Original Article

Bull Emerg Trauma 2025;13(4):2-11.

Bulletin of Emergency And Trauma

The Prognostic Value of D-Dimer Levels for Injury Outcomes in Trauma Patients: A Systematic Review and Meta-Analysis

Hooman Rezaei[1], Elham Navipour[2], Samaneh Zafarabadi[3], Mehrdad Karajizadeh[1], Fatemeh Javanmardi[4], Mahnaz Yadollahi[1], Maryam Hosseini[1*]

[1]Truama Research Center, Shahid Rajaee (Emtiaz) Trauma Hospital, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Department of Medical Education, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
[3]Student Research Committee, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[4]Department of Biostatistics, School of Medicine, Shiraz University of Medical Science, Shiraz, Iran

***Corresponding author:** Maryam Hosseini*
Address: Trauma Research Center, Shahid Rajaee (Emtiaz) Trauma Hospital, Shiraz University of Medical Sciences, Shiraz, Iran. **Tel:** +98 71 36254206;
e-mail: Hoseinism@sums.ac.ir

Received: May 06, 2025
Revised: August 03, 2025
Accepted: October 11, 2025

ABSTRACT

Objectives: This study aimed to systematically review and quantify the association between D-dimer levels and injury outcomes in trauma patients through a meta-analysis.
Methods: A systematic literature search of PubMed, MEDLINE/PubMed, and Web of Science was conducted from 2011 to 2023, supplemented by manual reference list searches. Two independent reviewers assessed the risk of bias using the Newcastle-Ottawa Scale. The primary outcomes were mortality and deep vein thrombosis (DVT).
Results: Of 84 identified articles, 17 were eligible for full-text assessment, and 12 were included in the final analysis. A random-effects model was used to pool the study results. The analysis revealed a statistically significant difference in mean D-dimer levels between patients with poor outcomes and those without poor outcomes (p=0.0003). The standardized mean difference (SMD) was 0.51 (95% confidence interval [CI]:0.24 to 0.79). Furthermore, a significant difference in mean D-dimer levels was observed between survivors and non-survivors (p=0.03, SMD:0.42, 95% CI:0.04-0.79) and between patients with DVT and those without DVT (p=0.0008, SMD:0.79, 95% CI:0.32-1.25).
Conclusion: This meta-analysis indicated that elevated D-dimer levels upon admission could be a valuable prognostic marker in trauma patients and might help predict poor outcomes.

Keywords: D-dimer, Meta-analysis, Mortality, Trauma brain injury, Deep vein thrombosis.

Please cite this paper as:
Rezaei H, Navipour E, Zafarabadi S, Karajizadeh M, Javanmardi F, Yadollahi M, Hosseini M. The Prognostic Value of D-Dimer Levels for Injury Outcomes in Trauma Patients: A Systematic Review and Meta-Analysis. *Bull Emerg Trauma*. 2025;13(4):2-11. doi: 10.30476/beat.2025.106988.1605.

Introduction

Trauma is a leading cause of global mortality and disability, representing the sixth most common underlying cause of mortality and the fifth leading cause of moderate and severe disability worldwide. It results in the highest rates of moderate and severe disability and mortality among young people [1, 2]. Although the Glasgow Coma Score (GCS) [3, 4] and repeated computed tomography (CT) scans

are conventional approaches for evaluating trauma injuries [5-7], reliable prognostic markers are required to assist in the immediate diagnosis of complications and predict patient recovery [8].

Acquired coagulopathy disorders are common consequences of tissue injury, hypoperfusion, hypothermia, and acidosis in trauma patients. These disorders result from an imbalance between anticoagulant and procoagulant factors, platelet dysfunction, and, most importantly, fibrinolysis during the acute phase of trauma. They are associated with a wide range of life-threatening outcomes, from progressive hemorrhagic injury (PHI) to mortality [9-11]. Hyperfibrinolysis is a critical aspect of trauma-induced coagulopathy, characterized by drastically elevated levels of fibrinogen/fibrin degradation products (FDPs), particularly D-dimer. This elevation is integrally linked to poor prognosis and severe outcomes [12, 13]. Previous studies demonstrated that alterations in D-dimer concentration could disrupt the fibrinolytic system by unbalancing coagulation factors, which could ultimately increase the need for massive transfusion due to extreme bleeding [14, 15]. Several investigations evaluated the prognostic role of D-dimer levels in different types of traumatic injury, including traumatic brain injury (TBI), but have failed to reach a decisive conclusion due to discrepant findings [16, 17]. For instance, a prospective study (n=205) found that a D-dimer>1,793 ng/mL at admission predicted mortality (OR=5.87) [18]. Another meta-analysis highlighted D-dimer's superiority over INR/PT for predicting disseminated intravascular coagulation (DIC) and hemorrhagic progression in TBI [19]. Moreover, a systematic review and meta-analysis by Zhang *et al.,* confirmed the prognostic role of D-dimer levels upon admission in patients with TBI, revealing a direct association between higher D-dimer levels upon admission and the risk of PHI [10]. While the study by Zhang *et al.,* focused exclusively on TBI patients [10], the present study was designed to systematically review and quantify the association between D-dimer levels and injury outcomes in a broader population of trauma patients by conducting a meta-analysis.

Materials and Methods

This study was conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Search Strategy and Selection Studies

Relevant publications were identified through a comprehensive and systematic search of PubMed, MEDLINE/PubMed, and Web of Science databases. The search strategy utilized keywords such as "D-dimer levels", "fibrin fragment D", "traumatic injury", "trauma", "outcome", "mortality", "deep vein thrombosis", and "DVT". The Boolean operators ("AND" and "OR") were used to combine these terms. The initial screening of records was based on titles and abstracts. The full texts of potentially eligible studies were then independently assessed by two reviewers. Any disagreements were resolved through discussion until a consensus was reached. The search was restricted to English-language articles published between January 2011 and January 2023.

Eligibility Criteria

Studies meeting the following criteria were included in the meta-analysis:

1) Study types: Case-control, cross-sectional, and cohort studies.

2) Population: Trauma patients.

