Review Article

J Trauma Inj 2024;37(2):97-105
https://doi.org/10.20408/jti.2024.0015

Journal of Trauma and Injury JTI

pISSN 2799-4317 • eISSN 2287-1683

Predictors of massive transfusion protocols activation in patients with trauma in Korea: a systematic review

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Purpose: Massive transfusion protocols (MTPs) implementation improves clinical outcomes of the patient's resuscitation with hemorrhagic trauma. Various predictive scoring system have been used and studied worldwide to improve clinical decision. However, such research has not yet been studied in Korea. This systematic review aimed to assess the predictors of MTPs activation in patients with trauma in Korea.

Methods: The PubMed, Embase, Cochrane Library, Research Information Sharing Service databases, KoreaMed, and KMbase were searched from November 2022. All studies conducted in Korea that utilized predictors of MTPs activation in adult patients with trauma were included.

Results: Ten articles were eligible for analysis, and the predictors were assessed. Clinical assessments such as systolic and diastolic blood pressure, shock index (SI), prehospital modified SI, modified early warning system (MEWS) and reverse SI multiplied by the Glasgow Coma Scale (rSIG) were used. Laboratory values such as lactate level, fibrinogen degradation product/fibrinogen ratio, and rotational thromboelastometry (ROTEM) were used. Imaging examinations such as pelvic bleeding score were used as predictors of MTPs activation.

Conclusions: Our systematic review identified predictors of MTPs activation in patients with trauma in Korea; predictions were performed using tools that requires clinical assessments, laboratory values or imaging examinations only. Among them, ROTEM, rSIG, MEWS, SI, and lactate level showed good effects for predictions of MTPs activation. The application of predictors for MTP's activation should be individualized based on hospital resource and skill set, also should be performed as a clinical decision supporting tools.

Keywords: Wounds and injuries; Blood transfusion; Korea; Predictors; Systematic review

Received: March 5, 2024
Revised: April 16, 2024
Accepted: April 24, 2024

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INTRODUCTION

Background

Trauma is a major cause of death in Korea, and hemorrhage is a major cause of early death in trauma. Various studies have investigated blood transfusion strategies in patients with trauma [1,2]. In particular, because of the importance of developing a strategy to control hemorrhagic shock, many guidelines and studies have rec-

ommended that each institution should implement massive transfusion protocols (MTPs) [3,4]. The implementation of MTP reduces mortality and overall blood product usage in patients with trauma. Although predicting the need for MT is difficult, various predictive scores have been developed and validated, such as the Assessment of Blood Consumption (ABC) score, Trauma-Associated Severe Hemorrhage (TASH) score, and shock index (SI) [5–7]. However, these predictive scores are not often used in Korea. In Korea, regional trauma centers were designated in 2012 to organize a national trauma system for the first time, and it can be said that the government is currently designing and operating 17 regional trauma centers. Our institution is one of these trauma centers, and we have implemented and developed our own MTP [8]. Except for a few trauma centers, emergency medical institutions that apply MTPs are scarce. In an observational study conducted in Korea, only 14% of patients received MT due to trauma [9]. Recently, an increasing number of institutions have been started MTPs in patients with trauma, and related studies are investigated; However, these studies are lacking in Korea. Therefore, it is necessary to analyze the current influence of MTPs in patients with trauma. In particular, as MTPs activation at the appropriate time improves outcomes in patients with trauma, it is essential to investigate the related studies in our region.

Objectives

The aim of this systematic review was to identify and assess the predictors of MTPs activation in patients with trauma in Korea.

METHODS

This systematic review was conducted according to the protocol registered in PROSPERO (No. CRD42022377287).

Search strategy

The PubMed, Embase, Cochrane Library, Research Information Sharing Service databases, KoreaMed, and KMbase were searched from November 2022. Key terms such as "trauma," "Korea," "transfusion" and "massive transfusion" were sorted. The full search strategy is outlined in Material S1.

All studies conducted in Korea that utilized predictors of MTPs activation in adult patients with trauma were included. MT was defined as the presence of 10 or more packed red blood cells in the first 24 hours. Included studies were to require to have complete information: total number of patients, information on predictors, and methodology for developing the prediction score. The following studies were excluded: pediatric studies, small case studies (< 20 patients), gray literature, and articles mentioning MT for nontraumatic injuries, and articles that only predicted transfusion but not MT.

