Performance of 5 disseminated intravascular coagulation score systems in predicting mortality in patients with severe trauma

Dong Hun Lee, MD[a], Byung Kook Lee, MD, PhD[a,*], Kyung Woon Jeung, MD[a], Jung Soo Park, MD, PhD[b], Yong Deok Lim, MS[c], Yong Hun Jung, MD[a], Sung Min Lee, MD[a], Yong Soo Cho, MD[a]

Abstract

The present study aimed to analyze and compare the prognostic performances of the Japanese Ministry of Health and Welfare (JMHW) score, the Korean Society on Thrombosis and Hemostasis (KSTH) score, the International Society on Thrombosis and Haemostasis (ISTH) score, the Japanese Association for Acute Medicine (JAAM) score, and the revised JAAM (rJAAM) score, for 28-day mortality in severe trauma.

This retrospective observational study included patients admitted for severe trauma between 2012 and 2015. Receiver operating characteristics analysis was performed to examine the prognostic performance of the 5 different DIC score systems. The primary outcome was 28-day mortality following an injury.

Of the 1266 patients included in the study, 28-day mortality rate was 19.7% (n = 249). The area under the curves (AUCs) of JMHW, KSTH, ISTH, JAAM, and rJAAM scores for 28-day mortality were 0.751 [95% confidence interval (95% CI), 0.726–0.775], 0.726 (95% CI, 0.701–0.750), 0.700 (95% CI, 0.674–0.725), 0.673 (95% CI, 0.646–0.699), and 0.676 (95% CI, 0.649–0.701), respectively. The AUC of JMHW score was significantly different from those of the other score systems. Fibrinogen levels ≤1.0 g/L [odds ratio (OR), 1.824; 95% CI, 1.029–3.232] and 1.0 to 1.5 g/L (OR, 1.697; 95% CI, 1.058–2.724) were independently associated with 28-day mortality compared with fibrinogen level above 1.5 g/L.

JMHW score has the highest prognostic performance for 28-day mortality among DIC score systems in severe trauma. Fibrinogen level seemed to have a role in greater discrimination of JMHW scores than the other DIC score systems.

Abbreviations: AIS = Abbreviated Injury Scale, aPTT = activated partial thromboplastin time, AUC = areas under the curve, CI = confidence interval, DIC = disseminated intravascular coagulation, ED = emergency department, FDP = fibrin degradation product, FFP = fresh frozen plasma, GCS = Glasgow Coma Scale, IQR = interquartile ranges, ISS = Injury Severity Score, ISTH = International Society on Thrombosis and Haemostasis, JAAM = Japanese Association for Acute Medicine, JMHW = Japanese Ministry of Health and Welfare, KSTH = Korean Society on Thrombosis and Hemostasis, OR = odds ratio, PC = platelet concentrates, PRC = packed red blood cells, PT-INR = international normalized ratio of prothrombin time, rJAAM = revised JAAM, ROC = receiver operating characteristic, RTS = revised trauma score, SIRS = systemic inflammatory response syndrome.

Keywords: criteria, disseminated intravascular coagulation, mortality, scoring, trauma

1. Introduction

The incidence of disseminated intravascular coagulation (DIC) induced by trauma may vary according to the criteria used in its diagnosis, but approximately 21% to 47% of all cases occur in trauma patients.[1–3] Although DIC caused by trauma is a hypercoagulable state similar to DIC caused by sepsis, its early phase after trauma involves a hemorrhagic phenotype due to a consumption coagulopathy rather than a thrombotic phenotype. DIC enhances the inflammatory response and causes the systemic inflammatory response syndrome (SIRS) and microvascular thrombosis, which result in multiple organ dysfunction syndrome.[4]

In this regard, several DIC scoring systems have been developed to predict the risk of mortality in critically ill patients. Of these, the Japanese Ministry of Health and Welfare (JMHW) score, the International Society on Thrombosis and Haemostasis (ISTH) score, the Japanese Association for Acute Medicine (JAAM) score, and the Korean Society on Thrombosis and Hemostasis (KSTH) score are commonly used to predict the risk of mortality in various diseases.[5] The JMHW score was the earliest developed scoring system for DIC,[6] and has shown efficiency in various diseases.[7–9] However, there has been no study on the use of the JMHW score for predicting the outcome of trauma. Gando et al[10] revised the JAAM score in 2006 and showed that the revised JAAM (rJAAM) score had a better prognostic performance than the JAAM score in critically ill patients. The ISTH score, which is internationally used,[11] and the rJAAM score possessed a high efficiency in the diagnosis of

DIC after trauma, whereas DIC diagnosed by the ISTH and rJAAM scores were also associated with a high risk of mortality.[1,2,12] In addition, the KSTH score, established in 1993, showed 85% concordance in the diagnosis of DIC compared with the ISTH score.[13] Most previous studies evaluated the performance for outcome in critically ill patients, but there was a lack of studies about the prognostic performance of DIC scores only in trauma patients.

Therefore, the aim of this study was to analyze and compare the prognostic performances of the JMHW, KSTH, ISTH, JAAM, and rJAAM scores in patients with severe trauma.