3) Exposure/Outcome: Literature examining the association between D-dimer levels and clinical outcomes, with outcome rates (number or percentage of trauma patients with the outcome) clearly stated.

4) Comparison: Studies reporting D-dimer levels in trauma patients for at least two distinct comparison groups (e.g., poor vs. good outcome, survivors vs. non-survivors).

5) Original studies providing the number of participants in each group, the timing of D-dimer evaluation, and the mean and standard deviation of D-dimer levels for each group.

Studies with incomplete or irrelevant data were excluded from this meta-analysis.

Quality Assessment

The risk of bias was assessed independently by two reviewers using the Newcastle-Ottawa Scale (NOS). The NOS evaluates three domains: subject selection (0-4 points), comparability of subjects (0-2 points), and exposure (for case-control studies) or outcome (for cohort studies) (0-3 points) [20]. Total scores range from 0 to 9, with studies scoring ≥6 being considered high-quality. Any disagreements between the two reviewers were resolved through discussion with a third reviewer to reach a consensus (Table 1). Studies scoring below 6 were considered low-quality and were excluded from the analysis.

Statistical Analysis

The association between D-dimer levels and injury outcomes in trauma patients was examined by synthesizing data from the included studies. The means, standard deviations, and sample sizes from each study were used to calculate the standardized mean difference (SMD). Notably, the control groups in these studies typically consisted of trauma patients with good functional outcomes. Consequently, the D-dimer levels in these control groups were expected to be elevated compared to healthy reference values (<250 ng/mL) [21], which contributed to heterogeneity across the studies. Heterogeneity was assessed using the I^2 statistic and the Chi-squared (Q) test.

Table 1. The characteristics of the 17 studies included in the systematic review

Study	Country	Type of Study	Patient (M/F)	Age (y)	Type of trauma	ISS score	D-dimer mean (ng/mL)	D-dimer SD (ng/mL)	Outcome	Outcome rate N (%)	Quality score	Reference
Jiang, *et al.* 2021	USA	Prospective	891(728/163)	36.4	TBI	19.6	20460	90.46	Mortality	61 (6.8)	8	[31]
Zang, *et al.* 2023	Japan	Prospective	106(43/63)	55.6	Lower extremity, Pelvis	Unknown	6397.5	4933.4	DVT	53 (50)	8	[17]
Fujiwara, *et al.* 2022	Japan	Retrospective	458(202/256)	62.53	TBI	Unknown	33675	17638	Mortality	67 (69.1)	8	[23]
Peng, *et al.* 2021	China	Retrospective	678(197/483)	45.94	Multiple trauma	16.26	13500	N/A	DVT	94 (13.8)	7	[28]
Juratli, *et al.* 2014	Germany	Retrospective	153(123/30)	52	TBI	Unknown	10000	N/A	Hemorrhage	70 (45.8)	7	[16]
Johansson, *et al.* 2012	Denmark	Prospective	75(56/19)	40.7	Unknown	22.3	39.6	13.5	Mortality	21 (28)	7	[52]
Lv, *et al.* 2020	China	Retrospective	2570 (1934/636)	48.54	TBI	15.35	7180	1112	Mortality	198 (7.7)	7	[26]
Ishii, *et al.* 2019	Japan	Retrospective	666 (459/207)	52	TBI, Multiple trauma	26	30075	15505.8	Mortality	69 (10.3)	7	[24]
C. Cardenas, *et al.* 2019	USA	Retrospective	547 (443/103)	34	TBI	26.9	9127.75	6786.5	Mortality	76 (13.8)	7	[22]
Yumoto, *et al.* 2017	Japan	Retrospective	204 (144/60)	49	TBI, face, thorax, abdomen, extremity	20	22525	11633.6	DVT	65(32)	7	[29]
Otsuka, *et al.* 2020	Japan	Retrospective	120 (81/39)	54.5	Multiple trauma	43	50175	23296.1	Mortality	59 (49.2)	6	[27]
Li, *et al.* 2020	China	Retrospective	50	Unknown	Multiple trauma	Unknown	1080.7	253	DIC	10 (20)	6	[23]
H. Shaz, *et al.* 2011	USA	Prospective	91 (73/18)	38	TBI	12	4186	5533.7	Mortality	3(8.1)	6	[34]
Nakama, *et al.* 2021	Japan	Retrospective	283(200/83)	47	Extremity, multiple trauma	4	10100	6177.6	The sensitivity, specificity of D-dimer for the prognosis of TBI without needing to whole body CT	76 (26.8)	6	[30]
Raza, *et al.* 2012	United Kingdom	Prospective	303 (248/55)	37	TBI, thorax, extremity	10	30544	4458.3	Mortality	27(8.9)	6	[32]
Rong, *et al.* 2016	China	Prospective	64 (44/20)	38	Lower extremity	Unknown	2000	1800	DVT	32 (50)	6	[33]
Yang, *et al.* 2022	China	Unknown	54(46/8)	36	Multiple trauma	21	6000	N/A	Mortality	4 (7.4)	6	[53]

DVT: Deep vein thrombosis; TBI: Traumatic brain injury; CT: Computerized tomography; DIC: Disseminated intravascular coagulation

The I^2 values were interpreted as follows: <0.25% low, 0.25-0.75% moderate, and >0.75 high heterogeneity. A random-effects model was employed for the meta-analysis due to the presence of significant heterogeneity. In cases where the I^2 statistic was 0%, indicating homogeneity, a fixed-effects model was applied. Publication bias was assessed using a funnel plot and Egger's test. All statistical analyses were conducted using STATA version 17, with a significance level set at $p<0.05$.

Results

The initial database search identified 84 articles. After removing 56 records due to irrelevance or duplication, 28 studies underwent title and abstract screening. This led to the exclusion of 11 studies. The full texts of the remaining 17 articles were assessed for eligibility, and 5 were excluded due to irrelevant or incomplete data. Consequently, 12 studies were included in the final meta-analysis. The study selection process is detailed in the PRISMA flow diagram (Figure 1).