Screening process and data extraction

All articles identified in the search were screened independently by two investigators. Full texts were reviewed and assessed for eligibility based on the defined inclusion and exclusion criteria. Disagreements were resolved independently by a third reviewer at all stages. Data were extracted through discussions with the third reviewer. The details collected from the data included year of publication, number of patients, study design (prospective/retrospective case-control or cohort study, randomized controlled trial), and the inclusion and exclusion criteria. The outcomes of this systematic review were the predictors of MTPs activation in patients with trauma in Korea. The parameters included for predictions were odds ratios with 95% confidence intervals, sensitivities, specificities, and areas under the receiver operating characteristic curve (AUROC).

Quality assessment and analysis

The quality of the observational studies was assessed using the Newcastle-Ottawa scale. A detailed assessment of the risk of bias is available in Table 1 [10–19]. The data analysis used was qualitative, allowing for an overall interpretation of the data based on a qualitative summary. It would not be appropriate to summarize the overall predictors because of the heterogeneity in patient numbers and predictors. The results were reported in accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines (Table S1).

RESULTS

Included studies

The literature search yielded 2,132 articles. After removing duplicated, 1,934 articles underwent title and abstract screening for eligibility, of which 24 articles underwent full-text assessment for eligibility. Fifteen more articles were excluded, one article was added through database of Korea, and 10 articles were finally eligible for inclusion. The agreement for the selection of articles after a full-text review by the two independent investigators (DS and JP) was reached before resolution by the third reviewer (KJ). Disagreement in selection was due to articles being excluded because they involved pediatric patients and not being chosen for MT but for transfusion. The PRISMA flowchart for this study is shown in Fig. 1.

https://doi.org/10.20408/jti.2024.0015

Table 1. Newcastle-Ottawa scale

Study	Selection				Comparability		Outcome			Total score
	Is the case definition adequate	Representativeness of the cases	Selection of controls	Definition of controls	Age	Other risk factor	Assessment of exposure	Same method of ascertainment for cases and controls	Nonresponse rate	
Park et al. [10] (2021)	☆	☆	-	☆	☆	☆	☆	☆	-	7/9
Lee et al. [11] (2021)	☆	☆	-	☆	☆	☆	☆	☆	-	7/9
Wang et al. [12] (2020)	☆	☆	-	☆	☆	-	☆	☆	-	6/9
Lee et al. [13] (2021)	☆	☆	-	☆	☆	-	☆	☆	-	6/9
Chae et al. [14] (2022)	☆	☆	-	☆	☆	☆	☆	☆	-	7/9
Kyoung et al. [15] (2016)	☆	☆	-	☆	☆	☆	☆	☆	-	7/9
Lee et al. [16] (2018)	☆	☆	-	☆	☆	☆	☆	☆	-	7/9
Baik et al. [17] (2022)	☆	☆	-	☆	☆	☆	☆	☆	-	7/9
Park et al. [18] (2019)	☆	☆	-	☆	☆	☆	☆	☆	-	7/9
Lee et al. [19] (2012)	☆	☆	-	☆	☆	-	☆	☆	-	6/9

Study description

The characteristics and predictive abilities of the included articles are shown in Tables 2 and 3 [10–19], respectively. Ten retrospective observational studies were identified by the search. Clinical assessments such as prehospital systolic blood pressure (SBP), shock index (SI), prehospital SI, modified SI (MSI), modified early warning system (MEWS), diastolic blood pressure (DBP), and reverse SI multiplied by the Glasgow Coma Scale (rSIG) were most frequently used, reported in five articles. Laboratory values, such as lactate level, fibrinogen degradation product (FDP) to fibrinogen ratio, and rotational thromboelastometry (ROTEM), were reported in four articles. Imaging examinations, such as evaluation of pelvic bleeding scores, were reported in one article.

Park et al. [10] validated the utility of prehospital SBP and SI in predicting the need for MT in a retrospective observational study. In this study, the patients were stratified by age and use of antihypertensive drugs. MT was predicted based on a prehospital SBP of 110 mmHg in patients older than 65 years who were using antihypertensive drugs (P = 0.024). In addition, MT was predicted based on an SI of 1.0 in patients older than 65 years who were not using antihypertensive drugs (P = 0.002) and those younger than 65 years who were not using antihypertensive drugs (P = 0.044). Lee et al. [11] evaluated all patients retrospectively utilizing DBP for predicting MT. The study reported that an initially decreased DBP was an independent predictor for MT (P < 0.001); the AUROC value for the prediction of MT was 0.777. Wang et al. [12] conducted a retrospective study. In this study, prehospital SI and prehospital MSI (heart rate [HR] / mean arterial blood pressure at the prehospital stage) were used as predictors of MT, with AUROC values of 0.773 and 0.765, respec-

