion group ($n = 1510$)	Massive transfusion group ($n = 117$)
Age (median[IQR])	53.00 [37.00, 63.00]	53.00 [36.00, 63.00]	56.00 [40.00, 65.00]
Sex, *n*(%)			
F	368 (22.6)	340 (22.5)	28 (23.9)
M	1259 (77.4)	1170 (77.5)	89 (76.1)
PT_INR (median[IQR])	1.03 [0.97, 1.11]	1.03 [0.97, 1.10]	1.20 [1.11, 1.35]
SBP (median[IQR])	120.00 [100.00, 140.00]	120.00 [100.00, 140.00]	80.00 [60.00, 100.00]
GCS (median[IQR])	15.00 [12.00, 15.00]	15.00 [12.00, 15.00]	9.00 [5.00, 14.00]
Coagulopathy (%)			
No	1382 (88.5)	1326 (91.7)	56 (48.7)
Yes	179 (11.5)	120 (8.3)	59 (51.3)
aPTT time (median[IQR])	27.60 [25.10, 30.90]	27.40 [25.00, 30.50]	33.50 [27.70, 45.75]
Hb (median[IQR])	13.70 [12.40, 14.90]	13.80 [12.50, 15.00]	12.60 [11.00, 13.40]
Lactic acid (median[IQR])	2.80 [1.80, 4.20]	2.60 [1.70, 3.90]	5.05 [3.52, 7.70]
SI (median[IQR])	0.73 [0.58, 0.97]	0.71 [0.57, 0.93]	1.24 [0.85, 1.84]
SIA (median[IQR])	35.41 [25.82, 49.40]	34.41 [25.15, 46.49]	60.00 [43.57, 88.35]
qSOFA (median[IQR])	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	2.00 [2.00, 3.00]
ISS (median[IQR])	17.00 [10.00, 26.00]	17.00 [9.00, 25.00]	30.00 [26.00, 38.00]
rSIG (median[IQR])	17.82 [11.82, 23.57]	18.56 [12.92, 24.14]	6.47 [3.80, 12.24]
Death (%)			
No	1490 (91.6)	1427 (94.5)	63 (53.8)
Yes	137 (8.4)	83 (5.5)	54 (46.2)
Death 24 h (%)			
No	1499 (92.1)	1433 (94.9)	66 (56.4)
Yes	128 (7.9)	77 (5.1)	51 (43.6)

IQR: interquartile ranges; SBP: Systolic blood pressure; GCS: Glasgow coma scale; SI: shock index; SIA: age shock index; rSIG: reverse shock index multiplied by Glasgow Coma scale; qSOFA: quick Sequential Organ Failure Assessment; ISS: injury severity score.

3.3. ROC analysis for predicting adverse outcomes

3.3.1. Massive transfusion

ROC analysis was done and AUROCs were calculated to assess the predictive values of SI, SIA, rSIG, and qSOFA for MT (Fig. 2a). The AUROCs for predicting MT with SI, SIA, rSIG, and qSOFA values were 0.796 (95% CI, 0.748–0.844), 0.792 (95% CI, 0.746–0.838), 0.842 (95% CI, 0.806–0.878), and 0.791 (95% CI, 0.751–0.830), respectively. rSIG showed the highest AUROC for predicting MT. The difference of rSIG with SI ($p < 0.022$) and SIA ($p < 0.024$) was significant.

3.3.2. Coagulopathy, in-hospital mortality, and 24-h mortality

For predicting coagulopathy (Fig. 2b), rSIG (AUROC 0.769; 95% CI, 0.728–0.809) showed the highest predictive power, followed by qSOFA (AUROC 0.716; 95% CI, 0.677–0.754), SI (AUROC 0.704; 95% CI, 0.656–0.752), and SIA (AUROC 0.693; 95% CI, 0.648–0.737) (Fig. 2b). Further, rSIG also showed the highest AUROCs among all indices for predicting in-hospital mortality (AUROC 0.812; 95% CI, 0.772–0.852) and 24-h mortality (AUROC 0.826; 95% CI, 0.789–0.864) (Fig. 3). Table 2 summarizes the AUROCs for all indices.