Study Characteristics and Quality Assessment

The characteristics of 17 studies included in the systematic review are summarized in Table 1. All studies were published between 2011 and 2023 and were conducted in six different countries, primarily in China and Japan. Of the 17 studies, 10 were retrospective [16, 22-30] and 6 were prospective [17, 21, 31-34]. The sample sizes ranged from 50 to 2,570 patients. The pooled study population consisted of 5,042 (68%) men and 2,371(32%) women. The outcomes of interest—including mortality, deep vein thrombosis (DVT), hemorrhage, and DIC—occurred in 981 (13.23%) patients, while 6,432 patients did not experience these outcomes.

Regarding patient populations, nine studies focused on traumatic brain injury (TBI), six on multiple trauma, and five on trauma to the extremities, pelvis, face, thorax, or abdomen. Blood samples for D-dimer measurement were obtained on the first day of admission for all patients.

In the methodological quality assessment, ten studies received a score of ≥7 (mean score=6.76) on the NOS and were considered high-quality. These studies met key criteria, including proper case selection, appropriate control groups, valid exposure/outcome assessment, control of confounders (such as age and trauma severity), and adequate follow-up, indicating a low risk of bias.

Comparison of D-dimer between Patients with and without Poor outcomes

A meta-analysis of 10 studies, using the SMD as the effect size, revealed significant heterogeneity (I^2=85.6%, $p<0.001$). Consequently, a random-effects model was employed. The pooled analysis demonstrated a statistically significant difference in the mean D-dimer levels between patients with poor outcomes (16,570.33 ng/mL) and those without poor outcomes and the control group (8,226.23 ng/mL) (p=0.0003). The SMD between the two groups was calculated at 0.51 (95% CI: 0.24 to 0.79, Figure 2).

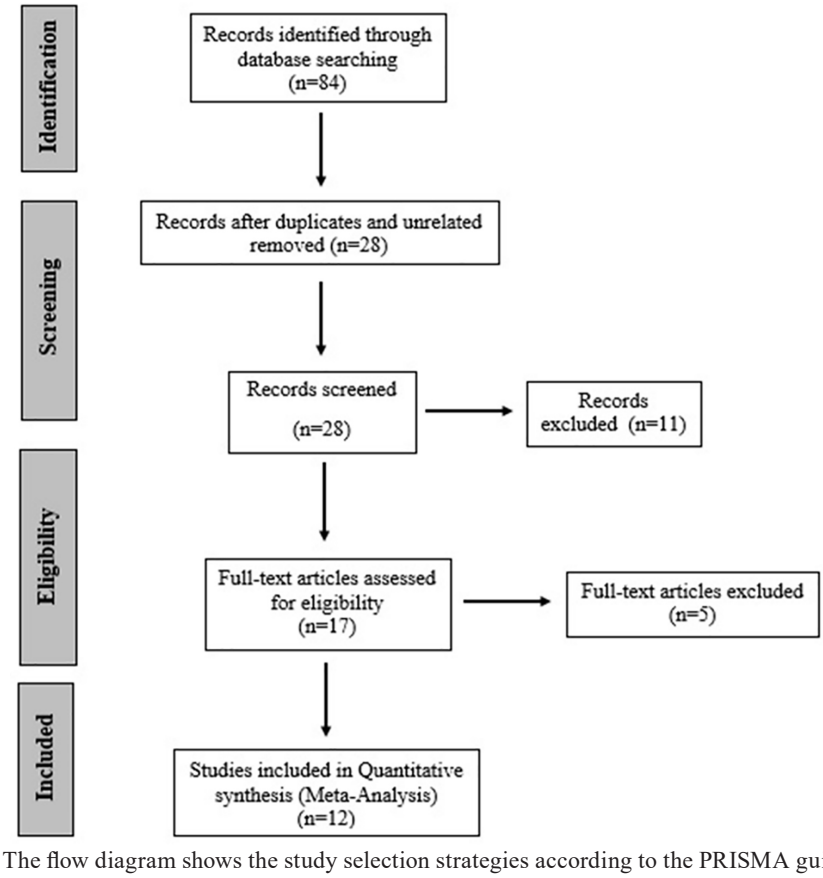

Fig. 1. The flow diagram shows the study selection strategies according to the PRISMA guidelines.

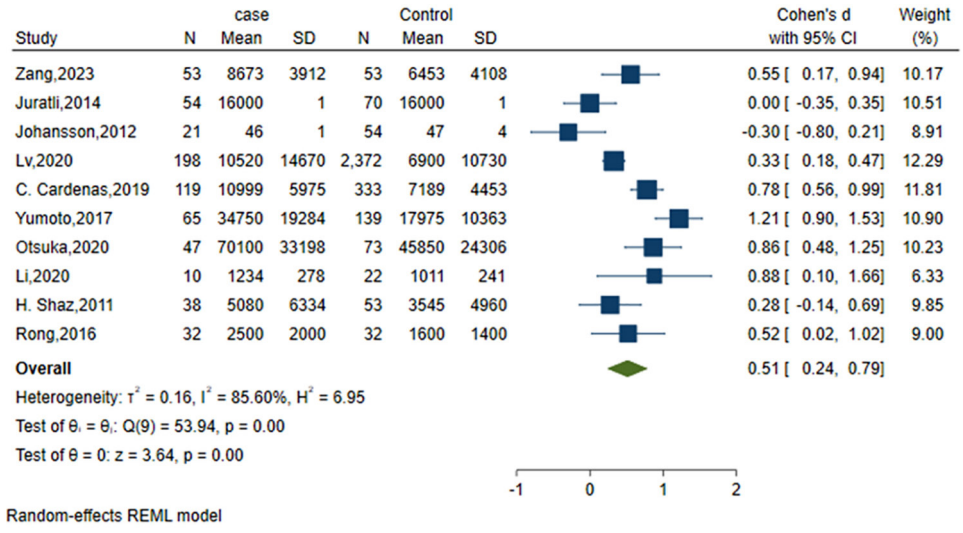

Fig. 2. A forest plot shows the standardized mean difference of D-dimer levels between trauma patients with poor outcomes (case) and those without poor outcomes (control).