2. Methods

2.1. Study design and population

We performed a retrospective observational study involving patients with severe trauma at Chonnam National University Hospital, Gwangju, South Korea, admitted between January 2012 and December 2015. Severe trauma was defined as an Injury Severity Score (ISS) greater than 16.[14] The following exclusion criteria were applied: age under 18 years; lack of coagulation laboratory tests [platelet count, activated partial thromboplastin time (aPTT), prothrombin time, fibrinogen, fibrin degradation product (FDP), and D-dimers] within 1 hour of admission; drowning or hanging; cardiac arrest following trauma; conditions resulting in coagulation abnormalities, such as hematologic malignancies, pregnancy, severe hepatic dysfunction, and the current use of anticoagulant agents; and patients with missing data. The study was approved by the Institutional Review Board of Chonnam National University Hospital (IRB # CNUH-2017–076).

2.2. Data collection

The following variables were obtained for each patient: age; sex; time interval between trauma and arrival at our emergency department (ED); vital signs on admission [systolic arterial blood pressure (mmHg), body temperature, heart rate, and respiratory rate]; initial Glasgow Coma Scale (GCS) score; laboratory data on admission [blood pH, $PaCO_2$, base excess, white blood cell count, hemoglobin, platelet count, aPTT, international normalized ratio of prothrombin time (PT-INR), fibrinogen level, FDP level, and D-dimer level]; the amounts of transfused packed red blood cells (PRC), fresh frozen plasma (FFP), and platelet concentrates (PCs) during the first 24 hours after trauma; and the 28-day mortality.

The SIRS score was calculated on the basis of the general SIRS criteria.[15] The revised trauma score (RTS) was calculated on the basis of the vital signs and GCS score. The Abbreviated Injury Scale (AIS) score and ISS were calculated on arrival. Massive transfusion was defined as the transfusion of ≥10 units of PRC from the initial presentation at the ED to 24 hours after arrival.[16] The JMHW, KSTH, ISTH, JAAM, and rJAAM scores were calculated using the data collected on admission. The diagnosis of DIC was based on the KSTH, ISTH, JAAM, revised JAAM, JMHW, and KSTH criteria, which are summarized in Table 1.[6,10,11,13] The 28-day mortality was selected as the primary outcome of trauma because in-hospital mortality does not reflect actual mortality.[17]

2.3. Statistical analysis

Continuous variables that did not satisfy the normality test are presented as median values with interquartile ranges (IQRs). Categorical variables are presented as frequencies and percentages. The difference between 2 groups was tested using the Mann–Whitney U test for continuous variables. The Fisher exact test or Chi-square test was used for the comparison of categorical variables, as appropriate.

Receiver operating characteristic (ROC) analysis was performed to examine the prognostic performance of the 5 different

Table 1

Summary of 5 different DIC scoring systems applied in the present study.

Parameters	Score	KSTH [13]	ISTH [11]	JAAM [10]	JMHW [6]
Platelets, ×10⁹/L	0	>100	>100	≥120	>120
	1	≤100	≤100	≥80 and <120 or >30% decrease within 24 h	80–120
	2		<50		50–80
	3			<80 or >50% decrease within 24 h	≤50
PT, s	0	<3	<3	<1.2 (PT ratio)	<1.25 (PT ratio)
	1	≥3 (or aPTT ≥5 s)	≥3 and <6	≥1.2	1.25–1.67
	2		≥6		≥1.67
Fibrin-related marker, mg/L	0	D-dimer <1.0	D-dimer <1.0	FDP <10	FDP <10
	1	D-dimer ≥1.0		10 ≤ FDP <25	10 ≤ FDP <20
	2		1.0 ≤ D-dimer <5.0		20 ≤ FDP <40
	3		D-dimer ≥5.0	FDP ≥25	FDP ≥40
Fibrinogen, g/L	0	>1.5	>1.0	>3.5	>1.5
	1	≤1.5	≤1.0	≤3.5	1.0–1.5
	2				≤1.0
SIRS score	0			0–2	
	1			≥3	
Underlying disease	1			Required	Present
Bleeding	1				Present
Organ failure	1				Present
Overt DIC		DIC ≥3	DIC ≥5	DIC ≥5	DIC ≥7

rJAAM criteria have same score system with JAAM except fibrinogen score.

aPTT = activated partial thromboplastin time, DIC = disseminated intravascular coagulation, FDP = fibrin/fibrinogen degradation product, ISTH = International Society on Thrombosis and Haemostasis, JAAM = Japanese Association for Acute Medicine, JMHW = Japanese Ministry of Health and Welfare, KSTH = Korean Society on Thrombosis and Hemostasis, PT = prothrombin time, rJAAM = revised JAAM, SIRS = systemic inflammatory response syndrome.

DIC scores regarding 28-day mortality. The comparison of dependent ROC curves was performed using the method proposed by DeLong et al.[18]

Multivariate logistic regression analysis was used to estimate the association between the 5 DIC scores and 28-day mortality, and to evaluate the association between fibrinogen levels and 28-day mortality after adjusting for relevant covariates. We put fibrinogen level as a continuous variable (model 1) and a categorical variable as ≤1.0, 1.0 to 1.5, and >1.5 g/L, defined according to the JMHW score[5] (model 2) to elucidate the type of association between fibrinogen level and 28-day mortality in the different logistic models. All variables with a P value of <.1 in the univariate analysis were selected for the multivariate logistic regression model. Multicollinearity between variables was assessed before modeling. Factors with a P value of <.05 in the multivariate logistic regression model were considered as final adjusted variables. Age, RTS, ISS, base excess, PT-INR, FDP, and D-dimer were selected as adjusted variables. The goodness-of-fit of the final model was evaluated using the Hosmer–Lemeshow test.[19] Backward selection was used to achieve the final model.

