

Original Article

Coagulation biomarkers as predictors of transfusion outcomes in trauma patients

Yude Jin¹, Liping Fei²

¹Department of General Surgery, First Affiliated Hospital of Huzhou University, Huzhou 313000, Zhejiang, China;

²Department of Intensive Care Unit, First Affiliated Hospital of Huzhou University, Huzhou 313000, Zhejiang, China

Received April 24, 2025; Accepted July 23, 2025; Epub August 15, 2025; Published August 30, 2025

Abstract: Objective: To investigate the role of coagulation biomarkers (fibrinogen [FIB], fibrin degradation products [FDP], D-dimer [D-D], FDP/FIB ratio) in predicting transfusion outcomes in trauma patients. Methods: A retrospective analysis of 112 trauma cases (May 2020-May 2024) stratified into good (n=80) and poor prognosis (n=32) groups based on transfusion outcomes was conducted. Pre-transfusion levels of coagulation biomarkers were compared between groups. Pearson correlation assessed associations among markers, and logistic regression identified outcome predictors. Clinical parameters, including blood pressure, complete blood count, and coagulation function, were also considered. The predictive value was evaluated through receiver operating characteristic curve analysis. Results: The poor prognosis group exhibited lower FIB but higher FDP, D-D, FDP/FIB ratio, and white blood cell count (WBC) (all $P<0.01$). Additionally, this group had longer prothrombin time and activated partial thromboplastin time (both $P<0.01$) as well as greater plasma transfusion volumes ($P<0.05$). An inverse relationship was identified between FIB and FDP/D-D levels across prognosis groups. However, positive FDP/D-D correlation was observed only in the poor prognosis group, with no significant FDP/D-D linkage found in the good prognosis group; moreover, these correlations were stronger in cases with worse clinical outcomes. Multivariate analysis identified FIB, FDP, D-D, and WBC as independent predictors. The combined biomarker model (area under the curve (AUC) =0.923) outperformed individual markers (AUC range: 0.691-0.809). Conclusion: FIB, FDP, D-D, and WBC are significant predictors of transfusion outcomes in trauma patients. A combined biomarker model demonstrates superior predictive performance, highlighting the importance of identifying coagulation dysregulation in trauma prognosis.

Keywords: Fibrinogen, fibrin degradation products, D-dimer, fibrin degradation products/fibrinogen ratio, trauma-induced coagulopathy, blood transfusion, outcome prediction

Introduction

Trauma, including any bodily injury resulting from external forces or internal mechanisms, whether accidental or deliberate, stands as both a predominant cause of death worldwide and a formidable challenge to global public health [1]. Current epidemiological evidence indicates that traumatic injuries claim approximately 6 million lives each year, representing nearly 10% of global mortality [2, 3]. Particularly alarming is the disproportionate impact on younger populations, where trauma-related deaths exceed the total mortality from all cancers combined [4]. In severe cases, substantial hemorrhage frequently occurs and may progress to life-threatening hemorrhagic shock,

with clinical evidence suggesting that uncontrolled bleeding contributes to over 30% of all trauma-associated deaths [5]. Transfusion therapy constitutes an indispensable life-saving intervention for such critically injured patients, fulfilling vital functions including circulatory volume restoration, hemodynamic stabilization, tissue perfusion improvement, and prevention of both immediate and delayed organ dysfunction [6]. Nevertheless, this treatment carries inherent risks, with a significant proportion of trauma patients developing transfusion-related complications ranging from relatively mild allergic reactions and febrile non-hemolytic transfusion reactions to severe outcomes like transfusion-related acute lung injury, circulatory overload, immune dysregulation, iron accu-

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mulation disorders, and even death [7, 8]. This clinical dilemma underscores the urgency for reliable predictive biomarkers.