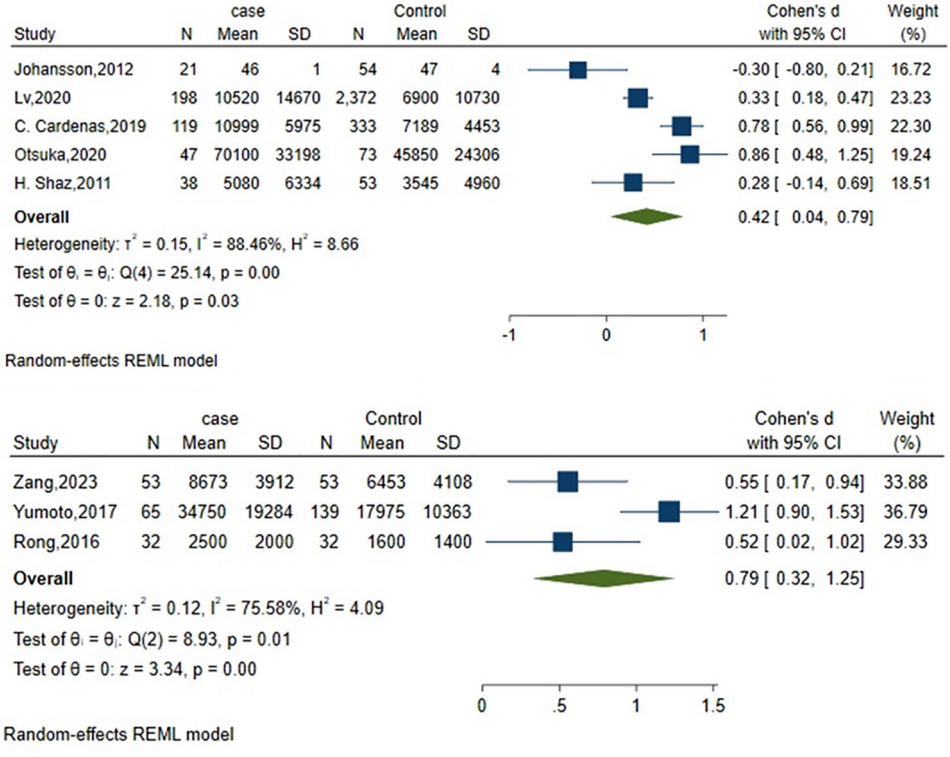

Fig. 3. A forest plot displays the standardized mean difference of D-dimer levels between trauma patients: (a) deceased (case) and survived (control), (b) with deep vein thrombosis (DVT) (case) and without DVT (control).

Comparison of D-dimer between Survivors and Non-Survivors

In the meta-analysis of 5 studies assessing mortality among trauma patients, the SMD also indicated significant heterogeneity (I^2=88.46%, p<0.001). A random-effects model was therefore applied. The analysis revealed a statistically significant difference in mean D-dimer levels between non-survivors (16,266 ng/mL) and survivors (7,729.01 ng/mL, p=0.03). The SMD was 0.42 with a confidence interval of 0.04 to 0.79 (Figure 3a).

Comparison of D-dimer between DVT Patients and Non-DVT Patients

The meta-analysis of 3 studies on DVT demonstrated heterogeneity (I^2=75.58%, p=0.01, Q=8.93). A random-effects model was used and indicated a statistically significant difference in mean D-dimer levels between patients with DVT (18,656.12 ng/mL) and those without DVT (12,909.52 ng/mL) (p=0.0008). The SMD was 0.79 (95% CI: 0.32 to 1.25, Figure 3b).

Comparison of D-dimer among Patients Based on Their Type of Trauma

A meta-analysis of five studies on TBI patients revealed significant heterogeneity (I^2=92.08%, p<0.001). The results of the random-effects model showed a statistically significant difference in mean D-dimer levels between the TBI patients

(14,151.12 ng /mL) and the control group (70,606.04 ng/mL, p=0.012). The SMD between these groups was 0.53, within a confidence interval of 0.11 to 0.94 (Figure 4a).

