

Original Article

Analysis of risk factors for trauma-induced coagulopathy in elderly major trauma patients

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BACKGROUND: Trauma-induced coagulopathy (TIC) due to serious injuries significantly leads to increased mortality and morbidity among elderly patients. However, the risk factors of TIC are not well elucidated. This study aimed to explore the risk factors of TIC in elderly patients who have major trauma.

METHODS: In this retrospective study, the risk factors for TIC in elderly trauma patients at a single trauma center were investigated between January 2015 and September 2020. The demographic information including gender, age, trauma parts, injury severity, use of blood products, use of vasopressors, need of emergency surgery, duration of mechanical ventilation, length of stay in the intensive care unit (ICU) and hospital, and clinical outcomes were extracted from electric medical records. Multivariate logistic regression analysis was performed to differentiate risk factors, and the performance of the model was evaluated using receiver operating characteristics (ROC) curves.

RESULTS: Among the 371 elderly trauma patients, 248 (66.8%) were male, with the age of 72.5 ± 6.8 years, median injury severity score (ISS) of 24 (IQR: 17–29), and Glasgow coma score (GCS) of 14 (IQR: 7–15). Of these patients, 129 (34.8%) were diagnosed with TIC, whereas 242 (65.2%) were diagnosed with non-TIC. The severity scores such as ISS (25 [20–34] vs. 21 [16–29], $P < 0.001$) and shock index (SI), (0.90 ± 0.66 vs. 0.58 ± 0.18 , $P < 0.001$) was significantly higher in the TIC group than in the non-TIC group. Serum calcium levels (1.97 ± 0.19 mmol/L vs. 2.15 ± 0.16 mmol/L, $P < 0.001$), fibrinogen levels (1.7 ± 0.8 g/L vs. 2.8 ± 0.9 g/L, $P < 0.001$), and base excess (BE, -4.9 ± 4.6 mmol/L vs. -1.2 ± 3.1 mmol/L, $P < 0.001$) were significantly lower in the TIC group than in the non-TIC group. Multivariate logistic regression analysis revealed that ISS > 16 (OR: 3.404, 95%CI: 1.471–7.880; $P = 0.004$), SI > 1 (OR: 5.641, 95%CI: 1.700–18.719; $P = 0.005$), low BE (OR: 0.868, 95%CI: 0.760–0.991; $P = 0.037$), hypocalcemia (OR: 0.060, 95%CI: 0.009–0.392; $P = 0.003$), and hypofibrinogenemia (OR: 0.266, 95%CI: 0.168–0.419; $P < 0.001$) were independent risk factors for TIC in elderly trauma patients. The AUC of the prediction model included all these risk factors was 0.887 (95%CI: 0.851–0.923) with a sensitivity and specificity of 83.6% and 82.6%, respectively.

CONCLUSION: Higher ISS (more than 16), higher SI (more than 1), acidosis, hypocalcemia, and hypofibrinogenemia emerged as independent risk factors for TIC in elderly trauma patients.

KEYWORDS: Trauma; Elderly patients; Trauma-induced coagulopathy; Hypocalcemia

World J Emerg Med 2024;15(6):475–480
DOI: 10.5847/wjem.j.1920-8642.2024.093

INTRODUCTION

Trauma represents a significant global health concern, resulting in 4–6 million fatalities annually.^[1-3] Uncontrolled bleeding remains the primary cause of potentially avoidable death among individuals with severe injuries, with one-third of such patients experiencing coagulopathy upon hospital admission.^[4-6] Throughout the course of severe trauma, trauma-induced coagulopathy (TIC) manifests across a spectrum from reduced blood clotting to excessive clotting, and is influenced by factors such as extensive tissue damage and severe hemorrhagic shock.^[1,7-9] Patients with TIC are at greater risk of multiple organ failure, elevated rates of morbidity and mortality compared with trauma patients without coagulation disorders.^[1,7,10,11] Additionally, advanced age is a significant predictor of worse outcomes following severe trauma.^[12,13] Elderly individuals are more susceptible to coagulation abnormalities due to age-related physiological changes, severe injuries, comorbidities, and less effective therapeutic interventions post-trauma.^[12,14] Consequently, elderly trauma patients, particularly those with TIC, experience poorer outcomes.^[9,13,15,16] While conventional coagulation tests (CCTs) and viscoelastography tests (VETs) are commonly used for TIC assessment, there remains a need for rapid and convenient indicators to facilitate effective resuscitation strategies.^[3,17] Despite extensive research on coagulopathy resulting from severe hemorrhagic shock and tissue injury, there is still no unified definition of TIC. Risk factors such as serum calcium play a crucial role in traumatic coagulation abnormalities;^[18,19] however, little information exists regarding the relationships between these factors and TIC in elderly trauma patients.