Data were analyzed using SPSS software, version 18 (IBM Inc., Chicago, IL). The ROC curves were created and compared using MedCalc version 16.1 (MedCalc Software bvba; Ostend, Belgium). A 2-sided significance level of 0.05 was used for statistical significance.

3. Results

3.1. Patient selection and characteristics

A total of 2165 patients with severe trauma were identified during the study period. After applying the exclusion criteria, 1266 patients were included in this study (Fig. 1). There were 914 (72.2%) male patients and the median age was 57.0 years (range: 45.0–70.0 years). The 28-day mortality rate was 19.7% (n=249). Massive transfusion was performed on 100 (7.9%) patients.

### 3.2. Comparison of baseline and clinical characteristics between survivors and nonsurvivors

There were significant differences between the survivor and nonsurvivor groups in terms of RTS and ISS values. The survivors were younger, had higher levels of hemoglobin and base excess, and had arrived at our ED significantly later after trauma than nonsurvivors (Table 2). Fibrinogen levels were significantly lower in nonsurvivors. FDP and D-dimer levels were significantly higher among nonsurvivors (Table 2). The scores of the JMHW [3 (2–3) vs 4 (3–5); $P<.001$], KSTH [1 (1–2) vs 2 (1–3); $P<.001$], ISTH [3 (2–3) vs 3 (3–4); $P<.001$], JAAM [4 (2–4) vs 4 (4–5); $P<.001$], and rJAAM [3 (2–3) vs 3 (3–4); $P<.001$] were significantly lower among the survivors (Table 2).

3.3. Prognostic performance of the 5 DIC scores in terms of 28-day mortality

Figure 2 shows the ROC curves of the 5 DIC scores in terms of 28-day mortality. The areas under the curve (AUCs) for JMHW, KSTH, ISTH, JAAM, and rJAAM scores were 0.751 [95% confidence interval (95% CI), 0.726–0.775], 0.726 (95% CI, 0.701–0.750), 0.700 (95% CI, 0.674–0.725), 0.673 (95% CI, 0.646–0.699), and 0.676 (95% CI, 0.649–0.701), respectively. The AUC of the JMHW score was significantly different from those of the other four DIC scores.

3.4. Association between the 5 DIC scores and 28-day mortality

Table 3 summarizes the association between the 5 DIC scores and 28-day mortality. After adjusting for confounders, the values of the JMHW, KSTH, ISTH, and rJAAM scores were independently associated with 28-day mortality [JMHW score; odds ratio (OR), 1.393; 95% CI, 1.207–1.607; KSTH score; OR, 1.717; 95% CI, 1.329–2.217; ISTH score; OR, 1.375; 95% CI, 1.147–1.648;
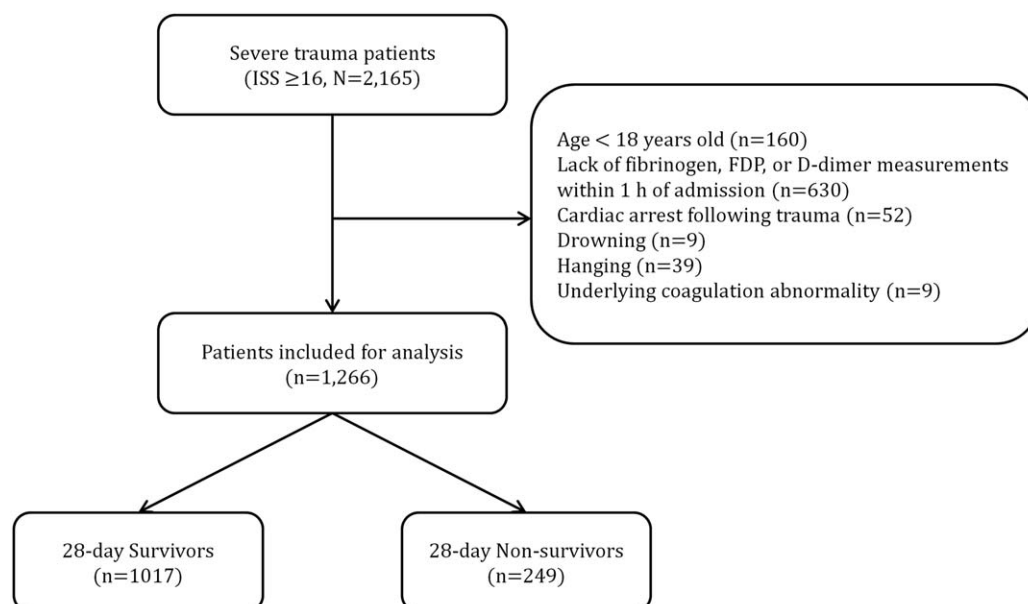
Figure 1. Schematic diagram showing the number of patients with severe trauma included in the present study. FDP=fibrin degradation product, ISS=Injury Severity Score.