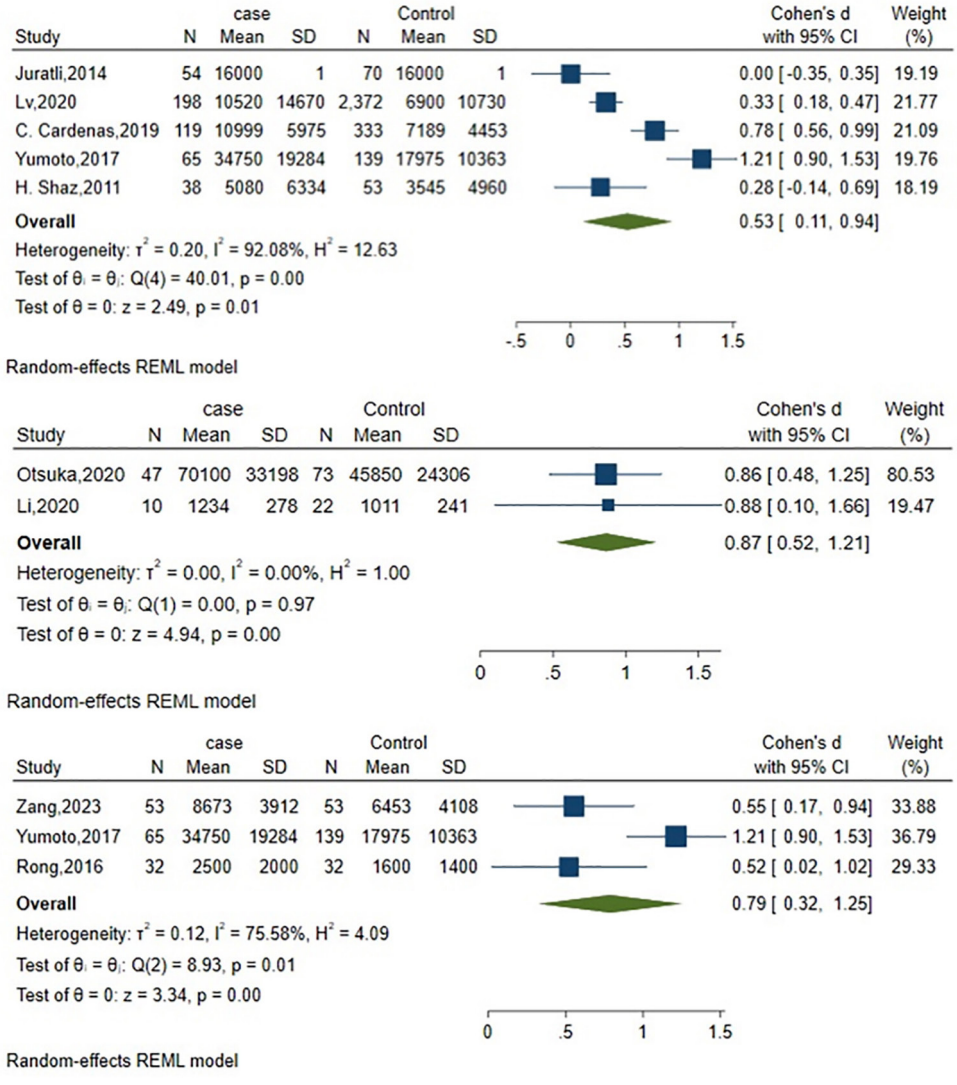

Fig. 4. A forest plot presents the standardized mean difference of D-dimer levels among (a) TBI patients, (b) multiple trauma patients, and (c) lower extremity trauma individuals.

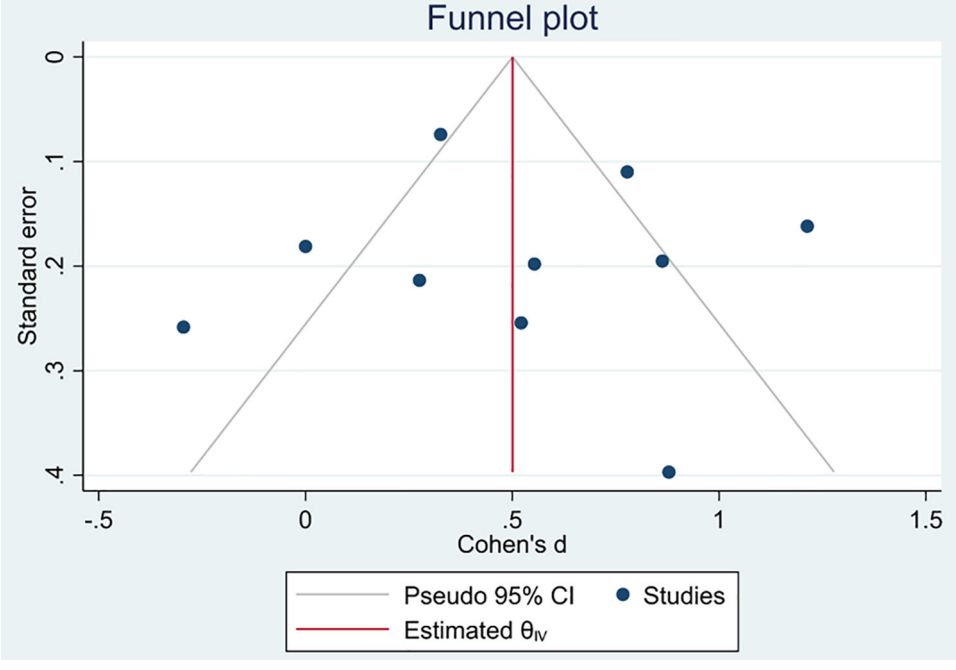

Fig. 5. Funnel plot assessing the publication bias

The analysis of two studies on multiple traumas demonstrated homogeneity (I^2=0%, p=0.97), leading to the use of a fixed-effects model. A statistically significant difference in mean D-dimer levels was found between patients with multiple trauma (58,018.24 ng /mL) and the control group (35,466.23 ng /mL, p<0.001). The SMD was 0.87, with a confidence interval of 0.52 to 1.21 (Figure 4b).

The meta-analysis of three studies on lower extremity injuries demonstrated heterogeneity (I^2=75.58%, p=0.01); consequently, a random-effects model was used. The analysis revealed a statistically significant difference in mean D-dimer levels between patients with lower extremity injuries (18,656.12 ng/mL) and controls (12,909.52 ng/mL, p=0.0008). The SMD was 0.79 (95% CI: 0.32 to 1.25, Figure 4c).

Publication bias was assessed using Begg's and Egger's tests across the included studies. The results indicated no significant publication bias for the analysis of the prognostic role of D-dimer levels (Egger's test p=0.87, Figure 5).

Discussion

This systematic review and meta-analysis confirmed that elevated D-dimer levels upon hospital admission are a significant prognostic biomarker for poor outcomes in a broad population of trauma patients. The pooled data demonstrated a consistent and statistically significant association between high D-dimer concentrations and critical endpoints, including mortality and DVT. Although significant heterogeneity was observed across the included studies, the application of robust methodologies, including random-effects modeling and subgroup analyses, strengthened the validity of these findings.

Numerous studies indicated that the risk of DVT in trauma patients ranged from 2.5% to 18.91% [22, 35-38]. Consistent with this, Zang *et al.,* [17] reported significantly higher D-dimer levels in trauma patients with DVT than both healthy individuals and non-DVT patients, suggesting its utility as a predictive biomarker. Elevated D-dimer levels were also linked to worse prognoses, with studies correlating higher levels with increased risks of both short-term [39, 40] and long-term [12] mortality. Indeed, trauma patients with elevated D-dimer levels have significantly higher odds of mortality [41]. While the present meta-analysis confirmed these associations, revealing significant differences between case and control groups, considerable heterogeneity was observed across the studies. To investigate this, we performed subgroup analyses based on trauma type (TBI, multiple trauma, and lower extremity injuries). This approach substantially reduced heterogeneity, even eliminating it in one subgroup, indicating that the type and mechanism of trauma may contribute to heterogeneity may contribute to heterogeneity.

