ORIGINAL ARTICLE

Predictive value of modified early warning score for massive transfusion in patients with traumatic brain injury

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ABSTRACT

BACKGROUND: Exsanguination can be fatal in patients with traumatic brain injury (TBI). We aimed to analyze and compare the prognostic performances of injury severity score (ISS), revised trauma score (RTS), shock index (SI), and modified early warning score (MEWS) for predicting massive transfusion (MT) in severe trauma patients with TBI.

METHODS: In this retrospective observational study, severe trauma patients with TBI who visited our emergency department between January 2018 and December 2020 were included in the study. TBI was considered when abbreviated injury scale was 3 or higher. The primary outcome was MT.

RESULTS: A total of 1108 patients were included, and MT was performed in 92 (8.3%) patients. Receiver operating characteristic analyses were performed to evaluate the accuracy of ISS, RTS, SI, and MEWS for predicting MT. The area under curves (AUCs) of ISS, SI, RTS, and MEWS for predicting MT were 0.725 (95% confidence interval [CI], 0.698–0.751), 0.676 (95% CI, 0.648–0.704), 0.769 (95% CI, 0.743–0.793), and 0.808 (95% CI, 0.784–0.831), respectively. The AUC of MEWS was significantly different from the AUCs of ISS and SI but not the AUC of RTS for predicting MT. In a multivariate analysis, Glasgow Coma Scale (odds ratio [OR], 0.856; 95% CI, 0.803–0.911), body temperature (OR, 0.596; 95% CI, 0.386–0.920), and fresh frozen plasma (OR, 2.031; 95% CI, 1.794–2.299) were independently associated with MT. MEWS (OR, 1.425; 95% CI, 1.256–1.618) was independently associated with MT after adjustment for confounders.

CONCLUSION: MEWS may be a useful tool for predicting MT in severe trauma patients with TBI.

Keywords: Massive transfusion; prognosis; scoring; trauma.

INTRODUCTION

Exsanguination, along with central nervous system injury, is the leading cause of death in trauma cases and accounts for approximately 30–40% of all trauma-related deaths.[1] Identifying patients who may experience sudden massive bleeding and providing them intensive care can be important to improve the prognosis of trauma patients. Several studies have shown that early and adequate massive transfusion (MT) is related to improved prognosis in trauma patients.[2–4]

It has been shown that massive bleeding is not rare after traumatic brain injury (TBI) and is related to the prognosis of patients with TBI.[5,6] A previous study has demonstrated the potential benefit of transfusion strategies, including an early transfusion, in patients with TBI.[6] Therefore, it may be important to classify patients, even those with TBI, who need MT early. Injury severity score (ISS) and revised trauma score (RTS), which are often used to determine the severity of trauma, have been shown to be significantly associated with MT in trauma patients.[7,8] High shock index (SI) can be a trigger for initiation of blood transfusion in trauma patients.[9] The modified early warning score (MEWS), which includes several vital signs and the Alert, Verbal, Painful, and Unresponsive scale, is related to trauma severity and in-hospital mortality.[10] However, there have been only few studies on the association between various triage tools and need for MT in severe trauma patients with TBI. Therefore, the aim of

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this study was to analyze and compare the prognostic performances of RTS, ISS, SI, and MEWS in severe trauma patients with TBI.

MATERIALS AND METHODS

Study Design and Population

We performed a retrospective observational study involving severe trauma patients with TBI who were admitted to Chonnam National University Hospital, Gwangju, South Korea, between January 2018 and December 2020. Severe trauma was defined as having an ISS >15.[11] TBI was considered when the Abbreviated Injury Scale (AIS) score was three or higher.[12] The following exclusion criteria were applied: age <18 years; cardiac arrest following trauma before emergency department visit; specific trauma mechanisms, such as drowning or hanging; and missing data. Our hospital's Institutional Review Board approved the study. Informed consent was waived since this was a retrospective study.

Data Collection

The following variables were obtained for each patient: Age; sex; mechanism of trauma; systolic blood pressure (SBP, mmHg), respiratory rate, pulse rate, and body temperature (BT, °C) on admission; initial Glasgow Coma Scale (GCS) score; transfusion amount of packed red blood cells (PRC), fresh frozen plasma (FFP), and platelet concentrates (PC) during the first 24 h after admission; and in-hospital mortality. The RTS and MEWS were calculated based on the vital signs and GCS.[13] SI was defined as pulse rate divided by SBP.[8] The AIS score and ISS were measured on arrival. MT was defined as transfusion of >10 units of PRCs within the first 24 h of admission or more than 4 units in 1 h.[14] The primary outcome was MT.

