

## Original Article

# Effects of coagulation dysfunction and platelet changes on rebleeding and prognosis in acute subdural hematoma

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**Abstract:** Objective: To explore the correlation between coagulation indices (prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (APTT), fibrinogen (FIB), and D-dimer) and platelet indices (platelet count, mean platelet volume (MPV), and platelet distribution width (PDW)) and early rebleeding and 2-year prognosis in patients with acute subdural hematoma (aSDH), and to identify independent predictive factors. Methods: A retrospective analysis was performed on 413 aSDH patients treated in the neurosurgery department from February 2018 to February 2021 (training set: 314 patients; validation set: 99 patients). Relevant indices, baseline data, surgical procedures, and 2-year survival rates were recorded. Multivariate logistic/Cox regression analysis was used, and a nomogram model was constructed and validated using ROC curves. Results: There were no significant differences in baseline data between the two groups. The rebleeding rate in the training set was 29.3%. Patients with rebleeding had lower Glasgow Coma Scale (GCS) scores, higher PT, APTT, and MPV, lower FIB and platelet count, and a higher proportion undergoing craniotomy (all  $P < 0.05$ ). PT, APTT, and MPV were independent risk factors for rebleeding, while craniotomy, FIB, PLT, and GCS were protective factors. The AUC of the nomogram was 0.955 in the training set and 0.928 in the validation set. The 2-year survival rate was 33.70% in the rebleeding group and 88.29% in the non-rebleeding group ( $P < 0.001$ ). Rebleeding, traffic injuries, and prolonged PT were associated with higher mortality. Conclusion: Prolonged PT, INR, decreased FIB, and decreased platelet counts were associated with an increased risk of early rebleeding and poor 2-year prognosis in aSDH patients. Joint models can effectively stratify risks, but external validation is still required.

**Keywords:** Acute subdural hematoma, coagulation function, platelet indices, rebleeding, prognosis

## Introduction

Acute subdural hematoma (aSDH) is a high-mortality subtype of traumatic brain injury (TBI). In contemporary study series, aSDH accounts for approximately 15%-20% of traumatic intracranial hemorrhage, and despite modern treatment, the mortality rate in the most severe cases remains 30%-60% [1, 2]. Blood rapidly accumulates between the dura mater and arachnoid mater, often accompanied by cortical contusion and small vessel injury; edema and early inflammatory response further promote hematoma enlargement [3]. Even with decom-

pressive craniectomy (DC) or hematoma evacuation, approximately 20%-35% of cases experience early rebleeding (usually defined as CT-confirmed recurrent/progressive hemorrhage within 72 hours), which is associated with worse functional outcomes and higher mortality [4]. The causes of rebleeding cannot be explained solely by anatomic structure. Disruption of the blood-brain barrier (BBB), trauma-related coagulation dysfunction, and thrombin-fibrin homeostasis often coexist [5, 6]. In TBI, trauma-induced coagulation dysfunction manifests as prolonged prothrombin time (PT)/international normalized ratio (INR) or activated partial

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thromboplastin time (APTT), decreased fibrinogen, increased D-dimer, and platelet count/quality defects (decreased count, altered mean platelet volume (MPV)/platelet distribution width (PDW)). These abnormalities may increase the risk of early hematoma expansion and may also affect long-term prognosis. Traumatic coagulation dysfunction (TIC), characterized by coagulation abnormalities and hyperfibrinolysis, occurs in 20% to 50% of severe TBI cases and is independently associated with increased hemorrhagic complications and mortality [7, 8]. Coagulation indices such as PT, APTT, and FIB are widely used to assess hemostatic function: prolonged PT and APTT indicate impaired extrinsic and intrinsic coagulation pathways, respectively, while decreased FIB reflects the depletion of coagulation substrates [9]. Previous studies have shown that abnormalities in these indicators are associated with the expansion of hemorrhage in intracranial injury, but their specific role in rebleeding from aSDH remains unclear [10]. Platelets, as key mediators of primary hemostasis, play a crucial role in preventing the progression of bleeding by adhering to and aggregating at the site of vascular injury to form thrombi [11, 12]. In traumatic brain injury, the incidence of thrombocytopenia (platelet count (PLT)  $<150 \times 10^9/L$ ) and platelet dysfunction ranges from 15% to 30%, and these conditions are associated with increased bleeding risk and poor prognosis [13, 14]. In addition to platelet count, indicators such as MPV and plateletcrit (PCT) can reflect the activation status and reactivity of platelets: an elevated MPV indicates the presence of more immature, highly active platelets, while PCT is related to platelet quality and functional capacity [15, 16]. However, the clinical value of these indices in predicting rebleeding or long-term survival in aSDH remains controversial, with inconsistent results from small-scale studies.