Table 2

Comparison of baseline characteristics according to 28-day mortality.

	All patients (N=1266)	Survivor (n=1017)	Nonsurvivor (n=249)	P
Age, y	57 (45–70)	55 (44–68)	67 (53–76)	<.001
Male, n (%)	914 (72.2%)	735 (72.3%)	179 (71.9%)	.904
Mechanism of trauma				.326
Blunt	1234 (97.5%)	990 (97.3%)	244 (98.0%)	
Penetrating	22 (1.7%)	20 (2.0%)	2 (0.8%)	
Burns	10 (0.8%)	7 (0.7%)	3 (1.2%)	
Time from trauma to ED visit, min	180 (60–300)	180 (120–300)	120 (60–180)	<.001
Injury Severity Score	22 (17–26)	20 (17–25)	25 (22–34)	<.001
SIRS criteria	1 (1–2)	1 (1–2)	2 (1–2)	<.001
Revised Trauma Score	7.841 (5.967–7.841)	7.841 (6.904–7.841)	4.944 (4.094–6.376)	<.001
Glasgow Coma Scale	15 (9–15)	15 (14–15)	5 (3–11)	<.001
Body temperature, °C	36.2 (36.0–36.5)	36.2 (36.0–36.5)	36.0 (36.0–36.4)	<.001
Systolic BP, mm Hg	110 (80–130)	110 (90–130)	100 (70–130)	<.001
Heart rate, /min	86 (76–98)	84 (76–96)	90 (78–108)	<.001
Respiratory rate, /min	20 (20–22)	20 (20–22)	20 (20–22)	.060
Arterial blood gas analyses				
pH	7.39 (7.34–7.43)	7.40 (7.35–7.43)	7.36 (7.25–7.42)	<.001
$PaCO_2$, mm Hg	35.6 (31.9–39.2)	36.0 (32.3–39.2)	34.0 (29.0–39.0)	<.001
Base excess	-3.2 (-7.1–0.5)	-2.6 (-6.1–0.2)	-6.6 (-12.3–3.0)	<.001
Laboratory tests				
White blood cell count, ×10^9/L	13.7 (10.2–18.2)	13.5 (10.2–18.0)	14.4 (9.8–19.7)	.189
Hemoglobin, g/dL	11.8 (10.0–13.5)	12.2 (10.4–13.6)	11.0 (8.6–12.3)	<.001
Platelet count, ×10^9/L	189 (149–231)	193 (155–238)	165 (128–212)	<.001
APTT, s	31.6 (27.9–37.3)	30.6 (27.4–35.0)	39.6 (32.0–55.2)	<.001
PT-INR	1.11 (1.03–1.25)	1.09 (1.02–1.19)	1.28 (1.12–1.59)	<.001
Fibrinogen, g/L	1.9 (1.3–2.4)	2.0 (1.5–2.4)	1.3 (0.8–1.9)	<.001
FDP, mg/L	72.7 (26.7–158.0)	58.7 (22.1–129.5)	161.5 (99.6–338.8)	<.001
D-dimer, mg/L	24.1 (6.1–35.2)	18.3 (4.8–35.2)	35.2 (29.2–35.2)	<.001
ISTH scores	3 (2–3)	3 (2–3)	3 (3–4)	<.001
JAAM scores	4 (4–4)	4 (2–4)	4 (4–5)	<.001
rJAAM scores	3 (3–4)	3 (2–3)	3 (3–4)	<.001
KSTH scores	1 (1–2)	1 (1–2)	2 (1–3)	<.001
JMHW scores	3 (2–4)	3 (2–3)	4 (3–5)	<.001
Massive transfusion	100 (7.9%)	55 (5.4%)	45 (18.1%)	<.001
PRC, unit	2 (0–4)	0 (0–4)	4 (0–8)	<.001
FFP, unit	0 (0–2)	0 (0–2)	2 (0–4)	<.001
PC, unit	0 (0–0)	0 (0–0)	0 (0–8)	<.001

aPTT = activated partial thromboplastin time, BP = blood pressure, ED = emergency department, FDP = fibrin degradation product, FFP = fresh frozen plasma, ISTH = International Society on Thrombosis and Haemostasis, JAAM = Japanese Association for Acute Medicine, JMHW = Japanese Ministry of Health and Welfare, KSTH = Korean Society on Thrombosis and Hemostasis, PC = platelet concentrates, PRC = packed red blood cell, PT-INR = international normalized ratio of prothrombin time, rJAAM = revised JAAM, SIRS = systemic inflammatory response syndrome.

rJAAM score; OR, 1.201; 95% CI, 1.026–1.405]. The JAAM score was associated with 28-day mortality in the univariate analysis but was not independently associated with 28-day mortality in the multivariate analysis.

### 3.5. Association between fibrinogen level and 28-day mortality

Fibrinogen level as a continuous variable was not associated with 28-day mortality in the multivariate analysis (OR, 0.999; 95% CI, 0.997–1.002) (Table 4). However, when fibrinogen level was categorized, fibrinogen levels ≤1.0 g/L (OR, 1.824; 95% CI, 1.029–3.232) and 1.0–1.5 g/L (OR, 1.697; 95% CI, 1.058–2.724) were independently associated with 28-day mortality compared with fibrinogen levels above 1.5 g/L.