Therefore, we conducted a retrospective study at a single center to investigate the risk factors associated with TIC in elderly individuals with major trauma. Our findings aim to increase the accuracy of diagnosis and the timely initiation of treatment for elderly patients with TIC.

METHODS

Study design

A retrospective, observational, single-center study was conducted on elderly trauma patients admitted to the Second Affiliated Hospital of Zhejiang University School of Medicine between January 2015 and September 2020.

The inclusion criteria were as follows: patients older than 65 years, with major trauma requiring intensive care unit (ICU) hospitalization. The exclusion criteria were as follows: (1) use of anticoagulants or anti-platelet

medication before the traumatic incident; (2) coagulation disorders resulting from pre-existing medical conditions; (3) cardiac arrest and death within 3 h of admission; (4) malignant tumor; (5) incomplete medical records; (6) transfusion of blood products prior to admission.

Demographic information, including patient gender, age, trauma parts, injury severity, therapeutic interventions, and clinical outcomes, such as the use of blood products, vasopressors, acute surgeries, duration of mechanical ventilation, length of stay in the ICU and hospital, and in-hospital mortality, were extracted.

Data were retrieved from electronic medical records of our hospital. The Institutional Review Board approved the study and waived the requirement for informed consent from patients ([2020] IRB-976) and their legal representatives (ClinicalTrials.gov, NCT05530161).

Definition of TIC

In this study, TIC was defined as a history of trauma and an international normalized ratio (INR) > 1.2. For additional analysis, the TIC group was categorized into severe TIC (INR > 1.5) and non-severe TIC.^[4, 20-23]

Statistical analysis

Statistical analysis was conducted via SPSS, version 26.0 (IBM, USA). The normality of continuous data was assessed using the Kolmogorov-Smirnov test. Normally distributed continuous data are presented as mean \pm standard deviation, while non-normally distributed data are presented as medians and interquartile ranges. Nominal variables are reported as numbers and proportions (%). Categorical variables were analyzed using the Chi-square test or Fisher's exact test, and continuous variables were analyzed using the Mann-Whitney *U*-test or Student's *t*-test, as appropriate. Multivariate logistic regression analysis was performed to identify risk factors, and receiver operating characteristics (ROC) curves were utilized to assess the predictive ability of the model. A two-sided *P*-value < 0.05 was considered statistically significant for all tests.

RESULTS

General information

A total of 371 elderly trauma patients were included in the study, comprising 248 (66.8%) male individuals, with a mean age of 72.5 ± 6.8 years. The median injury severity score (ISS) was 24, and the median Glasgow coma score (GCS) score was 14. All patients

were admitted to the ICU, with 59.8% requiring mechanical ventilation. Within the cohort, 129 (34.8%) patients were in the TIC group, while 242 (65.2%) were in the non-TIC group. The TIC group was subsequently categorized into severe and non-severe TIC groups based on a cutoff value of INR at 1.5. There were 38 (29.5%) patients in the severe TIC group, and 91 (70.5%) were in the non-severe TIC group (Figure 1).

Characteristics of the elderly trauma patients

In our cohort, the heart rate (HR), ISS, and shock index (SI) in the TIC group were significantly higher than those in the non-TIC group ($P<0.001$). Additionally, the TIC group presented significantly higher serum lactate levels, activated partial thromboplastin time (APTT), and PT than the non-TIC group ($P<0.001$). Conversely, BE, pH, serum calcium, fibrinogen, platelets, hemoglobin, initial systolic blood pressure (SBP), and body temperature were significantly lower in the TIC group ($P<0.001$). Furthermore, the TIC group had a significantly higher ratio of blood product transfusions, vasopressor use, acute surgeries, in-hospital death, and duration of mechanical ventilation (MV) compared to the non-TIC group ($P<0.001$) (Table 1).