4. Discussion

The present study was performed to evaluate the ability of rSIG to predict MT in severe trauma patients and to compare the predictive ability of rSIG with SI, SIA, and qSOFA. The findings of the present study suggested that the prognostic performance of rSIG for MT was significantly higher than SI, SIA, and qSOFA. Additionally, rSIG showed better AUROC for predicting coagulopathy, in-hospital mortality, and 24-h mortality as compared to other indices.

The rSIG can be measured using the reverse shock index and GCS. SI is very practical and useful for assessing the hemodynamic status of trauma patients. However, SI is calculated as the ratio of HR to SBP, which contradicts the basic concept of shock. In general, hemodynamic instability refers to a state in which SBP is lower than the HR, but as indicated by SI, it does not mean a state in which HR is lower than the SBP. To improve this, Chung et al. introduced the concept of reverse shock index [26], which is calculated by dividing SBP by HR, and a small rSI value means that the patient's condition is critical. Meanwhile, the GCS, which assesses the level of consciousness, is known to be a stronger predictor of mortality in trauma patients [27]. rSIG is a combination of simple but powerful predictors: reverse shock index and GCS.

The rSIG was first introduced by Kimura and Tanaka in 2018 [16]. They evaluated the trauma patients from 256 hospitals in Japan between 2006 and 2015 to find a better predictor than SI for post-injury mortality and requirement of early blood transfusion. They compared several modified models based on SI and identified that rSIG was a reliable triage tool for assessing the risk in trauma patients. They reported that the AUROC of rSIG was 0.901 for in-hospital mortality. Wu et al. externally validated the rSIG in patients admitted to a level 1 trauma center in Taiwan [18]. The results of the study showed that rSIG had higher predictive accuracy of mortality than SI in trauma patients, and the AUROC of rSIG was 0.83 for predicting mortality. Recently, Chu et al. applied rSIG to evaluate the in-hospital mortality in severe trauma patients with head injury [17]. They founded that rSIG was useful for predicting the mortality risk in severe trauma patients with head injury. In the present study, the AUROC of rSIG for in-hospital mortality was 0.812, and the predictive value of rSIG for mortality was superior to SI, SIA, and qSOFA. These findings are consistent with the results of the previous studies, which suggest that rSIG is a useful predictor of mortality in trauma patients. Another interesting feature of our study is that all tools, including rSIG, have low PPV and high NPV for MT and mortality. We believe this is due to the low incidence of MT (7.2%) and in-hospital mortality (8.4%) [28].

Of note, most of the previous studies have studied the relationship between rSIG and mortality in trauma patients. To the best of our knowledge, no study has reported the prediction of MT in severe trauma patients. In our study, the AUROC of rSIG for MT was 0.842, which indicated a better predictive value of rSIG than SI, SIA, and qSOFA. The underlying reason for this result is unclear. A possible explanation is that traumatic brain injury can be accompanied by scalp lacerations, facial bone fractures, and oronasal bleeding, which can be the source of bleeding [29]; and significant mental deterioration can occur without brain injury if a trauma patient falls into severe shock [30]. Thus, the combination of both a measure of bleeding (rSI) and consciousness (GCS) more fully encompasses the patient's trauma status.

One strength of our study is that we have identified that rSIG can be used as a predictor of coagulopathy. Coagulopathy occurs in about one-third of trauma patients admitted through the ED and causes multiple organ failure and high mortality [2,22]. Trauma-