The interaction between rebleeding and systemic factors such as age and comorbidities further complicates the prognostic assessment of aSDH [17, 18]. Although existing scoring systems (e.g., Marshall score, Glasgow Outcome Scale (GOS)) are used for risk stratification, their predictive accuracy is limited due to the lack of integration of hemostatic indices [19]. Recent cohort studies have indicated that coagulation abnormalities at admission (such

as prolonged PT/APTT or hypofibrinogenemia) are strong independent predictors of adverse outcome in traumatic brain injury [20, 21], but relevant data for aSDH remain scarce. Furthermore, the prognostic value of combining platelet indices with coagulation indices in this patient population has not been systematically evaluated. Therefore, this study aims to investigate the relationship between coagulation function (PT, APTT, FIB), platelet indices (PLT, PCT, MPV), and the risk of rebleeding and long-term survival in patients with acute subdural hematoma. Through multivariate regression and ROC curve analysis, we seek to identify reliable biomarkers to guide clinical decision-making, provide a basis for targeted interventions (such as fibrinogen supplementation and platelet transfusion), to ultimately improve patient outcome.

### Materials and methods

#### *General data*

This study retrospectively analyzed 413 patients with aSDH treated in the Department of Neurosurgery of Zhangye Second People's Hospital from February 2018 to February 2021 (training set: 314 cases; validation set: 99 cases). This study was conducted after approval by the Medical Ethics Committee of the Zhangye Second People's Hospital. The inclusion criteria were as follows: (1) confirmed by imaging examinations such as cranial CT or MRI [3]; (2) time from onset to admission  $\leq 24$  hours; (3) patients who underwent craniotomy for hematoma evacuation or burr hole drainage.

The exclusion criteria were as follows: (1) patients with severe liver and kidney failure, hematologic diseases or other diseases that may affect coagulation function; (2) patients with a history of coagulation dysfunction or long-term use of anticoagulants without sufficient discontinuation time; (3) patients with other severe intracranial injuries; (4) patients who were brain dead at admission or whose expected survival time was  $< 24$  hours.

#### *Data collection*

(1) Baseline Data: Baseline information of patients was collected (training set and validation set), including age, gender, cause of injury, Glasgow Coma Scale (GCS) score, and whether

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there were any concurrent injuries. (2) Fasting venous blood samples (5 mL) were collected from patients within 24 hours of admission. Coagulation indices - PT, APTT, and FIB - were measured using a fully automated coagulation analyzer (Sysmex CS-5100). Platelet parameters - platelet count (PLT), plateletcrit (PCT), and mean platelet volume (MPV) - were measured using a fully automated blood analyzer (Abbott CELL-DYN Ruby). All procedures were performed strictly in accordance with the instrument operating procedures and reagent kit instructions. (3) Rebleeding assessment: Rebleeding was defined as a  $\geq 20\%$  increase in hematoma volume or a  $\geq 2$ -point decrease in GCS score on CT scan within 48 hours after craniotomy [22]. Based on the occurrence of rebleeding, the training set was further divided into a rebleeding group (n=92) and a non-rebleeding group (n=222). (4) Prognostic follow-up: Patients in the training set were followed up for 2 years. Survival outcomes were tracked through outpatient follow-ups and telephone follow-ups, and 2-year survival rates were recorded.

### *Surgical methods*

Different surgical methods were selected based on the patient's condition, as follows: Craniotomy for hematoma evacuation (suitable for patients with high-density hematomas, combined with cerebral contusion, or increased intracranial pressure (ICP)): (1) Based on the maximum hematoma level located by CT, a frontotemporoparietal curved incision was made (starting from the upper edge of the zygomatic arch and extending posteriorly to the anterior aspect of the parietal tubercle), with a length of 10-12 cm; (2) 4-5 burr holes were drilled, and a bone flap with a diameter of 6-8 cm was formed using a craniotome. DCf was performed when ICP  $> 30$  mmHg; (3) The dura mater was incised, and the hematoma was removed under a microscope. Hemostasis was achieved using 15-20 W bipolar electrocoagulation, and hemostatic gauze was applied if necessary; (4) After irrigation, a drainage tube was placed. For patients who retain the bone flap, the bone flap was fixed, and the galea aponeurotica and skin are sutured in layers.