For further analysis, the TIC group was categorized into the severe and non-severe TIC groups. Compared with patients with non-severe TIC, patients with severe TIC were more critical, especially in terms of hemodynamics and acidosis, required more vasopressors and surgical support, and have a higher in-hospital

mortality (22.0% vs. 42.1%, $P=0.020$, Table 2).

Risk factors for the elderly TIC patients

Multivariate logistic regression analysis revealed that $ISS>16$ ($OR: 3.404$, $95\%CI: 1.471-7.880$; $P=0.004$), $SI>1$ ($OR: 5.641$, $95\%CI: 1.700-18.719$; $P=0.005$), low BE ($OR: 0.868$, $95\%CI: 0.760-0.991$; $P=0.037$), hypocalcemia ($OR: 0.060$, $95\%CI: 0.009-0.392$; $P=0.003$), and hypofibrinogenemia ($OR: 0.266$, $95\%CI: 0.168-0.419$; $P<0.001$) were independent risk factors for TIC in elderly trauma patients (Table 3).

The AUC of the prediction model was 0.887 ($95\%CI: 0.851-0.923$). The Youden's index was maximized with a sensitivity and specificity of 83.6% and 82.6%, respectively (Figure 2).

Table 1. Comparison between elderly trauma patients with and without trauma-induced coagulopathy (TIC)

Variables	Non-TIC (n=242)	TIC (n=129)	P- value
Age, years	72.5±7.0	72.6±6.3	0.853
Male, n (%)	160 (66.1)	88 (68.2)	0.682
Injured parts, n (%)			
Head and neck	207 (85.5)	97 (75.2)	0.014
Face	32 (13.2)	18 (14)	0.844
Thorax	128 (52.9)	82 (63.6)	0.048
Abdomen	30 (12.4)	34 (26.4)	0.001
Extremities	92 (38.0)	81 (62.8)	<0.001
Body surface	21 (8.7)	6 (4.7)	0.155
SBP, mmHg	150.4±29.1	122.3±39.3	<0.001
HR, beats/min	84.1±17.6	93.8±20.0	<0.001
Body temperature, °C	37.4±0.8	37.1±0.8	0.005
ISS	21 (16-29)	25 (20-34)	<0.001
GCS	14 (8-15)	14 (6-15)	0.156
SI	0.58±0.18	0.90±0.66	<0.001
Blood gas analysis			
Lactate, mmol/L	1.8 (1.3-2.9)	3.2 (2.1-4.9)	<0.001
BE, mmol/L	-1.2±3.1	-4.9±4.6	<0.001
pH	7.39±0.06	7.35±0.08	<0.001
Biochemical electrolyte			
Ca ²⁺ , mmol/L	2.15±0.16	1.97±0.19	<0.001
K ⁺ , mmol/L	4.00±0.55	3.99±0.58	0.888
Na ⁺ , mmol/L	140.0±3.76	140.3±3.72	0.440
Coagulation parameters			
INR	1.1±0.1	1.5±0.4	<0.001
Fibrinogen, g/L	2.8±0.9	1.7±0.8	<0.001
APTT, s	33.8±4.1	47.6±21.8	<0.001
PT, s	13.7±0.8	18.0±3.9	<0.001
Blood routine			
Platelet, ×10 ⁹ /L	163.7±54.2	139.4±53.4	<0.001
Hemoglobin, g/L	123.3±19.8	96.8±25.2	<0.001
Blood products, n (%)	7 (2.9)	12 (9.3)	0.008
Vasopressors, n (%)	53 (21.9)	61 (47.3)	<0.001
Acute surgery, n (%)	6 (2.5)	20 (15.5)	<0.001
In-hospital mortality, n (%)	33 (13.6)	36 (27.9)	<0.001
MV, n (%)	127 (52.5)	95 (73.6)	<0.001
Duration of MV, d	2.7±5.0	4.6±8.0	0.017
LOS in ICU, d	4.5±4.9	5.6±6.1	0.080
LOS in hospital, d	15.9±12.3	17.6±13.8	0.218