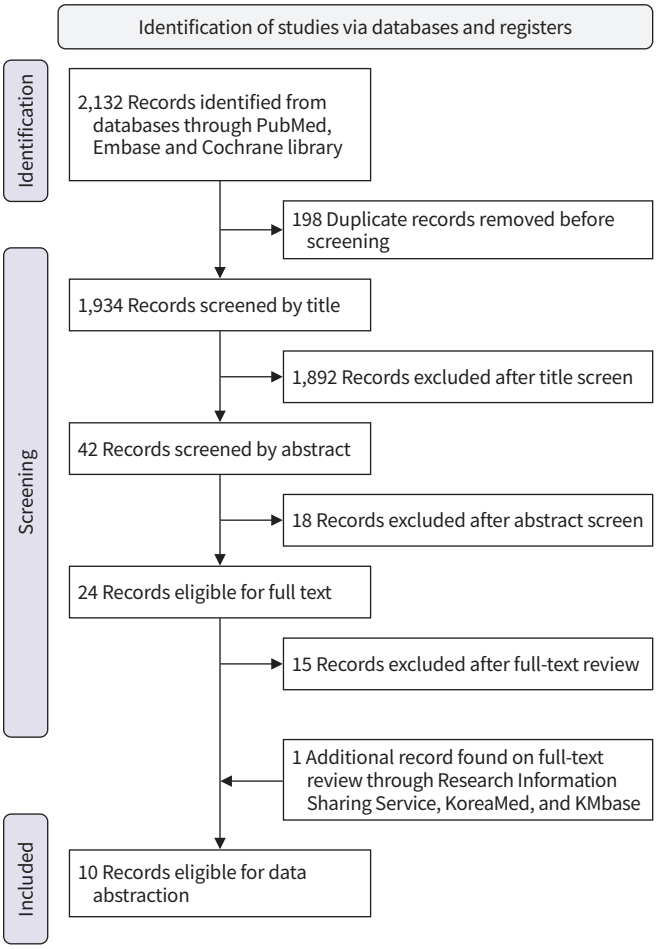

Fig. 1. PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) flowchart of literature search.

Table 2. Characteristics of studies in the systematic review

Study	Study setting	Date of recruitment	No. of participants	Inclusion criteria	Definition of MT	Intervention
Validated predictors requiring clinical assessment						
Park et al. [10] (2021)	Retrospective, observational study Single-center trauma center	Jan 2017– Dec 2018	4, 681 (137 MTs)	Age ≥15 yr Direct from injury scene Measurement SBP and HR	pRBC ≥10 in the first 24 hr pRBC ≥4 in the first 4 hr	Prehospital SBP <110 mmHg SI >1.0 Group: age >65 yr using antihypertensive drugs, age <65 yr using antihypertensive drugs, age >65 yr not using antihypertensive drugs, age <65 yr not using antihypertensive drugs
Lee et al. [11] (2021)	Retrospective, observational study Single-center ED	Jan 2016–Dec 2017	827 (64 MTs)	Age ≥18 yr ISS ≥16	pRBC ≥10 in the first 24 hr	DBP DBP, 41–60 mmHg DBP, 21–40 mmHg DBP, ≤20 mmHg
Wang et al. [12] (2020)	Retrospective, observational study Single-center trauma center	Jan 2016–Dec 2017	1,007 (78 MTs)	Age ≥15 yr Direct from injury scene Measurement SBP, DBP, and HR	pRBC ≥10 in the first 24 hr	Prehospital SI Prehospital MSI
Lee et al. [13] (2021)	Retrospective, observational study Single-center trauma center	Jan 2016–Dec 2018	1,627 (117 MTs)	Age ≥16 yr Direct from injury scene Measurement SBP, HR, RR, and GCS	pRBC ≥10 in the first 24 hr	SI SIA rSIG
Chae et al. [14] (2022)	Retrospective, observational study Single-center ED	Jan 2018–Dec 2020	1,108 (101 MTs)	Age ≥18 yr ISS ≥16 Head AIS ≥3	pRBC ≥10 in the first 24 hr pRBC ≥4 in the first 4 hr	MEWS
Validated predictors requiring laboratory values						
Kyoung et al. [15] (2016)	Retrospective, observational study Single-center ED	Jan 2008–Jun 2010	71 (15 early MTs)	Age ≥18 yr Direct from injury scene	Early MT (pRBC ≥10 in the first 6 hr)	Lactate level within a few minutes in ED
Lee et al. [16] (2018)	Retrospective, observational study Single-center ED	Jan 2012–Dec 2015	1,266 (100 MTs)	Age ≥18 yr ISS ≥16 Fibrinogen, FDP, D-dimer measurement within 1 hr	pRBC ≥10 in the first 24 hr	FDP/fibrinogen ratio
Baik et al. [17] (2022)	Retrospective, observational study Singe-center trauma center	2016–2020	969 (196 MTs)	Age ≥15 yr Underwent ROTEM	pRBC ≥10 in the first 24 hr	ROTEM at ED: EXTEM clotting time, EXTEM maximum clot firmness, EXTEM maximum lysis
Park et al. [18] (2019)	Retrospective, observational study Single-center ED	Jan 2016–Dec 2017	553 (62 MTs)	Age ≥18 yr ISS ≥16 Measurement lactate level	pRBC ≥10 in the first 24 hr	Lactate level in ED