4. Discussion

In this retrospective observational study, the JMHW score showed the highest prognostic performance in predicting 28-day

mortality in patients with severe trauma. Fibrinogen level seemed to have a role in greater discrimination of JMHW scores than the other DIC scores. JMHW, KSTH, ISTH, and rJAAM scores, but not JAAM score, were independently associated with the 28-day mortality after adjusting for confounders in patients with severe trauma.

In the present study, both JAAM and rJAAM scores were significantly different between survivors and nonsurvivors. However, in multivariate analysis, rJAAM score, but not JAAM score, was independently associated with mortality in the present study. Previous studies also showed that rJAAM could diagnose DIC, and may affect the outcome during the early phase of severe trauma.[1,2,12] Sawamura et al[1] showed that rJAAM score was an independent predictor of in-hospital mortality in trauma patients (OR; 1.459, P=.032). In the same study, the rJAAM score had a good discrimination power (AUC of 0.802) for poor outcomes in the early phase of trauma, which is higher than that of the present study.[1] The better prognostic performance of rJAAM in the previous study was thought to be due to the different definitions of the outcomes as in-hospital mortality and
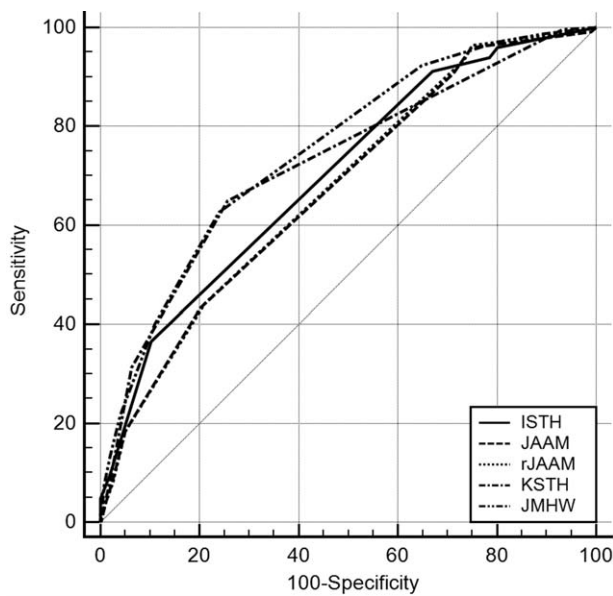
Figure 2. Receiver operating characteristic analyses of the 5 disseminated intravascular coagulation (DIC) scores in terms of 28-day mortality. The area under the curves (AUCs) of JMHW, KSTH, ISTH, JAAM, and rJAAM were 0.751 [95% confidence interval (95% CI), 0.726–0.775), 0.726 (95% CI, 0.701–0.750), 0.700 (95% CI, 0.674–0.725), 0.673 (95% CI, 0.646–0.699), and 0.676 (95% CI, 0.649–0.701)], respectively. The AUC of JMHW score was significantly different from the other DIC score systems. ISTH = International Society on Thrombosis and Haemostasis, JAAM = Japanese Association for Acute Medicine, JMHW = Japanese Ministry of Health and Welfare, KSTH = Korean Society on Thrombosis and Hemostasis, rJAAM = revised JAAM.

massive transfusion. In the previous study, the outcomes of the ROC analysis were death and massive transfusion, and not just death, and the maximum value of rJAAM score was seen within 24 hours of admission.[1]

Several studies have revealed that ISTH score is useful for outcome prediction in severe trauma.[1,12,20] Two studies showed that patients with overt DIC according to the ISTH criteria had a higher mortality rate and received more transfusions in the early phase of trauma, although DIC diagnosed by ISTH criteria was not consistent with anatomical findings.[12,20] Sawamura et al[1] demonstrated that the nonsurvivor group had higher ISTH scores and proportions of patients with overt DIC according to the ISTH criteria in the early phase of trauma. We could not find a study demonstrating ROC analysis of ISTH for the mortality in trauma, but there were few studies regarding outcome prediction of ISTH in postcardiac arrest patients.[21,22] The AUC values for predicting mortality in postcardiac arrest patients were 0.79 (95% CI, 0.69–0.88) and 0.76 (95% CI, 0.67–0.84).[21,22] The higher AUC values among cardiac arrest survivors than in the present study was thought to be due to the higher mortality rate in cardiac arrest survivors of about 48% to 79%.

The JMHW score was proposed in 1987.[6] Although we could not find a study regarding the relationship between JMHW score and outcomes in only trauma patients, it has been used to diagnose DIC in various fields. In critically ill patients, the prognostic performance for mortality using JMHW scores was higher than JAAM scores.[7,8] One retrospective study showed that JMHW score was more sensitive than the ISTH score for the diagnosis of DIC in critically ill patients and the concordance of diagnosing DIC by ISTH and JMHW was markedly high in

Table 3

Univariate and multivariate analysis of the 5 disseminated intravascular coagulation scores in the prediction of 28-day mortality.