Among potential biomarkers, the coagulation cascade shows particular promise. Fibrinogen (FIB), the crucial precursor of fibrin clots, has demonstrated prognostic value in massively transfused trauma cases and may have therapeutic potential [9]. Fibrin degradation products (FDP) have exhibited strong correlations with injury severity and mortality risk among varied trauma cohorts, independent of concomitant head injuries [10]. D-dimer (D-D), a reliable indicator of post-traumatic fibrinolytic activation, reflects tissue damage extent and has been validated for predicting both early mortality and massive transfusion requirements [11]. The FDP/FIB ratio has shown unique predictive capabilities for transfusion requirements of packed red blood cells (RBCs) in blunt trauma and for early hemorrhagic complications in newly diagnosed acute promyelocytic leukemia [12, 13]. Despite these individual associations, the existing literature lacks comprehensive predictive models for transfusion outcomes in trauma populations. This study, therefore, aims to evaluate the combined predictive value of FIB, FDP, D-D, and FDP/FIB ratio for transfusion outcomes in trauma patients, with the ultimate goal of facilitating more precise and personalized transfusion strategies and lowering mortality.

Materials and methods

Case selection

Stringent inclusion and exclusion criteria were established to ensure study validity. Inclusion criteria required patients to: (1) be adults (≥ 18); (2) present to trauma center within 24 hours post-injury; (3) demonstrate clinical indications for transfusion therapy; (4) complete all treatment at the First Affiliated Hospital of Huzhou University without inter-facility transfer; (5) receive initial medical intervention exclusively by our team; and (6) have intact medical records. Exclusion criteria systematically eliminated potential confounders, including: (1) recent use of anticoagulants or fibrinolytic agents; (2) pregnancy or lactation; (3) fatal injuries (e.g., decapitation, postmortem changes); (4) preexisting hematologic disorders (e.g.,

coagulopathies, leukemias, or anemias); (5) severe chronic organ dysfunction (cardiac, cerebral, or renal); and (6) malignancies. Following approval by the Institutional Ethics Committee of First Affiliated Hospital of Huzhou University, we identified 112 eligible trauma patients treated between May 2020 and May 2024 through rigorous screening. Participants were categorized by transfusion outcomes into two prognostic groups: good prognosis ($n=80$) and poor prognosis ($n=32$). Poor prognosis was operationally defined as encompassing three specific endpoints: (1) in-hospital mortality or (2) discharge due to therapeutic futility; (3) all other outcomes were considered favorable.

Intervention methods

All enrolled patients received immediate stabilization according to our institutional trauma protocol, which included: (1) supplemental oxygen administration, (2) continuous vital sign monitoring, (3) peripheral intravenous access establishment, and (4) initial volume resuscitation with lactated Ringer's solution. Transfusion strategies were dynamically adjusted according to quantitative blood loss assessment. In cases of blood loss exceeding 1,000 mL, the protocol mandated transfusion of leukoreduced packed RBCs coupled with fresh frozen plasma (FFP), with the therapeutic target of maintaining hemoglobin levels between 80-100 g/L through serial monitoring. For patients with catastrophic hemorrhage (defined as $>80\%$ total blood volume loss), we implemented an enhanced massive transfusion protocol comprising three essential adjuncts to RBCs and FFP: (1) weight-adjusted platelet concentrates (1.0-1.5 units/10 kg), (2) cryoprecipitate, and (3) continuous central venous pressure monitoring targeting 8.9-11.0 mmHg (1.18-1.47 kPa).

Data collection and outcome measures

(1) Coagulation biomarkers: Morning fasting venous blood samples (3 mL) were collected from patients. Following centrifugation, serum samples were obtained for analysis. FIB and FDP levels were measured using the clotting technique, with the FDP/FIB ratio subsequently computed. D-D expression was determined by an immunoturbidimetric assay.

(2) Blood pressure: All participants underwent blood pressure measurement using a sphyg-

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Table 1. Comparison of baseline clinical characteristics

Indicators	Good prognosis group (n=80)	Poor prognosis group (n=32)	χ^2/t	P
Gender			0.306	0.580
Male	48 (60.00)	21 (65.63)		
Female	32 (40.00)	11 (34.38)		
Age (years)	49.64±10.28	52.00±7.63	1.174	0.243
Body mass index (kg/m ²)	22.98±2.31	23.19±2.52	0.423	0.673
Injury mechanism			3.307	0.347
Car accident	40 (50.00)	20 (62.50)		
Fall from height	22 (27.50)	4 (12.50)		
Ground-level fall	9 (11.25)	3 (9.38)		
Others	9 (11.25)	5 (15.63)		
Injury Severity Score (points)	21.36±3.51	21.16±2.86	0.286	0.775

momanometer, with both systolic (SBP) and diastolic blood pressure (DBP) recorded.