Statistical Analysis

Continuous variables that did not satisfy the normality test are presented as median values with interquartile ranges. Categorical variables are presented as frequencies and percentages. Differences between the two groups were tested using a Mann–Whitney U-test for continuous variables. A Fisher's exact test or Chi-square test was used for comparison of categorical variables, as appropriate. Receiver operating characteristics (ROC) analysis was performed to examine the prognostic performance of ISS, RTS, SI, and MEWS for MT. The comparison of dependent ROC curves was performed using the DeLong et al.[15] method. We conducted a multivariate analysis using logistic regression of relevant covariates for predicting MT. Variables with $p<0.20$ in univariate comparisons were included in the multivariate regression model. We used a backward stepwise approach, sequentially eliminating variables with a threshold of $p>0.10$ to build a final adjusted regression model. We put each of the prognostic tools (MEWS, RTS, ISS, and SI) into the final model and performed the analysis separately. We have presented logistic regression analysis results as odds ratio (OR) and 95% confidence interval (CI). All analyses were performed using PASW/SPSS™ software, version 18 (IBM Inc., Chicago, IL, USA) and MedCalc version 19.0 (MedCalc Software, bvba, Ostend, Belgium). A two-sided significance level of 0.05 was defined as a statistically significant value.

RESULTS

Patient Selection and Characteristics

In total, 1190 patients with severe trauma were identified during the study period who met the inclusion criteria. Based on the exclusion criteria, 1108 patients were finally included in this study (Fig. 1), including 822 (74.2%) men, with a median age of 64.1 years (53.0–75.0 years). MT was performed in 101 (9.1%) patients.

Comparison of Baseline and Clinical Characteristics between MT and no MT Groups

Table 1 shows baseline and clinical characteristics between the MT and no MT groups. The MT group was younger than

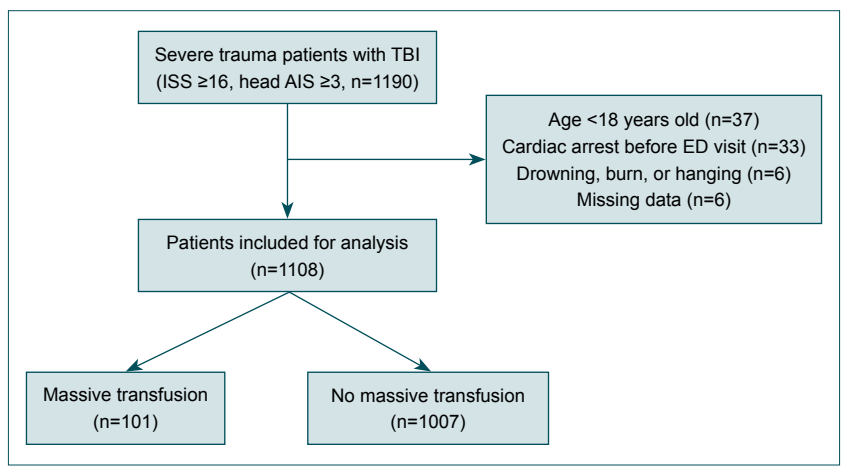

Figure 1. Schematic diagram showing the number of patients with TBI included in the present study.

Table 1. Comparison of baseline characteristics of patients with TBI according to MT