Burr hole drainage (applicable to patients with predominantly fluid-filled hematoma and GCS

score  $\geq 9$ ): (1) The thickest part of the hematoma was marked under CT guidance (avoiding lateral fissure vessels, selecting the frontal/temporal region 2-3 cm from the midline and 4 cm above the supraorbital crest); (2) Local anesthesia was administered (intravenous sedation was added for elderly/agitated patients). A 3 cm skin incision was made, a 1 cm burr hole was drilled, the dura mater was coagulated, and a "cross" incision was made. A 2 mm side-hole drainage tube was placed, aspirating no more than 50% of the total hematoma volume; (3) A closed drainage bag (10-15 cm below the head of the bed) was connected. Urokinase was injected 24 hours postoperatively, the tube was clamped for 2 hours and then was opened. The tube was removed when more than 80% of the hematoma had been cleared. The treatment plan employed a combination of "surgical-specific differentiated intervention + stratified dynamic monitoring": For craniotomy, complete hemostasis was achieved under direct vision, maintaining coagulation indices at near-critical levels (FIB  $\geq 1.535$  g/L, PLT  $\geq 147.655 \times 10^9$ /L), with monitoring at 24 and 48 hours post-surgery; for burr hole drainage, residual hematoma easily activated the fibrinolytic system, requiring an increased FIB target value of 1.8-2.2 g/L, with intensified monitoring at 6, 12, 24, and 48 hours post-surgery. For both surgical methods, interventions were adjusted promptly when indices became abnormal or approached critical levels, avoiding over-reliance on baseline data at admission.

### *Statistical analysis*

SPSS 26.0 software was used for statistical analysis. Quantitative data were expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ). Independent samples t-test was used for comparisons between two groups; one-way ANOVA was used for comparisons among multiple groups, and LSD-t tests were used for pairwise comparisons. Categorical data were expressed as number of cases (percentage) [n (%)], and chi-square tests were used for comparisons between groups. In the analysis of rebleeding risk factors, variables with  $P < 0.05$  in univariate analysis were included in a multivariate logistic regression model to identify independent risk factors for acute subdural hematoma rebleeding. Kaplan-Meier method was used for prog-

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**Table 1.** Comparison of baseline characteristics between the validation set and training set

| Variable                    | validation set (n=99)   | training set (n=314)    | Statistic | P value |
|-----------------------------|-------------------------|-------------------------|-----------|---------|
| Age (years)                 | 55.24±9.86              | 56.64±11.67             | -1.074    | 0.284   |
| Gender                      |                         |                         | 1.635     | 0.201   |
| Female                      | 29 (29.29%)             | 114 (36.31%)            |           |         |
| Male                        | 70 (70.71%)             | 200 (63.69%)            |           |         |
| Smoking history             |                         |                         |           |         |
| No                          | 69 (69.70%)             | 211 (67.20%)            | 0.215     | 0.643   |
| Yes                         | 30 (30.30%)             | 103 (32.80%)            |           |         |
| Alcohol consumption history |                         |                         |           |         |
| No                          | 64 (64.65%)             | 193 (61.46%)            | 0.324     | 0.569   |
| Yes                         | 35 (35.35%)             | 121 (38.54%)            |           |         |
| PT (s)                      | 14.39 [13.65, 15.00]    | 14.49 [13.14, 16.28]    | 1.039     | 0.299   |
| APTT (s)                    | 37.96 [36.48, 39.94]    | 38.84 [35.04, 42.56]    | 0.803     | 0.422   |
| FIB (g/L)                   | 1.91 [1.50, 2.23]       | 1.88 [1.46, 2.32]       | 0.555     | 0.579   |
| PLT ( $\times 10^9/L$ )     | 177.14 [145.88, 199.08] | 173.51 [142.12, 217.18] | 0.524     | 0.600   |
| PCT (%)                     | 0.19 [0.15, 0.21]       | 0.18 [0.16, 0.20]       | 1.202     | 0.229   |
| MPV (fL)                    | 10.64±1.09              | 10.77±1.71              | -0.727    | 0.468   |

Note: PT, Prothrombin Time; APTT, Activated Partial Thromboplastin Time; FIB, Fibrinogen; PLT, Platelet Count; PCT, Plateletcrit; MPV, Mean Platelet Volume.

nostic survival analysis, survival curves were plotted for the rebleeding group and the non-rebleeding group, and the prognostic differences between the two groups were compared using the Log-rank test. A multivariate Cox proportional hazards regression model was used to analyze prognostic risk factors to identify factors affecting patients' 2-year survival. To assess diagnostic efficacy, receiver operating characteristic (ROC) curves predicting 2-year survival outcomes for each indicator were plotted, and the area under the curve (AUC) was calculated. An AUC >0.7 indicates some diagnostic value, an AUC >0.8 indicates good diagnostic value, and an AUC >0.9 indicates high diagnostic value. Decision curve analysis (DCA) was used to assess the clinical utility of the model and clarify its applicability for various clinical decision-making scenarios. A *P* value <0.05 was considered significant.