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https://doi.org/10.20408/jti.2024.0015

Table 2. (Continued)

Study	Study setting	Date of recruitment	No. of participants	Inclusion criteria	Definition of MT	Intervention
Validated predictors requiring imaging examination						
Lee et al. [19] (2012)	Retrospective, observational study Single-center ED	Jan 2007–Mar 2012	97 (15 MTs)	Age ≥15 yr Not arterial bleeding of solid organ Pelvic bone fracture	pRBC ≥10 in the first 24 hr	Pelvic bleeding score (sacrum + pubis + ilium; 0 for no fracture, 1 for unilateral fractures, and 2 for bilateral fractures)

MT, massive transfusion; SBP, systolic blood pressure; HR, heart rate; pRBC, packed red blood cell; SI, shock index; ED, emergency department; ISS, Injury Severity Score; DBP, diastolic blood pressure; MSI, modified shock index; RR, respiratory rate; GCS, Glasgow Coma Scale; SIA, shock index multipled by age; rSIG, reverse shock index multipled by Glasgow Coma Scale; AIS, Abbreviated Injury Scale; MEWS, modified early warning system; FDP, fibrinogen degradation production; ROTEM, rotational thromboelastometry; EXTEM, extrinsically activated test.

tively. Lee et al. [13] validated the utility of the rSIG (SBP / HR × Glasgow Coma Scale) for predicting the need for MT in a retrospective observational study. This study reported that the rSIG was an independent predictor of MT, and the AUROC value for the prediction of MT was 0.842. Chae et al. [14] retrospectively evaluated patients with traumatic brain injury (TBI), utilizing MEWS to predict MT ($P < 0.001$); the AUROC value was 0.808. Kyoung et al. [15] conducted a retrospective study in which lactate levels were used as a predictor of MT ($P = 0.039$); the AUROC value was 0.790. Lee et al. [16] retrospectively evaluated all patients using the FDP/fibrinogen ratio to predict MT ($P = 0.029$). Baik et al. [17] validated the utility of ROTEM for predicting the need for MT in a retrospective observational study, and the AUROC value of ROTEM was 0.860. Park et al. [18] retrospectively evaluated all patients, TBI patients (Abbreviated Injury Scale ≥3), and non-TBI patients using lactate levels to predict MT. This study reported that lactate levels were independent predictor of MT in all patients and non-TBI patients ($P < 0.001$), and the AUROC values for the prediction of MT were 0.779 and 0.842, respectively. Lee et al. [19] retrospectively evaluated patients with pelvic bone fractures utilizing pelvic bleeding score for predicting the need for MT; the AUROC value was 0.718.

Through our search, we identified studies conducted in Korea on predictors of MT and which used tools that requires clinical assessments, laboratory values, or imaging examinations only. ROTEM had the highest AUROC value of 0.86, followed by rSIG, MEWS, SI, and lactate level.

DISCUSSION

In our review, we identified various predictors in studies that used tools that requires clinical assessments only or laboratory values only or imaging examinations only in Korea. Although there are frequently used predictors such as SI, SBP, DBP, and lactate level, studies on infrequently used predictors such as rSIG, MEWS, FDP/fibrinogen ratio, ROTEM, and pelvic bleeding score have been conducted. The rSIG, MEWS, and SI had a better performance in clinical assessment whereas ROTEM and lactate level had distinguished result in laboratory values. In addition, our review found the validation of scores was mostly performed in single-center studies.