Data were presented as mean with standard deviation, median with interquartile range, or number with percentage. SBP: systolic blood pressure; HR: heart rate; ISS: injury severity score; GCS: Glasgow coma score; SI: shock index; BE: base excess; INR: international normalized ratio; APTT: activated partial thromboplastin time; PT: prothrombin time; MV: mechanical ventilation; LOS: length of stay; ICU: intensive care unit.

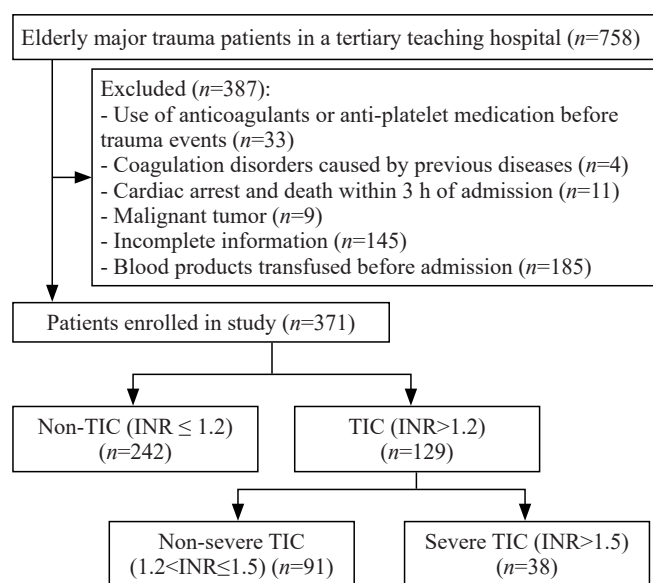


Figure 1. Flowchart of the study. TIC: trauma-induced coagulopathy; INR: international normalized ratio.

DISCUSSION

As the global population ages, the annual incidence of trauma among older patients is rising markedly.^[12] Unlike adult patients, elderly trauma patients experience distinct clinical outcomes due to physiological decline, pre-existing conditions, and less effective therapeutic

Table 2. Comparison of elderly trauma patients with and without severe trauma-induced coagulopathy (TIC)

Variables	severe TIC (n=38)	Non-severe TIC (n=91)	P- value
Age, year	72.0±6.1	72.9±6.4	0.448
Male, n (%)	30 (78.9)	58 (63.7)	0.091
Injured parts, n (%)			
Head and neck	24 (63.2)	73 (80.2)	0.041
Face	4 (10.5)	14 (15.4)	0.468
Thorax	24 (63.2)	58 (63.7)	0.950
Abdomen	10 (26.3)	24 (26.4)	0.995
Extremities	29 (76.3)	52 (57.1)	0.040
Body surface	2 (5.3)	4 (4.4)	1.000
SBP, mmHg	102.8±31.9	130.4±39.4	<0.001
HR, beats/min	97.5±20.9	92.2±19.5	0.169
Body temperature, °C	36.9±1.1	37.2±0.7	0.192
ISS	26 (17–30)	25 (20–34)	0.805
GCS	14 (3–15)	14 (7–15)	0.402
SI	1.18±1.08	0.78±0.30	0.030
Blood gas analysis			
Lactate, mmol/L	5.1 (3.2–7.6)	2.9 (1.7–4.1)	<0.001
BE, mmol/L	-7.6±5.3	-3.8±3.8	<0.001
pH	7.31±0.09	7.37±0.06	0.001
Biochemical electrolyte			
Ca ²⁺ , mmol/L	1.87±0.19	2.02±0.18	<0.001
K ⁺ , mmol/L	3.9±0.6	4.0±0.6	0.211
Na ⁺ , mmol/L	140.6±4.0	140.1±3.6	0.486
Coagulation parameters			
INR	2.0±0.5	1.3±0.1	<0.001
Fibrinogen, g/L	1.1±0.6	2.0±0.7	<0.001
APTT, s	65.3±31.7	40.3±8.5	<0.001
PT, s	22.5±4.6	16.1±0.9	<0.001
Blood routine			
Platelet, ×10 ⁹ /L	115.3±40.8	149.5±55.0	0.001
Hemoglobin, g/L	86.9±30.0	100.9±21.9	0.004
Blood products, n (%)	4 (10.5)	8 (8.8)	1.000
Vasopressors, n (%)	27 (71.1)	34 (37.4)	<0.001
Acute surgery, n (%)	12 (31.6)	8 (8.8)	0.001
In-hospital mortality, n (%)	16 (42.1)	20 (22.0)	0.020
MV, n (%)	31 (81.6)	64 (70.3)	0.186
Duration of MV, d	5.1±7.1	4.4±8.4	0.653
LOS in ICU, d	6.3±6.7	5.2±5.9	0.370
LOS in hospital, d	15.2±13.9	18.7±13.7	0.192