(3) Complete blood count: Serum samples were analyzed by an automated hematology analyzer for white blood cell count (WBC), platelet count, and hemoglobin levels.

(4) Coagulation function: An automated coagulation analyzer was utilized to document serum prothrombin time (PT), activated partial thromboplastin time (APTT), and international normalized ratio.

(5) Transfusion parameters: Transfusion-related data (packed RBCs, FFP, platelets, and cryoprecipitate) were prospectively collected.

Statistical analysis

Data analysis was performed using Statistical Product and Service Solutions 22.0 by International Business Machines Corporation for statistical computations and GraphPad Prism 7.0 by GraphPad Software for graphical representation. Continuous variables were expressed as mean \pm standard error of the mean and compared using independent Student's t-tests. Categorical variables were presented as frequencies (percentages) and assessed using χ^2 tests. Pearson correlation analysis was used to identify associations among FIB, FDP, and D-D. Multivariate binary logistic regression models were constructed to identify independent predictors of transfusion outcomes. Predictive performance was evaluated through receiver operating characteristic curve analysis, with area under the curve (AUC) values calculated. All statistical tests were two-sided, with $P < 0.05$ considered statistically significant.

Results

Comparison of baseline clinical characteristics

Comparative analysis of baseline characteristics revealed no significant differences between the poor and good prognosis groups in terms of demographic or clinical parameters (all $P > 0.05$). As detailed in **Table 1**, the two groups were well-matched with respect to sex distribution, age, body mass index, injury mechanisms, and Injury Severity Score.

Comparison of coagulation biomarkers

Comparative analysis of coagulation parameters (FIB, FDP, D-D, and FDP/FIB ratio) revealed significant differences between prognostic groups (all $P < 0.01$). As shown in **Figure 1**, patients with poor outcomes exhibited lower FIB levels but higher FDP, D-D, and FDP/FIB ratio compared to those in the good prognosis group (all $P < 0.01$).

Correlation analysis among FIB, FDP, and D-D

Pearson correlation analysis demonstrated significant interrelationships among FIB, FDP, and D-D in trauma patients (**Table 2**). Specifically, negative correlations were observed between FIB and both FDP and D-D (both $P < 0.05$), while a significant positive correlation was found between FDP and D-D ($P < 0.001$).

Comparison of correlations among FIB, FDP, and D-D

Negative correlations were identified between FIB and FDP/D-D in the good prognosis group (all $P < 0.05$), but without significant FDP/D-D

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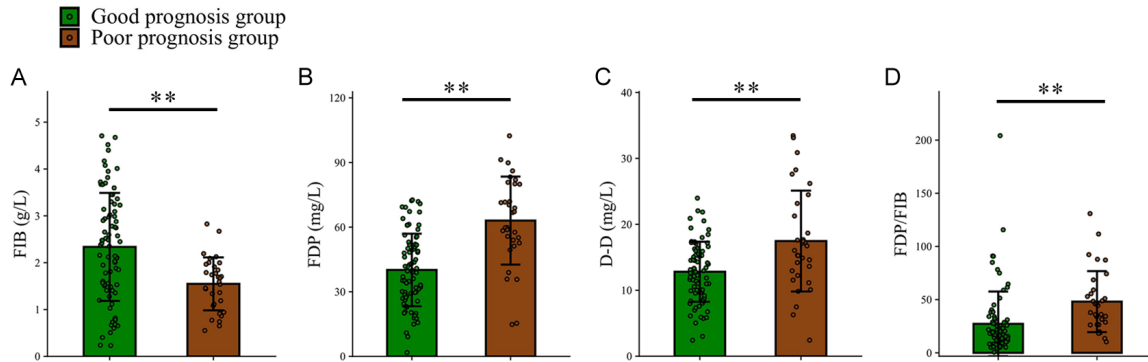


Figure 1. Comparison of coagulation biomarkers. A. FIB levels in good and poor prognosis groups. B. FDP levels in good and poor prognosis groups. C. D-D concentrations in good and poor prognosis groups. D. FDP/FIB ratio in good and poor prognosis groups. Note: **P<0.01; FIB, fibrinogen; FDP, fibrin degradation products; D-D, D-dimer.