In the subgroup analysis of five studies on TBI patients, a statistically significant difference in mean D-dimer levels was found between case and control groups. This finding is supported by previous research linking elevated D-dimer levels to a higher risk of PHI [16, 42, 43], poor functional outcomes, and increased in-hospital, 28-day, 30-day, and 90-day mortality [39, 44, 45]. A multicenter TBI database analysis further confirmed that admission D-dimer levels correlate with poor GOS scores and six-month mortality [12]. Moreover, Chen *et al.,* in a study with long-term follow-up (mean 2.8 years, maximum 6.9 years), demonstrated a relationship between high D-dimer levels and long-term mortality in TBI patients, reinforcing D-dimer's role as a poor prognostic indicator. A dose-response relationship was observed, wherein higher D-dimer levels corresponded to a significantly increasing mortality risk [41]. However, study heterogeneity remains, potentially due to varying outcomes and mortality prediction durations [41]. Despite this consistent association, heterogeneity persists among studies. Potential sources include variations in the specific outcomes measured, the timing of mortality prediction, the units for reporting D-dimer, and the assay methods used (e.g., ELISA versus immunoturbidimetric assays) [41, 46]. Furthermore, confounding variables, such as age and sex, are often unaccounted for, despite older age and female sex being known to independently elevate D-dimer levels. The failure of many studies to stratify by these factors likely contributes to variability. Additional confounders include anticoagulant use (e.g., warfarin, which may lower D-dimer levels) and comorbid conditions such as malignancy, which can increase them [46, 47].

In the analysis of studies on patients with multiple traumas, a significant difference was observed in mean D-dimer scores between the case and control groups, with an SMD of 0.87 (95%CI: 0.52, 1.21). Notably, no heterogeneity was detected (I^2=0%), suggesting that trauma type might be a valuable predictor of outcomes influencing the association between D-dimer and patient outcomes. This finding was supported by a 2016 multicenter retrospective study of 519 adult trauma patients, which reported higher mortality in those with elevated D-dimer levels [48]. Furthermore, elevated D-dimer levels were shown to correlate with the degree of trauma severity and tissue damage, serving as an important indicator of the ensuing inflammatory process [9].

Determining changes in D-dimer levels in patients with severe multiple traumas is crucial for predicting DIC. In one study, D-dimer levels were significantly higher in trauma patients with DIC than those without [49]. Supporting this, a 2019 prospective multicenter observational cohort study by Gall *et al.,* which involved 940 severely injured patients (mostly with TBI), reported that D-dimer levels were seven times higher in deceased patients than in survivors [50]. This strongly indicated that the

mean D-dimer level could be a powerful predictor of poor outcomes in multiple trauma patients. However, the precise mechanisms linking elevated D-dimer levels to poor outcomes, such as progressive PHI, thromboembolic complications, and multi-organ failure, remain unclear [51].

Furthermore, while the analysis of patients with lower extremity injuries [17] revealed heterogeneity, a statistically significant difference in mean D-dimer levels between case and control groups was still observed. Given its consistent predictive role for adverse outcomes in trauma patients, D-dimer levels measured at admission could serve as a valuable marker for clinical management [41]. This supports the potential for establishing specific D-dimer cut-off values to predict adverse outcomes in this patient population.

This study had several limitations. The exclusion of low-quality studies and the omission of the Google Scholar database might have contributed to heterogeneity and introduced a selection bias. Furthermore, the reliance on retrospective and observational study designs, inherent assay variability in D-dimer measurement, and potential generalizability issues were other important limitations.

The findings of this review confirmed that elevated D-dimer levels upon admission were significantly associated with adverse outcomes in trauma patients, including mortality, DIC, and DVT. Therefore, the routine evaluation of D-dimer levels upon admission could aid healthcare professionals in risk stratification and clinical decision-making. Future research is required to establish precise, validated cut-off points for D-dimer to predict specific adverse outcomes.

Declaration

Ethics approval: Not applicable.

Consent to participate: Not applicable.

Consent for publication: Not applicable.

Conflict of Interests: All authors declared that they have no conflict of interest.

Declaration of Generative AI in Scientific Writing: None.

Funding: The authors received no financial support for the research, authorship, and/or publication of this article.

Data availability: Data availability is not applicable to this article as no new data were generated or analyzed in this study.

Authors' Contribution: ENP: Drafting of the manuscript; SZA: Drafting of the manuscript; MK: Drafting of the manuscript; FM: Acquisition of the data; MH: Study concept, designing, drafting of the manuscript, critical revision of the manuscript for important intellectual content, and supervision.

Acknowledgments: The authors appreciate the staff of the trauma center at Shahid Rajaee Hospital, Shiraz, Iran.

References

1. Alberdi F, García I, Atutxa L, Zabarte M. Epidemiology of severe trauma. *Med Intensiva*. 2014;**38**(9):580–8.
2. James SL, Castle CD, Dingels ZV, Fox JT, Hamilton EB, Liu Z, et al. Global injury morbidity and mortality from 1990 to 2017: results from the Global Burden of Disease Study 2017. *Inj Prev*. 2020;**26**(Supp 1):i96–i114.
3. Huang YT, Huang YH, Hsieh CH, Li CJ, Chiu IM. Comparison of Injury Severity Score, Glasgow Coma Scale, and Revised Trauma Score in Predicting the Mortality and Prolonged ICU Stay of Traumatic Young Children: A Cross-Sectional Retrospective Study. *Emerg Med Int*. 2019;**2019**:5453624.
4. Salottolo K, Panchal R, Madayag RM, Dhakal L, Rosenberg W, Banton KL, et al. Incorporating age improves the Glasgow Coma Scale score for predicting mortality from traumatic brain injury. *Trauma Surg Acute Care Open*. 2021;**6**(1):e000641.
5. Soltanpour B, Akhgar A, Jalili MH. Chest computed tomography scan alters the management plan in multiple trauma patients with a prior chest X-ray. *Chinese Journal of Academic Radiology*. 2022;**6**:82 – 8.
6. Byerly SE, Jones MD, Lenart EK, Seger CP, Filiberto DM, Lewis RH, et al. Serial CT for Nonoperatively Managed Splenic Injuries. *Am Surg*. 2022;**88**(7):1504–9.
7. Shih YJ, Liu YL, Zhou JT, Zhang Y, Chen JH, Chen TY, et al. Usage of image registration and three-dimensional visualization tools on serial computed tomography for the analysis of patients with traumatic intraparenchymal hemorrhages. *J Clin Neurosci*. 2022;**98**:154–61.
8. Gan ZS, Stein SC, Swanson R, Guan S, Garcia L, Mehta D, et al. Blood Biomarkers for Traumatic Brain Injury: A Quantitative Assessment of Diagnostic and Prognostic Accuracy. *Front Neurol*. 2019;**10**:446.
9. Moore EE, Moore HB, Kornblith LZ, Neal MD, Hoffman M, Mutch NJ, et al. Trauma-induced coagulopathy. *Nat Rev Dis Primers*. 2021;**7**(1):30.
10. Zhang J, He M, Song Y, Xu J. Prognostic role of D-dimer level upon admission in patients with traumatic brain injury. *Medicine (Baltimore)*. 2018;**97**(31):e11774.
11. Savioli G, Ceresa IF, Caneva L, Gerosa S, Ricevuti G. Trauma-Induced Coagulopathy: Overview of an Emerging Medical Problem from Pathophysiology to Outcomes. *Medicines (Basel)*. 2021;**8**(4).
12. Fujiwara G, Okada Y, Sakakibara T, Yamaki T, Hashimoto N. The Association Between D-dimer Levels and Long-Term Neurological Outcomes of Patients with Traumatic Brain Injury: An Analysis of a Nationwide Observational Neurotrauma Database in Japan. *Neurocrit Care*. 2022;**36**(2):483–91.
13. Moresco RN, Vargas LC, Voegeli CF, Santos RC. D-dimer and its relationship to fibrinogen/fibrin degradation products (FDPs) in