	Crude OR (95% CI)	P	Adjusted OR (95% CI)*	P
JMHW score	1.767 (1.605–1.944)	<.001	1.393 (1.207–1.607)	<.001
KSTH score	2.679 (2.270–3.161)	<.001	1.717 (1.329–2.217)	<.001
ISTH score	2.070 (1.772–2.418)	<.001	1.375 (1.147–1.648)	<.001
JAAM score	1.632 (1.461–1.824)	<.001	1.161 (0.996–1.352)	.056
rJAAM score	1.697 (1.497–1.883)	<.001	1.201 (1.026–1.405)	.023

CI = confidence interval, ISTH = International Society on Thrombosis and Haemostasis, JAAM = Japanese Association for Acute Medicine, JMHW = Japanese Ministry of Health and Welfare, KSTH = Korean Society on Thrombosis and Hemostasis, OR = odds ratio, rJAAM = revised JAAM.
* Adjusted for age, time from accident to emergency department visit, Injury Severity Score, Revised Trauma Score, PaCO$_2$, base excess, and hemoglobin.

Table 4

Multivariate logistic regression analysis of 28-day mortality.

	Adjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
Age, y	1.048 (1.035–1.062)	<.001	1.050 (1.036–1.064)	<.001
Revised Trauma Score	0.447 (0.391–0.509)	<.001	0.448 (0.392–0.512)	<.001
Injury Severity Score	1.029 (1.006–1.053)	.013	1.025 (1.002–1.049)	.031
Base excess	0.930 (0.897–0.964)	<.001	0.943 (0.907–0.979)	.003
PT-INR	1.295 (1.042–1.610)	.020	1.219 (0.972–1.530)	.086
FDP, mg/L	1.002 (1.001–1.003)	.004	1.001 (1.000–1.003)	.021
D-dimer, mg/L	1.024 (1.006–1.042)	.010	1.023 (1.005–1.041)	.014
Fibrinogen, g/L	0.999 (0.997–1.002)	.594		
Fibrinogen >1.5 g/L			Reference	
Fibrinogen 1.0–1.5 g/L			1.697 (1.058–2.724)	.028
Fibrinogen ≤1.0 g/L			1.824 (1.029–3.232)	.040

Adjusted for age, Injury Severity Score, Revised Trauma Score, base excess, PT-INR, FDP, and D-dimer.
aPTT = activated partial thromboplastin time, CI = confidence interval, ED = emergency department, FDP = fibrin degradation product, OR = odds ratio, PT-INR = international normalized ratio of prothrombin time, SIRS = systemic inflammatory response syndrome.

patients with trauma or acute promyelocytic leukemia.[23] High sensitivity for DIC assumes that the JMHW score provides more details based on underlying disease, bleeding symptoms, organ failure, fibrinogen and FDP levels, and platelet count than the ISTH score.[6,11] Wada et al[9] showed that early treatment using JMHW score at the early stage of DIC could improve survival. JMWH had a lower OR of 28-day mortality than KSTH in the present study. However, KSTH has a narrow range of score (0–4) compared with JMWH score (0–14). Therefore, it does not mean that KSTH has a stronger association with 28-day mortality than JMWH.

Many studies demonstrated that low platelet counts were associated with in-hospital mortality in severe trauma.[24–26] For the 5 DIC scores, the threshold of platelet count is 100 to 120 × 10^9/L[5]; however, Hayakawa et al[24] showed that the mean platelet count on arrival was 186 (152–235) × 10^9/L in massively transfused patients or nonsurvivors, which is similar to the findings of the present study. Sawamura et al[1] thought that the consumed platelets were replaced by those released from extravascular sites and transfusion during the early phase of trauma. In addition, Gando[4] reported that a platelet counts markedly decreased at least 24 hours following trauma. Therefore, for the 5 DIC scores, the threshold for platelet counts was too low to reflect mortality in the early phase of trauma.

Fibrin-related markers were reported to be associated with outcome in patients with severe trauma. High D-dimer levels on admission were associated with in-hospital mortality in trauma patients.[1,24] For the KSTH and ISTH scores, the threshold of D-dimer levels were 1.0 or 5.0 mg/L.[5] However, in these 2 studies, the D-dimer levels of the nonsurvivor group were 113.1 ± 158.9 and 60 (28.2–120.4) mg/L, consistent with the present study.[1,24] Therefore, the threshold of the D-dimer level in KSTH and ISTH score is not appropriate to predict mortality in the early phase of trauma. FDP, another marker of fibrin derivatives, was also an independent predictor of in-hospital mortality in trauma patients.[1,2] Sawamura et al[1] showed that the FDP levels of the survivor group and nonsurvivors group were 38.2 ± 66.0 and 249.9 ± 314.9 mg/L, respectively. The threshold of FDP level was 25 mg/L for the JAAM and rJAAM scores, and 40 mg/L for the JMHW score.[5] This suggests that the FDP level in the JAAM, rJAAM, and JMHW scores are too low for trauma. However, the JMHW criteria for FDP level are better than others because the JMHW criteria for FDP level is strict and the reference values are higher.