Table 2. Correlation analysis among FIB, FDP, and D-D

Indicators	r	P
FIB vs. FDP	-0.323	0.010
FIB vs. D-D	-0.351	0.004
FDP vs. D-D	0.340	<0.001

Note: FIB, fibrinogen; FDP, fibrin degradation products; D-D, D-dimer.

linkage ($P>0.05$). Among those with poor prognoses, inverse correlations were noted between FIB and FDP/D-D (all $P<0.01$), along with positive FDP/D-D association ($P<0.05$). An important observation is that these correlations were less pronounced in the good prognosis group but strengthened markedly in the poor prognosis group (Table 3).

Comparison of blood pressure parameters

No statistically significant differences (both $P>0.05$) in either SBP or DBP measurements were found between the two groups (Figure 2).

Comparison of complete blood count parameters

WBC significantly differed between the good and poor prognosis groups ($P<0.01$), with higher values observed in the poor prognosis group. In contrast, platelet count and hemoglobin levels showed no obvious intergroup differences (both $P>0.05$) (Figure 3).

Comparison of coagulation function

PT and APTT were significantly prolonged in the poor prognosis group compared with the good

Table 3. Comparison of correlations among FIB, FDP, and D-D

Indicators	r	P
Good prognosis group		
FIB vs. FDP	-0.240	0.032
FIB vs. D-D	-0.237	0.035
FDP vs. D-D	0.209	0.063
Poor prognosis group		
FIB vs. FDP	-0.495	0.004
FIB vs. D-D	-0.554	0.001
FDP vs. D-D	0.444	0.011

Note: FIB, fibrinogen; FDP, fibrin degradation products; D-D, D-dimer.

prognosis group (both $P<0.01$). However, no evident intergroup difference was observed for international normalized ratio ($P>0.05$) (Figure 4).

Comparison of transfusion parameters

While no significant intergroup differences were found in transfusion volumes of packed RBCs, platelets, or cryoprecipitate ($P>0.05$), the poor prognosis group required greater volumes of FFP transfusion compared to the good prognosis group ($P<0.05$) (Table 4).

Analysis of factors influencing transfusion outcomes

The statistically significant factors identified in previous analyses - including FIB, FDP, D-D, FDP/FIB ratio, WBC, PT, APTT, and FFP transfusion volume - were selected as independent variables, with treatment outcomes as the dependent one. Multivariate logistic regression

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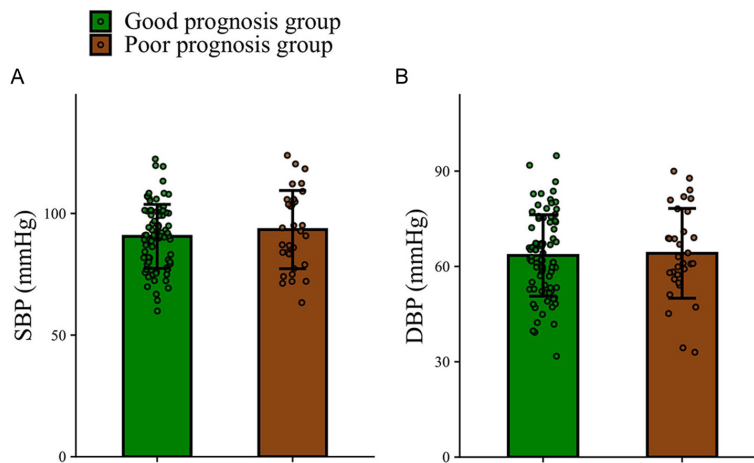


Figure 2. Comparison of blood pressure parameters. A. SBP in good and poor prognosis groups. B. DBP in good and poor prognosis groups. Note: SBP, systolic blood pressure; DBP, diastolic blood pressure.

analysis identified FIB, FDP, D-D, and WBC as independent predictors of transfusion outcomes (all $P < 0.05$), while FDP/FIB ratio, PT, APTT, and FFP transfusion volume showed no distinct association with transfusion outcomes (all $P > 0.05$) (Tables 5, 6).