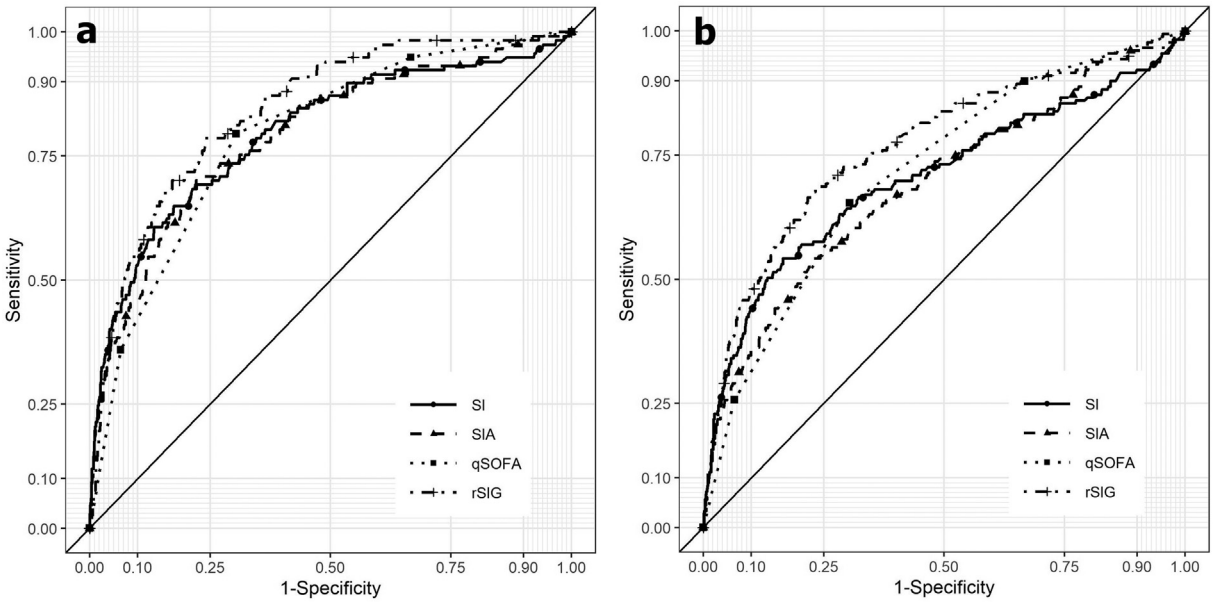

Fig. 2. Receiver Operating Characteristic Curve for massive transfusion (a) and coagulopathy (b).

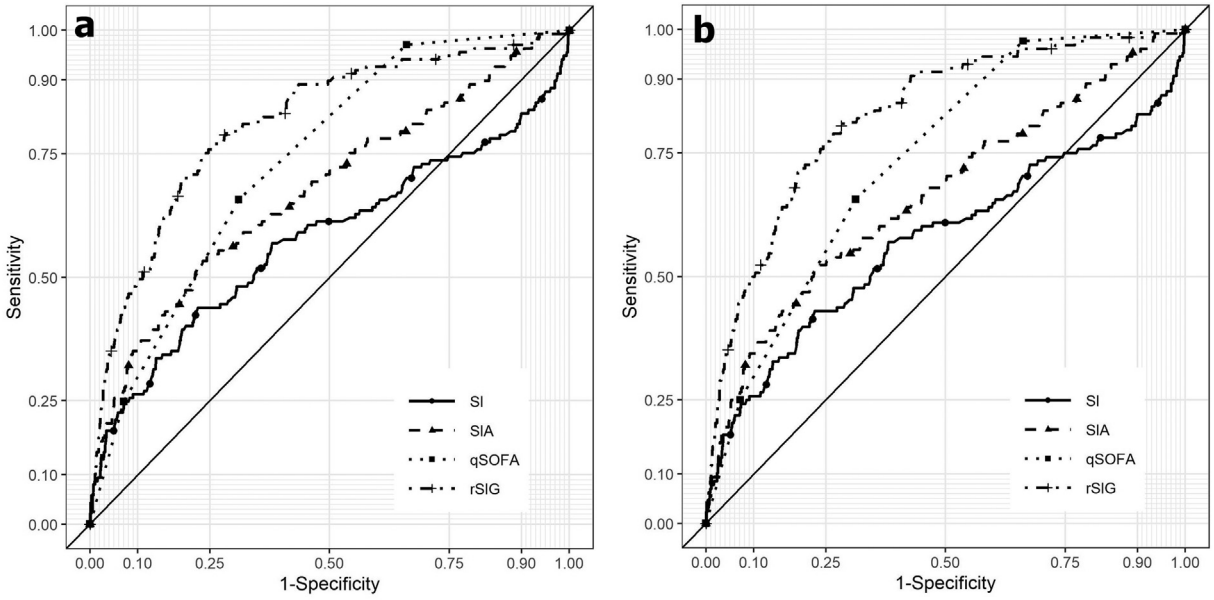

Fig. 3. Receiver Operating Characteristic Curve for in-hospital mortality (a) and 24-h mortality (b).

induced coagulopathy is of two types: acute traumatic coagulopathy (ATC) and resuscitation-associated coagulopathy. ATC in trauma patients is the coagulopathy induced directly from trauma, while resuscitation-associated coagulopathy is that exacerbated by hypothermia, metabolic acidosis, coagulating factor consumption, and hemo-dilution [31]. The early prediction of coagulopathy can lead to rapid implementation of rewarming, correction of acidosis, balanced transfusion, and MTP activation. To the best of our knowledge, the present study is the first to predict coagulopathy using rSIG. Additionally, our study showed that rSIG has a better predictive value than SI, SIA, and qSOFA.