disorders associated with activation of coagulation or fibrinolytic systems. *J Clin Lab Anal*. 2003;**17**(3):77–9.
14. Nakae R, Murai Y, Takayama Y, Namatame K, Matsumoto Y, Kanaya T, et al. Neurointensive Care of Traumatic Brain Injury Patients Based on Coagulation and Fibrinolytic Parameter Monitoring. *Neurol Med Chir (Tokyo)*. 2022;**62**(12):535–41.
15. Nakae R, Murai Y, Yokobori S. Biomarkers in neurological injury: fibrinogen, fibrinogen/fibrin degradation products (FDPs), and D-dimer. Biomarkers in Trauma, Injury and Critical Care: Springer; 2022. p. 1–15.
16. Juratli TA, Zang B, Litz RJ, Sitoci KH, Aschenbrenner U, Gottschlich B, et al. Early hemorrhagic progression of traumatic brain contusions: frequency, correlation with coagulation disorders, and patient outcome: a prospective study. *J Neurotrauma*. 2014;**31**(17):1521–7.
17. Zang X, Su Y, Zhang W, Cao X, Li C, Lu S, et al. Hepatocyte-derived Microparticles as Novel Biomarkers for the Diagnosis of Deep Venous Thrombosis in Trauma Patients. *Clin Appl Thromb Hemost*. 2023;**29**:10760296231153400.
18. Hazarika A, Kumar M, Ahluwalia J, Khurana BJK, Mahajan V, Bhatia N, et al. D-dimer levels at the time of admission to hospital as a predictor of outcome in trauma patients: A prospective observational study. *Saudi J Anaesth*. 2025;**19**(3):303–8.
19. Mohammadzadeh I, Niroomand B, Tajerian A, Shahnazian Z, Nouri Z, Mortezaei A. Coagulopathy at admission in traumatic brain injury and its association with hematoma progression: A systematic review and meta-analysis of 2411 patients. *Clin Neurol Neurosurg*. 2025;**249**:108699.
20. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol*. 2010;**25**(9):603–5.
21. Johnson ED, Schell JC, Rodgers GM. The D-dimer assay. *Am J Hematol*. 2019;**94**(7):833–9.
22. Cardenas JC, Wade CE, Cotton BA, George MJ, Holcomb JB, Schreiber MA, et al. TEG Lysis Shutdown Represents Coagulopathy in Bleeding Trauma Patients: Analysis of the PROPPR Cohort. *Shock*. 2019;**51**(3):273–83.
23. on between D-dimer levels and long-term neurological outcomes of patients with traumatic brain injury: an analysis of a nationwide observational neurotrauma database in Japan. *Neurocritical Care*. 2022;**36**(2):483–91.
24. Ishii K, Kinoshita T, Kiridume K, Watanabe A, Yamakawa K, Nakao S, et al. Impact of initial coagulation and fibrinolytic markers on mortality in patients with severe blunt trauma: a multicentre retrospective observational study. *Scand J Trauma Resusc Emerg Med*. 2019;**27**(1):25.
25. Li D, Fang F, Zhao G. Multiple trauma severity associated with levels of plasma thrombomodulin, activated protein c, and d-dimer. *Int J Clin Exp Med*. 2020;**13**(3):1973–8.
26. Lv K, Yuan Q, Fu P, Wu G, Wu X, Du Z, et al. Impact of fibrinogen level on the prognosis of patients with traumatic brain injury: a single-center analysis of 2570 patients. *World J Emerg Surg*. 2020;**15**(1):54.
27. Otsuka H, Sakoda N, Uehata A, Sato T, Sakurai K, Aoki H, et al. Indications for early plasma transfusion and its optimal use following trauma. *Acute Med Surg*. 2020;**7**(1):e593.
28. Peng G, Wang Q, Sun H, Gan L, Lu H, Deng Z, et al. Development and prospective validation of a novel risk score for predicting the risk of lower extremity deep vein thrombosis among multiple trauma patients. *Thromb Res*. 2021;**201**:116–22.
29. Yumoto T, Naito H, Yamakawa Y, Iida A, Tsukahara K, Nakao A. Venous thromboembolism in major trauma patients: a single-center retrospective cohort study of the epidemiology and utility of D-dimer for screening. *Acute medicine & surgery*. 2017;**4**(4):394–400.
30. Nakama R, Yamamoto R, Izawa Y, Tanimura K, Mato T. Serum D-dimer level as a biomarker for identifying patients with isolated injury to prevent unnecessary whole-body computed tomography in blunt trauma care. *Scand J Trauma Resusc Emerg Med*. 2021;**29**(1):12.
31. Jiang RM, Pourzanjani AA, Cohen MJ, Petzold L. Associations of longitudinal D-Dimer and Factor II on early trauma survival risk. *BMC Bioinformatics*. 2021;**22**(1):122.
32. Raza I, Davenport R, Rourke C, Platton S, Manson J, Spoors C, et al. The incidence and magnitude of fibrinolytic activation in trauma patients. *J Thromb Haemost*. 2013;**11**(2):307–14.
33. Rong Z, Yao Y, Chen D, Song K, Zheng M, Jiang Q. The incidence of deep venous thrombosis before arthroscopy among patients suffering from high-energy knee trauma. *Knee Surg Sports Traumatol Arthrosc*. 2016;**24**(5):1717–21.
34. Shaz BH, Winkler AM, James AB, Hillyer CD, MacLeod JB. Pathophysiology of early trauma-induced coagulopathy: emerging evidence for hemodilution and coagulation factor depletion. *J Trauma*. 2011;**70**(6):1401–7.
35. Knudson MM, Moore EE, Kornblith LZ, Shui AM, Brakenridge S, Bruns BR, et al. Challenging Traditional Paradigms in Posttraumatic Pulmonary Thromboembolism. *JAMA Surg*. 2022;**157**(2):e216356.
36. MacDonald DRW, Neilly D, Schneider PS, Bzovsky S, Sprague S, Axelrod D, et al. Venous Thromboembolism in Hip Fracture Patients: A Subanalysis of the FAITH and HEALTH Trials. *J Orthop Trauma*. 2020;**34 Suppl 3**:S70–s5.
37. Wang H, Pei H, Ding W, Yang D, Ma L. Risk factors of postoperative deep vein thrombosis (DVT) under low molecular weight heparin (LMWH) prophylaxis in patients with thoracolumbar fractures caused by high-energy injuries. *J Thromb Thrombolysis*. 2021;**51**(2):397–404.
38. Wang P, Yan X, Fei C, Zhang B, Xing J, Zhang K, et al. Incidence and risk factors of clinically important venous thromboembolism in tibial plateau fractures. *Sci Rep*. 2022;**12**(1):20206.
39. Allard CB, Scarpelini S, Rhind SG, Baker AJ, Shek PN, Tien H, et al. Abnormal coagulation tests are associated with progression of traumatic intracranial hemorrhage. *J Trauma*. 2009;**67**(5):959–67.
40. Lee DH, Lee BK, Noh SM, Cho YS. High fibrin/fibrinogen degradation product to fibrinogen ratio is associated with 28-day mortality and massive transfusion in severe trauma. *Eur J Trauma Emerg Surg*. 2018;**44**(2):291–8.
41. Chen X, Wang X, Liu Y, Guo X, Wu F, Yang Y, et al. Plasma D-dimer levels are a biomarker for in-hospital complications and long-term mortality in patients with traumatic brain injury. *Front Mol Neurosci*. 2023;**16**:1276726.
42. Tian HL, Chen H, Wu BS, Cao HL, Xu T, Hu J, et al. D-dimer as a predictor of progressive hemorrhagic injury in patients with traumatic brain injury: analysis of 194 cases. *Neurosurg Rev*. 2010;**33**(3):359–65; discussion 65–6.
43. Tong WS, Zheng P, Zeng JS, Guo YJ, Yang WJ, Li GY, et al. Prognosis analysis and risk factors related to progressive intracranial haemorrhage in patients with acute traumatic brain injury. *Brain Inj*. 2012;**26**(9):1136–42.
44. Yuan F, Ding J, Chen H, Guo Y, Wang G, Gao WW, et al. Predicting