Predictive value analysis for transfusion outcomes

Based on the results from the aforementioned logistic regression model, we evaluated the predictive performance of the identified independent factors (FIB, FDP, D-D, and WBC) both individually and in combination. Receiver operating characteristic curve analysis yielded the following detailed findings: FIB demonstrated moderate predictive capacity ($AUC = 0.712$), with an optimal cutoff at 2.27 g/L yielding 52.50% sensitivity and 93.75% specificity. FDP showed stronger predictive performance ($AUC = 0.809$), with a 52.50 mg/L cutoff providing 77.50% sensitivity and 78.13% specificity. D-D exhibited significant but relatively lower predictive ability ($AUC = 0.691$), achieving 65.00% sensitivity and 65.63% specificity at a 14.61 mg/L optimal cutoff. WBC displayed good predictive value ($AUC = 0.748$), with an $18.50 \times 10^9/L$ cutoff showing 83.75% sensitivity and 56.25% specificity. Most notably, the combined predictive model incorporating all four biomarkers demonstrated excellent performance ($AUC = 0.923$), with an optimal cutoff of 0.32 showing favorable sensitivity (85.00%) and specificity (87.50%) (Figure 5 and Table 7).

Discussion

Hemorrhage remains a leading cause of preventable mortality in trauma patients, with timely transfusion therapy serving as a critical intervention to mitigate this risk [14]. Despite advances in trauma care, suboptimal transfusion outcomes are observed in a substantial proportion of patients, underscoring the urgency for effective prognostic biomarkers [15]. Predictive modeling for transfusion outcomes has seen notable progress in recent years. Research by Borgman et al. [16] con-

firmed that using the trauma-associated severe hemorrhage (TASH) score to calculate optimal FFP/packed RBCs ratios significantly enhanced survival in major trauma cases. Similarly, Rijnhout et al. [17] established the efficacy of platelet-rich plasma/RBCs ratios in forecasting 30-day mortality in massive transfusion scenarios.

Our investigation shed light on the potential correlation and predictive implications of coagulation biomarkers (FIB, FDP, and D-D, as well as FDP/FIB ratio) for transfusion outcomes in trauma cases. The findings revealed that adverse prognostic outcomes correlated with lower FIB levels coupled with higher FDP, D-D, and FDP/FIB ratio, suggesting their potential utility in transfusion outcome predictions. Being an essential coagulation factor, FIB was predominantly produced in the liver and facilitated hemostasis by engaging in clot formation. However, therapeutic interventions like hypothermic or large-volume transfusion could markedly reduce FIB levels [18, 19]. FDP, a degradation product of FIB mediated by plasmin, correlated with fibrinolytic status. Elevated FDP concentrations were strongly associated with coagulopathy severity and increased bleeding risk [20]. D-D, a byproduct of cross-linked fibrin degradation, served as a specific marker for hyperfibrinolysis. Its elevated levels indicated concurrent activation of coagulation and fibrinolysis systems, and showed strong predictive value for unfavorable prognoses [21]. These alterations collectively contributed to increased

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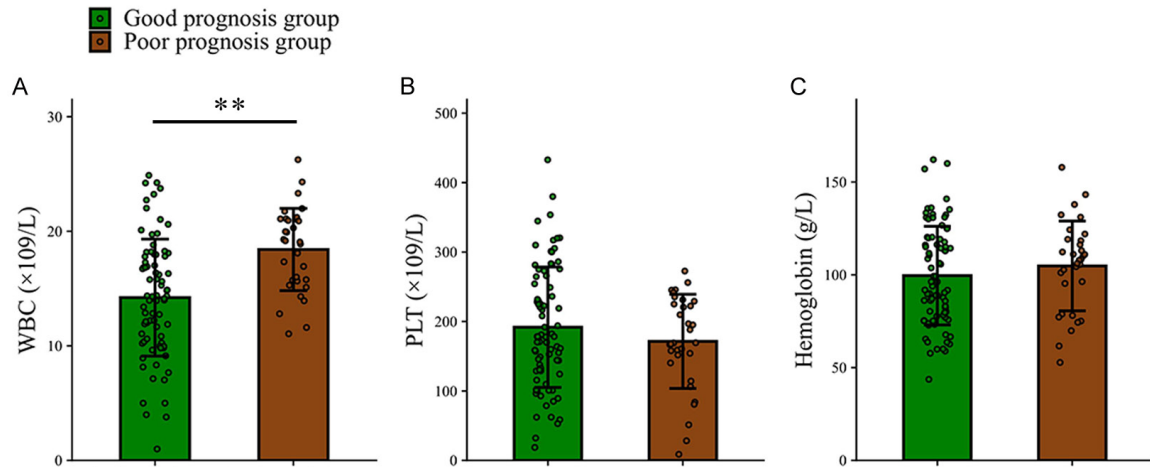


Figure 3. Comparison of complete blood count parameters. A. WBC in good and poor prognosis groups. B. Platelet count in good and poor prognosis groups. C. Hemoglobin concentration in good and poor prognosis groups. Note: ** $P < 0.01$; WBC, white blood cell count.