Data were presented as mean with standard deviation, median with interquartile range, or number with percentage. SBP: systolic blood pressure; HR: heart rate; ISS: injury severity score; GCS: Glasgow coma score; SI: shock index; BE: base excess; INR: international normalized ratio; APTT: activated partial thromboplastin time; PT: prothrombin time; MV: mechanical ventilation; LOS: length of stay; ICU: intensive care unit.

Table 3. Risk factors for TIC in elderly trauma patients

Factors	OR (95% CI)	P-value
Body temperature	0.767 (0.516–1.139)	0.189
ISS > 16	3.404 (1.471–7.880)	0.004
SI > 1	5.641 (1.700–18.719)	0.005
Platelet	0.995 (0.989–1.001)	0.112
pH	26.602 (0.085–8,329.401)	0.263
Hypocalcemia	0.060 (0.009–0.392)	0.003
Lactate	1.037 (0.864–1.245)	0.694
BE	0.868 (0.760–0.991)	0.037
Fibrinogen	0.266 (0.168–0.419)	<0.001

TIC: trauma-induced coagulopathy; ISS: injury severity score; SI: shock index; BE: base excess.

interventions following severe trauma.^[13-15,24,25] Severe coagulation disorders resulting from significant hemorrhage are common among severely injured elderly patients. However, few studies have investigated the risk factors of poor outcomes in elderly patients with TIC.^[3,4,6] Our findings revealed that elderly TIC patients exhibited significantly higher values of ISS, SI, lactate, APTT, and PT compared to non-TIC patients. Additionally, the levels of BE, pH, fibrinogen, platelets, and hemoglobin were notably lower in the TIC group, indicating traumatic acidosis and substantial blood component loss. Consequently, the administration of blood transfusions, vasopressors, and emergency surgeries is necessary for the effective management of elderly patients with major trauma. Compared with non-TIC patients, elderly TIC patients also required prolonged mechanical ventilation. Therefore, there is a critical need for prompt evaluation and treatment of elderly patients with TIC.

In this study, we confirmed that an ISS > 16 (indicative of major trauma), SI > 1 (indicating shock), low BE (indicating metabolic acidosis), hypocalcemia, and hypofibrinogenemia were independent risk factors of TIC in elderly trauma patients. Previous studies have consistently identified severe tissue injury, shock, and metabolic acidosis as risk factors for TIC.^[1,4] Comparing risk factors for TICs between elderly and young adult populations is difficult due to the absence of age stratification in previous studies. Both the ISS and the SI reflect the severity of injury in trauma patients