outcomes after traumatic brain injury: the development and validation of prognostic models based on admission characteristics. *J Trauma Acute Care Surg*. 2012;**73**(1):137–45.

45. Kotani S, Murakami N, Doi T, Ogawa T, Hashimoto N. Acute epidural vertex hematoma with good hemostasis using delayed surgery after monitoring of coagulation and fibrinolytic parameters: A case report. *Surg Neurol Int*. 2023;**14**:73.

46. Kabrhel C, Mark Courtney D, Camargo CA, Jr., Plewa MC, Nordenholz KE, Moore CL, et al. Factors associated with positive D-dimer results in patients evaluated for pulmonary embolism. *Acad Emerg Med*. 2010;**17**(6):589–97.

47. Sun C, Xi F, Li J, Yu W, Wang X. Longitudinal D-Dimer Trajectories and the Risk of Mortality in Abdominal Trauma Patients: A Group-Based Trajectory Modeling Analysis. *J Clin Med*. 2023;**12**(3).

48. Hayakawa M, Maekawa K, Kushimoto S, Kato H, Sasaki J, Ogura H, 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**(3):308–14.

49. Zhu YJ, Huang XK. Relationship between disseminated intravascular coagulation and levels of plasma thrombinogen segment 1+2, D-dimer, and thrombomodulin in patients with multiple injuries. *Chin J Traumatol*. 2009;**12**(4):203–9.

50. Gall LS, Vulliamy P, Gillespie S, Jones TF, Pierre RSJ, Breukers SE, et al. The S100A10 Pathway Mediates an Occult Hyperfibrinolytic Subtype in Trauma Patients. *Ann Surg*. 2019;**269**(6):1184–91.

51. Zanza C, Romenskaya T, Racca F, Rocca E, Piccolella F, Piccioni A, et al. Severe Trauma-Induced Coagulopathy: Molecular Mechanisms Underlying Critical Illness. *Int J Mol Sci*. 2023;**24**(8).

52. Johansson PI, Stensballe J, Rasmussen LS, Ostrowski SR. High circulating adrenaline levels at admission predict increased mortality after trauma. *J Trauma Acute Care Surg*. 2012;**72**(2):428–36.

53. Yang Z, Le TD, Simovic MO, Liu B, Fraker TL, Cancio TS, et al. Traumatized triad of complementopathy, endotheliopathy, and coagulopathy - Impact on clinical outcomes in severe polytrauma patients. *Front Immunol*. 2022;**13**:991048.