Variables	TBI patients (n=1108)	No MT (n=1007)	MT (n=101)	p
Age, years	64.1 (53.0–75.0)	65.0 (54.0–75.1)	60.0 (45.0–72.6)	0.010
Male, n (%)	822 (74.2)	748 (74.3)	74 (73.3)	0.918
Mechanism of trauma, n (%)				1.000
Blunt	1103 (99.5)	1002 (99.5)	101 (100.0)	
Penetrating	5 (0.5)	5 (0.5)	0 (0.0)	
Injury Severity Score	22 (16–25)	22 (16–25)	25 (22–34)	<0.001
Revised Trauma Score	5.97 (5.03–7.84)	5.97 (5.64–7.84)	4.09 (2.63–5.64)	<0.001
Glasgow Coma Scale score	14 (7–15)	14 (8–15)	5 (3–12)	<0.001
Systolic BP, mmHg	130 (110–140)	130 (110–150)	100 (80–130)	<0.001
Respiratory rate, /min	20 (20–20)	20 (20–20)	20 (20–24)	0.018
Pulse rate, /min	84 (74–96)	84 (74–94)	88 (72–108)	0.042
Body temperature, °C	36.4 (36.1–36.7)	36.4 (36.1–36.8)	36.2 (36.0–36.4)	<0.001
Shock index	0.65 (0.54–0.82)	0.65 (0.54–0.80)	0.88 (0.59–1.36)	<0.001
MEWS	2 (1–4)	2 (1–4)	5 (4–7)	<0.001
PRC, unit	0 (0–2)	0 (0–1)	7 (5–11)	<0.001
FFP, unit	0 (0–1)	0 (0–0)	5 (2–9)	<0.001
PC, unit	0 (0–0)	0 (0–0)	0 (0–10)	<0.001
In-hospital mortality, n (%)	183 (16.5)	128 (12.7)	55 (54.5)	<0.001

TBI: Traumatic brain injury; MT: Massive transfusion; BP: Blood pressure; MEWS: Modified early warning score; PRC: Packed red blood cell; FFP: Fresh frozen plasma; PC: Platelet concentrates.

Table 2. Multivariate logistic regression analysis for predicting MT in patients with TBI

	Adjusted OR (95% CI)	p
Age, years	0.986 (0.969–1.002)	0.094
Glasgow Coma Scale score	0.856 (0.803–0.911)	<0.001
Systolic blood pressure, mmHg	0.998 (0.991–1.006)	0.689
Respiratory rate, /min	1.044 (0.946–1.152)	0.392
Pulse rate, /min	1.007 (0.993–1.020)	0.328
Body temperature, °C	0.596 (0.386–0.920)	0.020
FFP, unit	2.031 (1.794–2.299)	<0.001
PC, unit	0.994 (0.964–1.026)	0.721

MT: Massive transfusion; TBI: Traumatic brain injury; OR: Odds ratio; CI: Confidence interval; FFP: Fresh frozen plasma; PC: Platelet concentrates.

Table 3. Multivariate logistic regression analyses of MEWS, RTS, ISS, and SI for predicting MT in patients with TBI

	Adjusted OR (95% CI)	p
MEWS	1.425 (1.256–1.618)[a]	<0.001
RTS	0.599 (0.506–0.708)[b]	<0.001
ISS	1.050 (1.005–1.097)[c]	0.028
SI	1.391 (0.754–2.568)[c]	0.291

Each prognostic tool was individually entered into the final model and analyzed separately. The analysis for each prognostic tool was not adjusted for other tools. MEWS: Modified early warning score; RTS: Revised trauma score; ISS: Injury severity score; SI: Shock index; MT: Massive transfusion; TBI: Traumatic brain injury; OR: Odds ratio; CI: Confidence interval; FFP: Fresh frozen plasma; GCS: Glasgow Coma Scale. [a]Adjusted for age and FFP; [b]Adjusted for age, body temperature, and FFP; [c]Adjusted for age, GCS, body temperature, and FFP.

the no-MT group, and they had higher ISS and SI values and lower RTS, GCS, SBP, and BT values than those of the no-MT group. The MEWS (5 [4–7] vs. 2 [1–4]; p<0.001) in the MT group was significantly higher than that in the no MT group. Amount of PRC, FFP, and PC transfusion during the first 24 h after admission were significantly higher in the MT group than in the no-MT group. In-hospital mortality (54.5% vs. 12.7%; p<0.001) in the MT group was higher than that in the no MT group.

Prognostic Performance of ISS, RTS, SI, and MEWS for MT

The area under curves (AUCs) of ISS, SI, RTS, and MEWS for predicting MT were 0.725 (95% CI, 0.698–0.751), 0.676 (95% CI, 0.648–0.704), 0.769 (95% CI, 0.743–0.793), and 0.808 (95% CI, 0.784–0.831), respectively. The AUC of MEWS was significantly different from those of ISS and SI but not the AUC of RTS for predicting MT (Fig. 2).