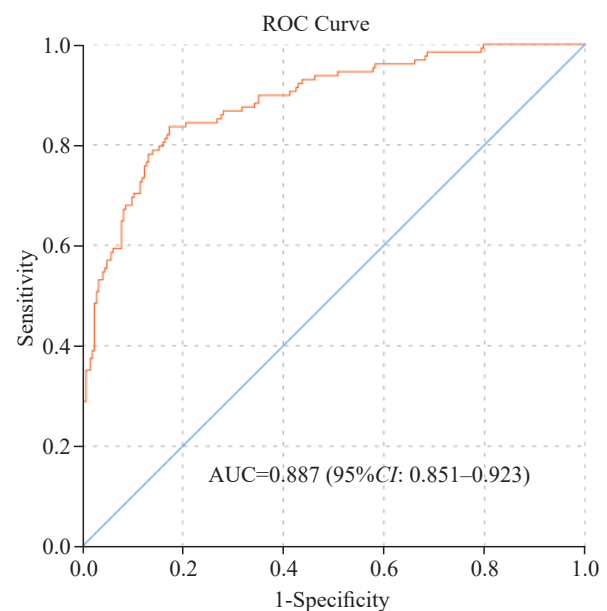


Figure 2. ROC curve of regression model for predicting trauma-induced coagulopathy. The regression model included ISS, SI, serum calcium, base excess and fibrinogen as risk factors.

and indicate the occurrence of coagulation dysfunction and metabolic acidosis. Patients with severe injuries and ongoing bleeding or profound hemorrhagic shock usually have a poor prognosis.^[1] Prompt management of hemorrhage and appropriate resuscitation are crucial measures for rectifying coagulation disorders.

TIC is characterized by hypofibrinogenemia and often elevated fibrinolytic activity.^[4,26,27] Effective cessation of bleeding primarily depends on the formation of stable clots, which relies on adequate fibrinogen and platelet levels rather than the speed of coagulation initiation.^[27,28] Khan et al^[29] found that neither lactate levels nor any viscoelastic parameter exhibited improvement in patients who received mixed transfusion packages with delayed or no fibrinogen supplementation. In addition to early administration of tranexamic acid, early fibrinogen administration is crucial, ideally guided by a fibrinogen concentration < 1.5 g/L or viscoelastic evidence of functional fibrinogen deficiency.^[4]

Previous studies have thoroughly investigated variations in serum calcium levels as an indicator for evaluating coagulation function in trauma patients.^[30-33] However, the relationship between hypocalcemia and the “lethal triad symptoms” has been poorly elucidated in prior research. Early prevention of hypocalcemia may offer benefits for elderly patients with TIC. Therefore, it is essential to closely monitor and maintain normal serum calcium levels in elderly TIC patients.^[18, 33-35] However, the identification and treatment algorithms for hypocalcemia in TIC patients remain limited.^[31, 32]

Several limitations should be acknowledged in this study. First, it was a single-center retrospective study, potentially introducing selection bias. Multicenter prospective studies are required for further evaluate risk factors for TIC in elderly patients. Second, the lack of data in this study, such as ionized calcium levels, serum protein levels, calcium supplementation, and trauma mechanisms, hindered further analysis of the correlation between calcium levels and TIC in elderly patients.

CONCLUSION

In conclusion, higher ISS (>16), higher SI (>1), acidosis, hypocalcemia, and hypofibrinogenemia were identified as independent risk factors for TIC in elderly trauma patients. Prompt and effective correction of shock, acidosis, hypocalcemia, and hypofibrinogenemia in elderly TIC patients could significantly improve clinical outcomes.

Funding: This work was supported by National Natural Science Foundation of China (81571916), Key Research and Development (R&D) Program of Zhejiang Province (2024C03186) and Major Project of National-Zhejiang Provincial Administration of Traditional Chinese Medicine (GZY-ZJ-KJ-24030).

Ethical approval: This study was approved by the Second Affiliated Hospital of Zhejiang University School of Medicine. The institutional review board waived the requirement for informed consent ([2020] IRB-976) from patients and their relatives, given the observational nature of the study.

Conflicts of interest: The authors have no conflicts of interest related to this study.

Author contributions: YBK, QY, and HBD contributed equally to this paper and are co-first authors. YBK and YAX conceived the study and carried out the study design. YBK, JSS, QY, YFH, YCJ, SXX, HBD, FR, BJC, YPF and LBJ participated in the data acquisition. YBK, LBJ, GRW and YAX interpreted the data. YBK edited the manuscript. All the authors read and approved the final version of the manuscript.

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Received December 29, 2023

Accepted after revision June 30, 2024