Fibrinogen level was rapidly reduced than the other coagulation markers during the early phase of severe trauma.[27,28] In contrast, fibrinogen level was maintained at a moderate level in sepsis,[28,29] because trauma was characterized by a consumptive coagulopathy, unlike sepsis. In the present study, multivariate analysis revealed that fibrinogen level as a continuous variable was not an independent predictor of mortality. However, fibrinogen level ≤1.5 g/L was an independent predictor of mortality in the present study. Several studies also showed that fibrinogen level ≤1.5 g/L was associated with a worse outcome.[26,27,30] McQuilten et al[26] demonstrated that fibrinogen level ≤1.5 g/L was associated with in-hospital mortality, but fibrinogen level >1.6 g/L was not. However, they showed that only 10% of patients with severe trauma had a fibrinogen level ≤1.5 g/L, while 31% had a fibrinogen level ≤1.5 g/L in the present study. The reasons for the difference between studies remain unclear. However, a possible explanation is that the median time from trauma to ED visit was 1.12 hours in the previous study, while patients visited the ED at a median time of 3 hours after trauma in the present study. In animal studies, the rate of fibrinogen breakdown was increased over the rate of fibrinogen synthesis by the liver, eventually accelerating fibrinogen degradation over time.[31] Hayakawa et al[27] showed that fibrinogen level ≤1.5 g/L was associated with the development of DIC and massive transfusion. The European trauma guideline recommends treatment with fibrinogen concentrate or cryoprecipitate if significant bleeding occurs with a fibrinogen level of less than 1.5 to 2.0 g/L.[30] Therefore, the threshold level of fibrinogen (3.5 g/L) in the JAAM criteria is too high to apply to patients with severe trauma. In contrast to the JAAM criteria, the threshold level of fibrinogen in ISTH criteria was 1.0 g/L. Therefore, ISTH criteria had a disadvantage; a fibrinogen level of 1.0 to 1.5 g/L could not be reflected. In the JMHW score, fibrinogen level was categorized as >1.5, 1.0 to 1.5, and ≤1.0 g/L. Therefore, the JMHW score is appropriate for predicting mortality in patients with severe trauma in relation to their fibrinogen level.

The present study has several limitations. First, it was retrospective and single centered study; therefore, to assess generalizability and causation, further studies will be needed that include larger sample sizes, multiple centers, and a prospective design. Second, 630 patients with severe trauma were excluded because their fibrinolytic biomarkers were not measured within 1 hour of admission. The reasons for this included delayed blood sampling due to resuscitation, resampling due to hemolysis, the relatively high cost of coagulation biomarker tests, and insurance issues. Third, ED arrival was significantly later for the survivor group than the nonsurvivor group. This may be because patients with more severe conditions were transferred more promptly to the ED. This finding was comparable to the observations made by Hayakawa et al.[24] Fourth, the maximum hospital D-dimer value was 35.2 mg/L fibrinogen-equivalent units. Therefore, the predictive value of the D-dimer was not sufficiently analyzed. However, multivariate analysis revealed that D-dimer level was an independent predictor of 28-day mortality. Finally, we did not investigate the relationship between the serial change of DIC score and the prognosis of trauma.

5. Conclusion

JMHW score has the highest prognostic performance for 28-day mortality among the DIC score systems in patients with severe trauma. Fibrinogen level seemed to have a role in greater discrimination of JMHW scores than the other DIC score systems.

Author contributions

Conceptualization: DongHun Lee, Byung Kook Lee, Yong Soo Cho.
Data curation: DongHun Lee, Yong Hun Jung, Sung Min Lee, Yong Soo Cho.
Investigation: Byung Kook Lee.
Methodology: Byung Kook Lee, Jung Soo Park.
Project administration: Byung Kook Lee.
Software: Yong Hun Jung.
Supervision: Kyung Woon Jeung.
Validation: Sung Min Lee.
Writing – original draft: DongHun Lee.
Writing – review & editing: Byung Kook Lee, Kyung Woon Jeung, Yong Deok Lim.

References

[1] Sawamura A, Hayakawa M, Gando S, et al. Disseminated intravascular coagulation with a fibrinolytic phenotype at an early phase of trauma predicts mortality. Thromb Res 2009;124:608–13.

[2] Oshiro A, Yanagida Y, Gando S, et al. Hemostasis during the early stages of trauma: comparison with disseminated intravascular coagulation. Crit Care 2014;18:R61.

[3] Hayakawa M, Sawamura A, Gando S, et al. Disseminated intravascular coagulation at an early phase of trauma is associated with consumption coagulopathy and excessive fibrinolysis both by plasmin and neutrophil elastase. Surgery 2011;149:221–30.

[4] Gando S. Disseminated intravascular coagulation in trauma patients. Semin Thromb Hemost 2001;27:585–92.

[5] Di Nisio M, Baudo F, Cosmi B, et al. Diagnosis and treatment of disseminated intravascular coagulation: guidelines of the Italian Society for Haemostasis and Thrombosis (SISET). Thromb Res 2012;129: e177–84.

[6] Kobayashi N, Maegawa K, Takada M, et al. Criteria for diagnosis of DIC based on the analysis of clinical and laboratory findings in 345 DIC patients collected by the Research Committee on DIC in Japan. Bibl Haematol 1987;49:265–75.

[7] Takemitsu T, Wada H, Hatada T, et al. Prospective evaluation of three different diagnostic criteria for disseminated intravascular coagulation. Thromb Haemost 2011;105:40–4.