MTP implementation improves clinical outcomes in patients with trauma. First, the application of MTP in a trauma center is independently associated with lower mortality rates [20,21]. Second, the implementation of MTP reduces the occurrence of severe disseminated intravascular coagulation [22]. Third, MTP reduces the use of blood components [23]. Therefore, it is important to activate the MTP at an appropriate time.

One systematic review revealed that validated and unvalidated scores were identified by utilizing elements of clinical assessment, laboratory values, and ultrasound assessment [24]. This review included all studies that utilized scores or predictors of MTPs in adult patients with trauma. The study presented an approach for choosing a prediction score for MTPs activation based on experience level, resources, and skill set. In addition, the modified Traumatic Bleeding Severity Score (TBSS), TASH score, ABC score, and SI were introduced.

The modified TBSS was defined according to age, SBP on arrival, focused assessment with sonography for trauma (FAST), pelvic fracture, and lactate level. The modified TBSS had a high predictive value in determining the need for MT, with an AUROC value of 0.915 [25]. The TASH score has been validated in several studies, supporting its use in different patients, and it was defined according to sex, SBP, HR, FAST, pelvic fracture, femur fracture, hemoglobin, and base excess. The TASH score is con-

Table 3. Performance of predictors to activate massive transfusion protocol

Study	Outcome	OR (95% CI)	P-value	Sensitivity	Specificity	AUROC
Validated predictors requiring clinical assessment						
Park et al. [10] (2021)	Prehospital SBP <110 mmHg: age >65 yr using antihypertensive drugs	28.10 (1.75–52.00)	0.024*	NA	NA	NA
	SI >1.0: age >65 yr not using antihypertensive drugs	10.30 (2.27–46.30)	0.002*	NA	NA	NA
	SI >1.0: age <65 yr not using antihypertensive drugs	3.87 (1.36–11.00)	0.044*	NA	NA	NA
Lee et al. [11] (2021)	DBP	0.96 (0.95–0.97)	<0.001*	NA	NA	0.777
	DBP, 41–60 mmHg	2.74 (1.30–5.78)	0.008*	NA	NA	NA
	DBP, 21–40 mmHg	6.98 (3.19–15.28)	<0.001*	NA	NA	NA
	DBP, ≤20 mmHg	19.47 (7.71–49.20)	<0.001*	NA	NA	NA
Wang et al. [12] (2020)	Prehosptial SI	NA	NA	0.65	0.77	0.773
	Prehospital MSI	NA	NA	0.60	0.82	0.765
Lee et al. [13] (2021)	SI	NA	NA	0.67	0.84	0.796
	SIA	NA	NA	0.70	0.78	0.792
	rSIG	NA	NA	0.79	0.77	0.842
Chae et al. [14] (2022)	RTS	0.60 (0.51–0.71)	<0.001*	NA	NA	0.769
	ISS	1.05 (1.01–1.10)	0.028*	NA	NA	0.725
	SI	1.39 (0.75–2.57)	0.291	NA	NA	0.676
	MEWS	1.43 (1.26–1.62)	<0.001*	NA	NA	0.808
Validated predictors requiring laboratory values						
Kyoung et al. [15] (2016)	SBP	11.71 (1.83–74.77)	0.009*	NA	NA	0.717
	ISS	23.39 (1.87–293.23)	0.015*	NA	NA	0.785
	Base deficit	4.19 (0.88–19.91)	0.072	NA	NA	0.755
	Lactate level	6.99 (1.10–44.33)	0.039*	NA	NA	0.790
Lee et al. [16] (2018)	FDP/fibrinogen ratio	1.01 (1.00–1.01)	0.029*	NA	NA	NA
Baik et al. [17] (2022)	ROTEM (EXTEM maximum clot firmness)	NA	0.023*	NA	NA	0.860
Park et al. [18] (2019)	Lactate level					
	Total patients	1.18 (1.07–1.30)	<0.001*	0.76	0.68	0.779
	TBI patients (AIS ≥3)	1.00 (0.84–1.19)	0.985	0.60	0.75	0.690
	Non-TBI patients	1.47 (1.26–1.71)	<0.001*	0.81	0.77	0.842
Validated predictors requiring imaging examination						
Lee et al. [19] (2012)	ISS	NA	NA	NA	NA	0.731
	Pelvic bleeding score (sacrum + pubis + ilum; 0 for no fracture, 1 for unilateral fractures, and 2 for bilateral fractures)	NA	NA	0.71	0.70	0.718