Table 2
Predictive power of the rSIG, SI, SIA and qSOFA for MT, Coagulopathy, 24-h mortality and in-hospital mortality.

Variable	Cut off	Sensitivity	Specificity	PPV	NPV	AUROC (95% CI)
MT						
rSIG	9.52	0.79	0.77	0.21	0.98	0.842 (0.806–0.878)
SI	0.80	0.67	0.84	0.25	0.97	0.796 (0.748–0.844)
SIA	45.47	0.70	0.78	0.20	0.97	0.792 (0.746–0.838)
qSOFA	1.50	0.80	0.70	0.17	0.98	0.791 (0.751–0.830)
Coagulopathy						
rSIG	10.30	0.69	0.77	0.28	0.95	0.769 (0.728–0.809)
SI	0.84	0.54	0.85	0.31	0.93	0.704 (0.656–0.752)
SIA	40.81	0.56	0.77	0.24	0.93	0.693 (0.648–0.737)
qSOFA	1.50	0.65	0.70	0.22	0.94	0.716 (0.677–0.754)
24 h mortality						
rSIG	11.17	0.79	0.76	0.22	0.98	0.826 (0.789–0.864)
SI	0.80	0.43	0.78	0.14	0.94	0.574 (0.512–0.637)
SIA	39.90	0.51	0.78	0.17	0.95	0.666 (0.612–0.720)
qSOFA	0.50	0.69	0.68	0.15	0.96	0.738 (0.701–0.774)
In hospital mortality						
rSIG	10.20	0.76	0.77	0.23	0.97	0.812 (0.772–0.852)
SI	0.81	0.43	0.80	0.17	0.94	0.578 (0.517–0.638)
SIA	42.34	0.54	0.77	0.18	0.95	0.674 (0.623–0.726)
qSOFA	0.50	0.67	0.69	0.16	0.96	0.737 (0.701–0.773)

rSIG: reverse shock index multiplied by Glasgow Coma score; SI: shock index; SIA: age shock index; qSOFA: quick Sequential Organ MT: massive transfusion; PPV: positive predictive value; NPV: negative predictive value; AUROC: area under the receiver operating characteristic curve; CI: confidence interval.

Our study has some limitations. First, this study was a retrospective study; therefore, a potential bias can exist. Second, this study was a single trauma center ED study; therefore, the generalizability of the results may be limited because of the effect of regional and demographic variables. Third, we did not measure other prediction scores for MT, such as the Assessment of Blood Consumption score, Trauma Associated Severe Hemorrhage score, and Emergency Transfusion Score [32-34]. However, these scores are more complex to calculate than rSIG, and blood tests or ultrasound results are needed. In future studies, we intend to compare rSIG with other scoring systems for predicting MT, which include laboratory and sonographic results. Moreover, rSIG can be calculated at the prehospital stage. Since our region does not measure GCS at the prehospital stage, we cannot calculate prehospital rSIG in future studies.

5. Conclusion

The present study identified that rSIG is a useful indicator for predicting MT in severe trauma patients. Moreover, rSIG is more accurate than SI, SIA, and qSOFA in predicting in-hospital mortality, 24-h mortality, and coagulopathy. It is a simple bedside tool that can be easily calculated using only vital signs and GCS. Taken together, we believe that rSIG is a useful, rapid, and accurate predictor for MT, coagulopathy, in-hospital mortality, and 24-h mortality in trauma patients.

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Author statement

Young Tark Lee: study design, writing, data collection, data interpretation, critical revision.
Byung Kwan Bae: data analysis, data interpretation.
Young Mo Cho: literature search, critical revision.
Soon Chang Park: literature search, critical revision.
Chang Ho Jeon: data analysis.
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Dae-Sup Lee: data analysis.
Sung-Hwa Ko: data analysis, data interpretation.
Dong-Man Ryu: data analysis, data interpretation.
Il Jae Wang: study design, writing, data collection, data interpretation, critical revision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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