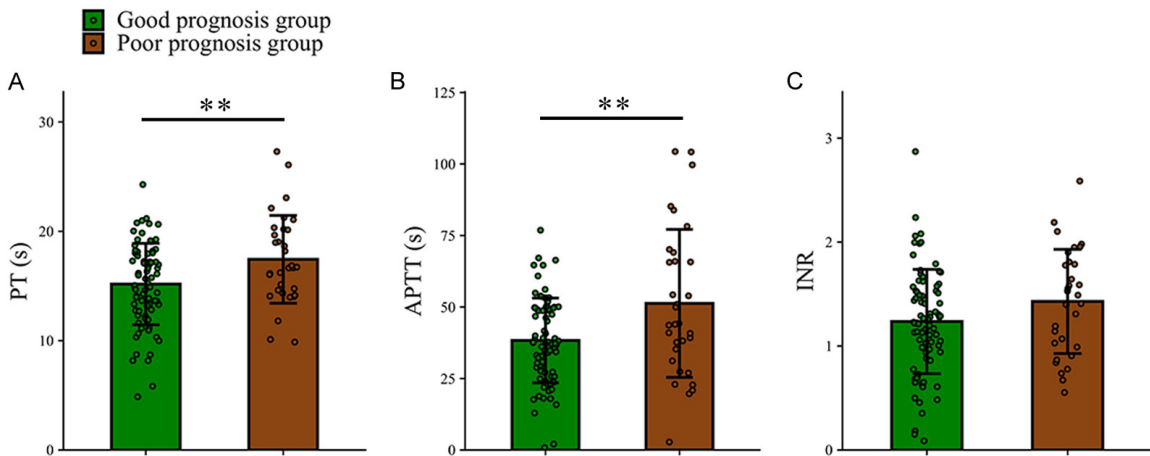


Figure 4. Comparison of Coagulation function. A. PT in good and poor prognosis groups. B. APTT in good and poor prognosis groups. C. International normalized ratio in good and poor prognosis groups. Note: ** $P < 0.01$; PT, Prothrombin time; APTT, activated partial thromboplastin time.

FDP/FIB ratios, indicating a critical imbalance between coagulation and fibrinolysis [13]. The correlation findings revealed that the negative association between FIB and FDP/D-D ratio in trauma patients with unfavorable outcomes, along with the positive correlation of FDP and D-D, fundamentally signified a breakdown in coagulation-fibrinolysis homeostasis, the degree of which correlated directly with clinical outcomes. The stronger negative correlation in the poor prognosis group further indicated that these patients faced a higher risk of trauma-induced coagulopathy, necessitating aggressive interventions such as massive transfusion or clotting factor replacement (e.g., cryoprecipi-

tate or antifibrinolytic agents). This subgroup might also be at increased risks of multi-organ dysfunction and mortality [22]. Conversely, the strong positive association detected in patients with adverse outcomes points to exaggerated fibrinolysis as a potential determinant of treatment failure [23].

Our extended observations revealed several clinically significant findings. Regarding blood pressure parameters, neither SBP nor DBP demonstrated any meaningful association with transfusion outcomes in our trauma cohort. In contrast, WBC served as an indicator of trauma severity, with higher levels often correlating

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Table 4. Comparison of transfusion parameters

Indicators	Good prognosis group (n=80)	Poor prognosis group (n=32)	χ^2/t	P
Packed RBCs transfusion volume (U)	6.58±4.00	8.34±4.88	1.972	0.051
FFP transfusion volume (mL)	578.65±253.03	731.55±230.62	2.960	0.004
Platelet transfusion volume			0.335	0.563
No	77 (96.25)	30 (93.75)		
Yes	3 (3.75)	2 (6.25)		
Cryoprecipitate transfusion volume			2.192	0.139
No	79 (98.75)	30 (93.75)		
Yes	1 (1.25)	2 (6.25)		

Note: RBCs, red blood cells; FFP, fresh frozen plasma.