[8] Gando S, Wada H, Asakura H, et al. Evaluation of new Japanese diagnostic criteria for disseminated intravascular coagulation in critically ill patients. Clin Appl Thromb Hemost 2005;11:71–6.

[9] Wada H, Wakita Y, Nakase T, et al. Outcome of disseminated intravascular coagulation in relation to the score when treatment was begun. Thromb Haemost 1995;74:848–52.

[10] Gando S, Iba T, Eguchi Y, et al. Japanese Association for Acute Medicine Disseminated Intravascular Coagulation (JAAM DIC) Study Group. A multicenter, prospective validation of disseminated intravascular coagulation diagnostic criteria for critically ill patients: comparing current criteria. Crit Care Med 2006;34:625–31.

[11] Bakhtiari K, Meijers JC, de Jonge E, et al. Prospective validation of the International Society of Thrombosis and Haemostasis scoring system for disseminated intravascular coagulation. Crit Care Med 2004;32: 2416–21.

[12] Sawamura A, Hayakawa M, Gando S, et al. Application of the Japanese Association for Acute Medicine disseminated intravascular coagulation diagnostic criteria for patients at an early phase of trauma. Thromb Res 2009;124:706–10.

[13] Lee JH, Song JW, Song KS. Diagnosis of overt disseminated intravascular coagulation: a comparative study using criteria from the International Society versus the Korean Society on Thrombosis and Hemostasis. Yonsei Med J 2007;48:595–600.

[14] Baker SP, O'Neill B, Haddon WJr, et al. The Injury Severity Score: a method for describing patients with multiple injuries and evaluating emergency care. J Trauma 1974;14:187–96.

[15] Members of the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference committee: American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: Definition for sepsis and organ failure and guidelines for the use innovative therapies in sepsis. Crit Care Med 1992; 20:864–874.

[16] Mitra B, Cameron PA, Gruen RL, et al. The definition of massive transfusion in trauma: a critical variable in examining evidence for resuscitation. Eur J Emerg Med 2011;18:137–42.

[17] Skaga NO, Eken T, Jones JM, et al. Different definitions of patient outcome: consequences for performance analysis in trauma. Injury 2008;39:612–22.

[18] DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics 1988;44:837–45.

[19] Lemeshow S, Hosmer DWJr. A review of goodness of fit statistics for use in the development of logistic regression models. Am J Epidemiol 1982;115:92–106.

[20] Rizoli S, Nascimento BJr, Key N, et al. Disseminated intravascular coagulopathy in the first 24 hours after trauma: the association between ISTH score and anatomopathologic evidence. J Trauma 2011;71: S441–7.

[21] Kim J, Kim K, Lee JH, et al. Prognostic implication of initial coagulopathy in out-of-hospital cardiac arrest. Resuscitation 2013;84: 48–53.

[22] Ono Y, Hayakawa M, Maekawa K, et al. Fibrin/fibrinogen degradation products (FDP) at hospital admission predict neurological outcomes in out-of-hospital cardiac arrest patients. Resuscitation 2017;111:62–7.

[23] Wada H, Gabazza EC, Asakura H, et al. Comparison of diagnostic criteria for disseminated intravascular coagulation (DIC): diagnostic criteria of the International Society of Thrombosis and Hemostasis and of the Japanese Ministry of Health and Welfare for overt DIC. Am J Hematol 2003;74:17–22.

[24] Hayakawa M, Maekawa K, Kushimoto S, et al. High d-dimer levels predict a poor outcome in patients with severe trauma, even with high fibrinogen levels on arrival: a multicenter retrospective study. Shock 2016;45:308–14.

[25] Brown LM, Call MS, Margaret Knudson M, et al. A normal platelet count may not be enough: the impact of admission platelet count on mortality and transfusion in severely injured trauma patients. J Trauma 2011;71:S337–42.

[26] McQuilten ZK, Wood EM, Bailey M, et al. Fibrinogen is an independent predictor of mortality in major trauma patients: a five-year statewide cohort study. Injury 2017;48:1074–81.

[27] Hayakawa M, Gando S, Ono Y, et al. Fibrinogen level deteriorates before other routine coagulation parameters and massive transfusion in the early phase of severe trauma: a retrospective observational study. Semin Thromb Hemost 2015;41:35–42.

[28] Koami H, Sakamoto Y, Sakurai R, et al. The thromboelastometric discrepancy between septic and trauma induced disseminated intravascular coagulation diagnosed by the scoring system from the Japanese association for acute medicine. Medicine (Baltimore) 2016;95:e4514.

[29] Gando S, Saitoh D, Ogura H, et al. A multicenter, prospective validation study of the Japanese Association for Acute Medicine disseminated intravascular coagulation scoring system in patients with severe sepsis. Crit Care 2013;17:R111.

[30] Spahn DR, Bouillon B, Cerny V, et al. Management of bleeding and coagulopathy following major trauma: an updated European guideline. Crit Care 2013;17:R76.

[31] Martini WZ, Chinkes DL, Pusateri AE, et al. Acute changes in fibrinogen metabolism and coagulation after hemorrhage in pigs. Am J Physiol Endocrinol Metab Nov 2005;289:E930–4.