OR, odds ratio; CI, confidence interval; AUROC, area under the receiver operating characteristic curve; SBP, systolic blood pressure; NA, not available; SI, shock index; DBP, diastolic blood pressure; MSI, modified shock index; SIA, shock index multipled by age; rSIG, reverse shock index multipled by Glasgow Coma Scale; RTS, Revised Trauma Score; ISS, Injury Severity Score; MEWS, modified early warning system; FDP, fibrinogen degradation production; ROTEM, rotational thromboelastometry; EXTEM, extrinsically activated test; TBI, traumatic brain injury; AIS, Abbreviated Injury Scale.
*P<0.05.

sidered reliable for predicting the need for MT [26]. In another study, the predictive value of the TASH score for MTPs implementation was sophisticated, with an AUROC value of 0.889 [27]. The ABC score was defined based on SBP, HR, penetration mechanism, and FAST. These four components were evaluated in a bedside assessment of patients with acute injuries early in the assessment phase. The ABC score had a high accuracy, with an AUROC value of 0.859 [5]. In another multicenter study, the AUROC values for each cohort were 0.903, 0.833, and 0.883 [28]. Therefore, our institution adopted the ABC score as a predictor of MT. The SI is easily implemented using HR and SBP, and increase in SI has been associated with a higher predictive value for MT [29]. In another study, the predictive value of SI for MTPs activation was high, with an AUROC value of 0.859 [30].

In Korea, the application of MTPs in patients with trauma has only begun recently. Some emergency medical institutions have

https://doi.org/10.20408/jti.2024.0015

not yet established MTPs nor do they have clear indicators of MTPs activation in each center. Therefore, studies related to MT, especially those on its predictors in Korea, are hard to find. According to our study, there are few studies on validated scores that incorporate clinical assessment, laboratory values, and ultrasound assessment, such as the TBSS, TASH, and ABC scores, in Korea. A prediction score derived from using various elements has a greater ability to discriminate between patients who require MTP activation and those who do not. However, most studies conducted in Korea used tools that requires clinical assessments only or laboratory values only or imaging examinations only. Our review identified emerging predictors and new approaches, such as ROTEM, MEWS, rSIG, and pelvic bleeding score in some local studies.

Other systematic reviews have attempted to address the topic regarding global trends; however, this is the first systematic review conducted on the predictors of MTP's implementation in patients with trauma in Korea. According to our study, these predictors cannot replace clinical judgment but may act as clinical decision support tools. This review also suggests that research on predictors incorporating clinical assessment, laboratory values, and ultrasound assessment is needed in the future. Furthermore, this review suggests that the establishment of a cohort of MT in patients with trauma and further research on MT in Korea are necessary.

Limitations

This systematic review has some limitations. First, the heterogeneity of the studies led to a qualitative, not quantitative, summation of the results. Second, all studies were retrospective and observational. Third, each study had different inclusion criteria, such as age, presence of TBI, and presence of pelvic bone fracture.

Conclusions

Our systematic review identified predictors of MTPs activation in patients with trauma in Korea; predictions were performed using tools that requires clinical assessments only, laboratory values only, or imaging examinations only. Among them, ROTEM, rSIG, MEWS, SI, and lactate level showed good effects for predicting the need for MT. The use of predictors for MTPs activation should be individualized based on hospital resource and skill set and should act as clinical decision support tools. In future studies, a comprehensive study on MT in patients with and without trauma in Korea is required. Furthermore, it would be helpful to establish a cohort of MT in Korea.

ARTICLE INFORMATION

Author contributions

Conceptualization: DS, KJ; Data curation: DS, JP, JK, HS; Formal analysis: DS, IH; Funding acquisition: KJ; Methodology: DS, KJ; Visualization: DS; Writing–original draft: DS, KJ; Writing–review & editing: all authors. All authors read and approved the final manuscript.

Conflicts of interest

Junsik Kwon is an Editorial Board member of the *Journal of Trauma and Injury*, but was not involved in the peer reviewer selection, evaluation, or decision process of this article. The authors have no other conflicts of interest to declare.

Funding

This study was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Korean Ministry of Health and Welfare (No. HI22C1806).

Acknowledgments

The authors thank Yujin Kwon (Ajou University Medical Information and Media Center, Suwon, Korea) for her technical assistance for this study.

Data availability

Data analyzed in this study are available from the corresponding author upon reasonable request.

Supplementary materials

Material S1. Search strategy.

Table S1. PRISMA 2020 checklist

Supplementary materials are available from https://doi.org/10.20408/jti.2024.0015.

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