Table 5. Analysis of variables influencing transfusion outcomes

Indicators	Variable	Assignment
FIB (g/L)	X1	Continuous variable
FDP (mg/L)	X2	Continuous variable
D-D (mg/L)	X3	Continuous variable
FDP/FIB ratio	X4	Continuous variable
WBC ($\times 10^9/L$)	X5	Continuous variable
PT (s)	X6	Continuous variable
APTT (s)	X7	Continuous variable
FFP transfusion volume (mL)	X8	Continuous variable
Transfusion outcome	Y	Good prognosis =0, poor prognosis =1

Note: FIB, fibrinogen; FDP, fibrin degradation products; D-D, D-dimer; WBC, white blood cell count; PT, prothrombin time; APTT, activated partial thromboplastin time; FFP, fresh frozen plasma.

Table 6. Multivariate analysis of factors influencing transfusion outcomes

Indicators	β	SE	Wald	P	OR	95% CI
FIB (g/L)	-1.997	0.883	5.113	0.024	0.136	0.024-0.766
FDP (mg/L)	0.092	0.031	8.896	0.003	1.097	1.032-1.165
D-D (mg/L)	0.176	0.056	9.964	0.002	1.192	1.069-1.330
FDP/FIB ratio	-0.038	0.027	2.057	0.152	0.962	0.913-1.014
WBC ($\times 10^9/L$)	0.236	0.095	6.193	0.013	1.266	1.051-1.525
PT (s)	0.121	0.103	1.359	0.244	1.128	0.921-1.382
APTT (s)	0.037	0.019	3.778	0.052	1.038	1.000-1.078
FFP transfusion volume (mL)	0.002	0.001	2.757	0.097	1.002	1.000-1.005

Note: FIB, fibrinogen; FDP, fibrin degradation products; D-D, D-dimer; WBC, white blood cell count; PT, prothrombin time; APTT, activated partial thromboplastin time; FFP, fresh frozen plasma.

with adverse clinical outcomes such as more severe injuries, increased hemorrhage, and greater impairment in coagulation function [24]. The prognostic value of WBC might stem from its role in immune modulation through its interactions with platelets and involvement in inflammatory cascades [25, 26]. Coagulation profiling further identified prolonged PT and APTT as significant predictors of poor progno-

sis, and these abnormalities potentially arose from multiple mechanisms, including dilutional coagulopathy from massive transfusion, trauma-induced disruption of coagulation-fibrinolysis equilibrium, and profound FIB depletion [27]. Transfusion therapy analysis yielded particularly noteworthy results. Patients with poor outcomes required substantially higher volumes of FFP transfusion compared to those

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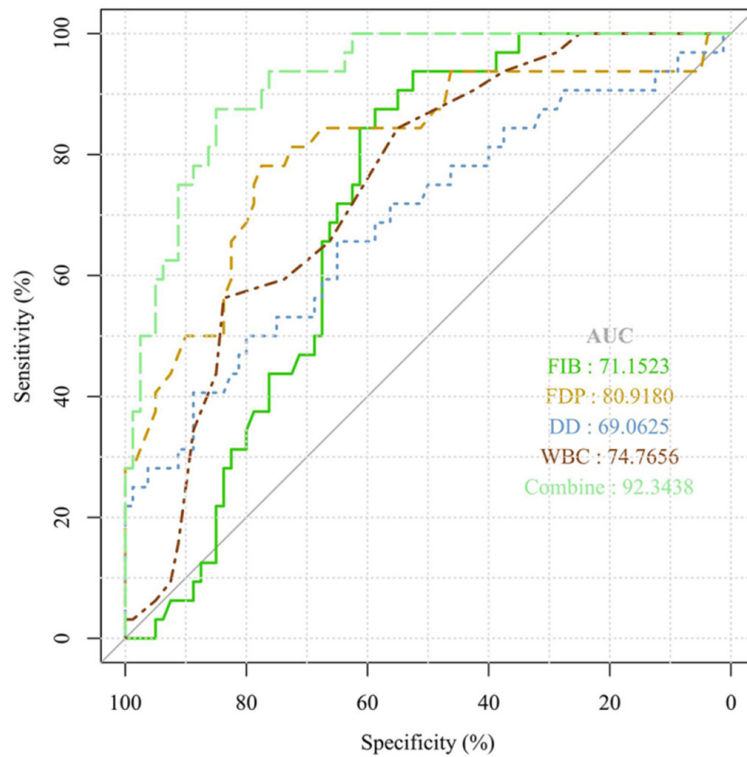