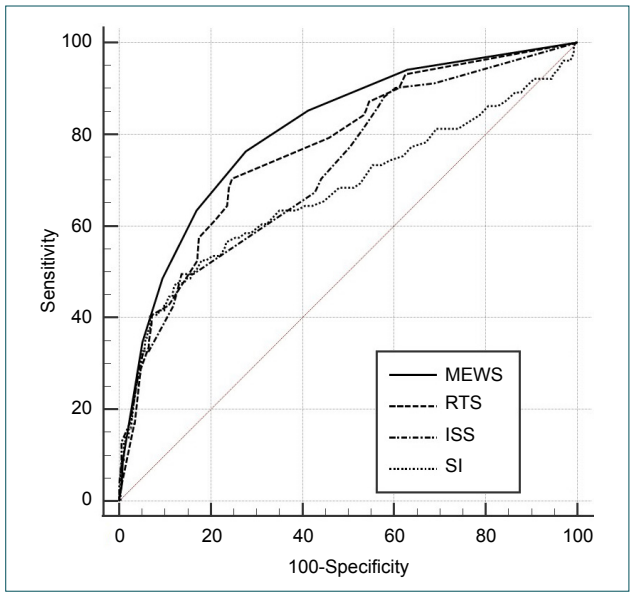

Figure 2. Receiver operating characteristic analyses of ISS, SI, RTS, and MEWS. The AUCs of ISS, SI, RTS, and MEWS for predicting MT were 0.725 (95% CI, 0.698–0.751), 0.676 (95% CI, 0.648–0.704), 0.769 (95% CI, 0.743–0.793), and 0.808 (95% CI, 0.784–0.831), respectively. The AUC of MEWS was significantly different from the AUCs of ISS and SI but not from that of RTS for predicting MT. ISS: Injury severity score; SI: Shock index; RTS: Revised trauma score; MEWS: Modified early warning score; AUC: Area under the curve; CI: Confidence interval.

Multivariate Analysis using Logistic Regression for Predicting MT

Table 2 shows the results of the multivariate analysis for predicting MT. After adjustment for confounders, GCS score (OR, 0.856; 95% CI, 0.803–0.911), BT (OR, 0.596; 95% CI, 0.386–0.920), and FFP (OR, 2.031; 95% CI, 1.794–2.299) were independently associated with MT.

Among the prognostic tools, MEWS (OR, 1.425; 95% CI, 1.256–1.618), RTS (OR, 0.599; 95% CI, 0.506–0.708), and ISS (OR, 1.050; 95% CI, 1.005–1.097) were independently associated with MT (Table 3).

DISCUSSION

In the present study, MEWS showed a good performance for predicting MT in severe trauma patients with TBI. MEWS was independently associated with MT in the multivariate analysis. GCS and BT values seemed to have a significant role in discrimination of MEWS for predicting MT than ISS and SI, but not RTS.

A study by Jiang et al.[10] demonstrated that MEWS of non-survivors was higher than that of survivors. Furthermore, MEWS of patients with severe trauma was higher than that of patients with minor trauma.[10] In another study, higher MEWS was related with injury severity, mortality, and intensive care unit (ICU) admission.[16] In patients with TBI, MEWS was related to early mortality, advanced airway management, hypotension on admission, and ICU admission.[17,18] Given that MT reflects the patient's injury severity, such as triage score or risk of mortality, MEWS might be associated with MT. Moreover, in the multivariate analysis of the present study, GCS and BT, which are components of MEWS, were associated with MT. Even in diseases related to bleeding, other than trauma, several studies have demonstrated that MEWS is related with MT.[19]

Boutin et al.[16] showed that GCS score of the group requiring blood transfusion was lower than that of the non-transfusion group. The low GCS score in patients with TBI may reflect more severe brain injury. Patients with lower GCS score may have more severe brain injury in cases of TBI. The previous studies demonstrated that coagulopathy following TBI is associated with the severity of injury.[20,21] It is postulated that TBI can activate the extrinsic pathway, which, in turn, leads to consumptive coagulopathy and hyperfibrinolysis.[20,21] Thereby, the more severe the TBI, the more hyperfibrinolysis proceeds, which can worsen the coagulopathy, and eventually the amount of transfusion required will increase, which is consistent with the findings of the present study.

In the present study, low BT was associated with MT in severe trauma patients with TBI. Hypothermia disturbs coagulation through platelet dysfunction and impaired enzymatic functions.[22] In trauma patients, hypovolemia resulting from bleeding makes them vulnerable to hypothermia, which further accelerates coagulation disorders.[22] The previous studies have showed that hypothermia on admission is related with severity and in-hospital mortality in severe TBI cases.[23,24] Therefore, given that hypothermia is known to cause coagulation disorders, more blood transfusion may be required in patients with TBI with low BT than in patients with high temperature.