Figure 5. Predictive value analysis for transfusion outcomes. Note: AUC, area under the curve; FIB, fibrinogen; FDP, fibrin degradation products; D-D, D-dimer; WBC, white blood cell count.

with favorable outcomes, likely reflecting the complex interplay among coagulation factor consumption, trauma-induced coagulopathy, and hyperfibrinolysis in severe trauma cases [28, 29]. Our multivariate logistic regression analysis provided crucial insights into risk stratification. FIB emerged as a significant protective factor, while elevated FDP, D-D, and WBC as independent risk factors for poor transfusion outcomes. Specifically, trauma patients with low FIB, elevated FDP, D-D, and WBC levels demonstrated significantly worse transfusion outcomes. These findings aligned well with existing literature. For example, Rourke et al. [30] similarly identified low admission FIB as predictive of increased 24-hour and 28-day mortality, suggesting that early FIB replacement could potentially improve outcomes. Our results regarding D-D mirrored those of Lee et al. [31], who established D-D as an independent predictor of 28-day mortality in severe trauma patients. Quantitative predictive modeling revealed that while individual biomarkers exhibited moderate predictive value (AUC: 0.691-0.809), their integration into a unified

predictive model achieved superior discriminatory power (AUC=0.923), with excellent sensitivity (85.0%) and specificity (87.5%) at the optimal cutoff (probability >0.32). This represented a statistically and clinically significant improvement over any single parameter.

This research has several limitations that warrant consideration. First, the limited sample size increases the risk of model overfitting. Additionally, the lack of precise documentation of the interval between hospital admission and transfusion initiation may affect the interpretation of the predictive value of coagulation markers. Furthermore, the analysis of temporal variations in FIB, D-D, and other parameters was limited. These limitations highlight key areas for future research. Subsequent studies should aim to expand the

sample size to enhance the generalizability and robustness of the predictive model. It is also crucial to systematically record critical treatment timelines. A more comprehensive investigation into how these biomarkers correlate with different stages of trauma management would enhance the clinical relevance of the findings.

In summary, this study provides robust evidence that FIB, FDP, D-D levels, and the FDP/FIB ratio are strongly associated with transfusion outcomes in trauma patients. Moreover, severe trauma was characterized by the simultaneous progression of coagulation factor depletion and hyperfibrinolysis. Notably, FIB, FDP, D-D, and WBC were identified as independent predictors of clinical outcomes. Most importantly, the combination of these four biomarkers demonstrated superior prognostic utility, achieving significantly higher predictive accuracy than any individual parameter. This integrated approach offers clinicians a powerful tool for prognostic assessment in trauma patients requiring transfusion therapy.

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Table 7. Predictive value analysis for transfusion outcomes

Indicators	AUC	P	Best Cut-off Value	Sensitivity	Specificity	Accuracy
FIB (g/L)	0.712	<0.001	2.27	52.50%	93.75%	64.29%
FDP (mg/L)	0.809	<0.001	52.50	77.50%	78.13%	77.68%
D-D (mg/L)	0.691	<0.001	14.61	65.00%	65.63%	65.18%
WBC ($\times 10^9/L$)	0.748	<0.001	18.50	83.75%	56.25%	75.89%
Joint prediction	0.923	<0.001	0.32	85.00%	87.50%	85.71%

Note: AUC, area under the curve; FIB, fibrinogen; FDP, fibrin degradation products; D-D, D-dimer; WBC, white blood cell count.

Disclosure of conflict of interest

None.

Address correspondence to: Liping Fei, Department of Intensive Care Unit, First Affiliated Hospital of Huzhou University, Huzhou 313000, Zhejiang, China. Tel: +86-0572-2039308; E-mail: nmqk10-426@163.com

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