This study had several limitations. First, it was a retrospective study that was performed at a single center. Therefore, its findings are not immediately generalizable to the overall population. Further multi-center studies with larger sample sizes and prospective designs are needed to substantiate our findings. Second, we did not analyze the effects of essential procedures (such as interventions, operations, and transfusions) on MT. Further, research is needed to address these effects. Finally, the present study did not compare with other triages for need for MT, such as activities-specific balance confidence scale and trauma-associated severe hemorrhage scores. As there was insufficient data on FAST results in ED and pelvic radiography data were missing, these could not be included in the analysis. Future studies may be needed to compare MEWS to these scores.

Conclusion

In the present study, MEWS showed a good performance for

predicting MT in severe trauma patients with TBI. MEWS was independently associated with MT in the multivariate analysis. Therefore, it may be a useful tool for predicting MT in cases of severe trauma with TBI.

Ethics Committee Approval: This study approved by the Chonnam National University Hospital University Hospital Institutional Review Board (Date: 05.03.2021, Decision No: CNUH-2021-064).

Peer-review: Internally peer-reviewed.

Authorship Contributions: Concept: D.H.L.; Design: D.H.L., D.K.K.; Supervision: B.K.L.; Resource: D.K.K.; Materials: D.K.K.; Data: H.R.C., D.K.K.; Analysis: H.R.C., D.H.L., B.K.L.; Literature search: H.R.C.; Writing: H.R.C., D.H.L.; Critical revision: D.H.L., B.K.L.

Conflict of Interest: None declared.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Travmatik beyin hasarı olan hastalarda masif transfüzyon için modifiye erken uyarı puanının tahmin değeri

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AMAÇ: Travmatik beyin hasarı (TBH) olan hastalarda ciddi kan kaybı ölümcül olabilir. Şiddetli travma hastalarında masif transfüzyonu (MT) öngörmek için, yaralanma şiddeti skoru (ISS), revize travma skoru (RTS), şok indeksi (SI) ve modifiye erken uyarı skoru (MEWS)'nun prognostik performanslarını analiz etmeyi ve karşılaştırmayı amaçladık.

GEREÇ VE YÖNTEM: Bu geriye dönük gözlemsel çalışmaya Ocak 2018–Aralık 2020 tarihleri arasında acil servisimize başvuran TBH'li ağır travma hastaları dahil edildi. Kısa travma ölçeği 3 veya daha yüksek olduğunda TBH kabul edildi. Birincil sonuç MT idi.

BULGULAR: Toplam 1.108 hasta dahil edildi ve 92 (%8.3) hastaya MT uygulandı. MT'yi öngörmek için ISS, RTS, SI ve MEWS'nin doğruluğunu değerlendirmek üzere alıcı işletim karakteristik analizleri yapıldı. ISS, SI, RTS ve MEWS'nin MT'yi tahmin etmek üzere eğri altında kalan alanları (AUC'ler) sırasıyla 0.725 (%95 güven aralığı [CI], 0.698–0.751), 0.676 (%95 CI, 0.648–0.704), 0.769 (%95 CI, 0.743–0.793) ve 0.808 (%95 CI, 0.784-0.831) idi. MEWS'nin AUC'si, ISS ve SI'nin AUC'lerinden önemli ölçüde farklıydı, ancak MT'yi tahmin etmek için RTS'nin AUC'sinden farklı değildi. Çok değişkenli bir analizde, Glasgow Koma Skalası (Odds oranı [OR], 0.856; %95 CI, 0.803–0.911), vücut ısısı (OR, 0.596; %95 CI, 0.386–0.920) ve taze donmuş plazma (OR, 2.031; %95 CI, 1.794–2.299) bağımsız olarak MT ile ilişkiliydi. MEWS (OR, 1.425; %95 CI, 1.256–1.618), araya giren faktörler için ayarlama yapıldıktan sonra bağımsız olarak MT ile ilişkili bulundu.

TARTIŞMA: MEWS, TBH'li ciddi travma hastalarında MT'yi öngörmek için yararlı bir araç olabilir.

Anahtar sözcükler: Masif transfüzyon; prognoz; puanlama; travma.

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