Based on the previous aSDH rebleeding rate (30%), the sample size was estimated using G\*Power 3.1 software, with  $\alpha=0.05$ ,  $\beta=0.2$ , and effect size=0.3. A training set of  $\geq 286$  cases was required, and the validation set was set to 20%-30% of the training set ( $\geq 57$  cases), which this study met. For Logistic/Cox regression, each variable corresponded to  $\geq 10$  events (92 rebleeding cases,  $\geq 60$  deaths), meeting the variable requirements of the model.

## Results

### Comparison of baseline data

There were no significant differences in age, gender, smoking history, alcohol consumption history, coagulation indices (PT, APTT, FIB), or platelet indices (PLT, PCT, and MPV) (all  $P>0.05$ ), demonstrating comparability between the two sets of patients in terms of baseline data. See **Table 1**.

As shown in **Table 2**, there were no statistically significant differences in age, gender, or cause of injury between the non-bleeding group and the rebleeding group (all  $P>0.05$ ). The rebleeding group had a lower GCS score ( $P<0.001$ ). Regarding coagulation indicators and platelet parameters, the rebleeding group had longer PT and APTT, lower FIB and PLT (all  $P<0.001$ ), and higher MPV ( $P<0.001$ ), with no statistically significant difference in PCT ( $P=0.068$ ). The rebleeding group had a higher proportion of craniotomy and less intraoperative blood loss than the non-bleeding group (both  $P<0.05$ ).

### Independent factors influencing rebleeding within 48 hours after surgery in patients

The variables selected through univariate analysis (**Table 2**) were included in multivariate

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**Table 2.** Comparison of characteristics between the rebleeding and non-rebleeding groups in the training set

| Variable                           | Non-bleeding group<br>(n=222) | Rebleeding group<br>(n=92) | Statistic | P value |
|------------------------------------|-------------------------------|----------------------------|-----------|---------|
| <b>Baseline data</b>               |                               |                            |           |         |
| Age (years)                        | 59.00±12.32                   | 54.50±9.03                 | 1.948     | 0.051   |
| Gender                             |                               |                            | 0.861     | 0.353   |
| Female                             | 77 (34.68%)                   | 37 (40.22%)                |           |         |
| Male                               | 145 (65.32%)                  | 55 (59.78%)                |           |         |
| GCS score (points)                 | 9.00 [7.00, 10.00]            | 7.00 [5.00, 8.00]          | 7.862     | <0.001  |
| Cause of injury                    |                               |                            | 2.715     | 0.438   |
| Traffic accident                   | 95 (42.79%)                   | 42 (45.65%)                |           |         |
| Falling from height                | 56 (25.23%)                   | 28 (30.43%)                |           |         |
| Blunt trauma                       | 42 (18.92%)                   | 15 (16.30%)                |           |         |
| Others                             | 29 (13.06%)                   | 7 (7.61%)                  |           |         |
| <b>Coagulation indicators</b>      |                               |                            |           |         |
| PT (s)                             | 13.79 [12.98, 14.97]          | 16.34 [15.40, 18.41]       | 8.020     | <0.001  |
| APTT (s)                           | 36.86 [33.41, 40.13]          | 43.70 [42.31, 45.02]       | 9.160     | <0.001  |
| FIB (g/L)                          | 2.02 [1.73, 2.37]             | 1.35 [1.11, 1.52]          | 7.387     | <0.001  |
| <b>Platelet parameters</b>         |                               |                            |           |         |
| PLT ( $\times 10^9/L$ )            | 199.06 [165.62, 220.88]       | 129.97 [83.44, 144.76]     | 9.057     | <0.001  |
| PCT (%)                            | 0.18 [0.17, 0.21]             | 0.18 [0.16, 0.19]          | 1.385     | 0.068   |
| MPV (fL)                           | 10.46 [9.39, 11.15]           | 12.29 [11.88, 12.76]       | 8.353     | <0.001  |
| <b>Surgery-related indicators</b>  |                               |                            |           |         |
| Surgical method                    |                               |                            | 3.969     | 0.046   |
| Burr hole drainage                 | 55 (24.77%)                   | 33 (35.87%)                |           |         |
| Craniotomy for hematoma evacuation | 167 (75.23%)                  | 59 (64.13%)                |           |         |
| Intraoperative blood loss (ml)     | 368.5±132.6                   | 202.8±89.3                 | 12.47     | <0.001  |

Note: PT, Prothrombin Time; APTT, Activated Partial Thromboplastin Time; FIB, Fibrinogen; PLT, Platelet Count; PCT, Plateletcrit; MPV, Mean Platelet Volume; GCS, Glasgow Coma Scale.

logistic regression analysis. The results showed that surgical procedure, PT, APTT, FIB, PLT, MPV, and GCS score were all independent influencing factors for rebleeding within 48 hours after surgery (all  $P < 0.05$ ). Among the risk factors for rebleeding, APTT (HR=1.393, 95% CI=1.214-1.598,  $P < 0.001$ ), PT (HR=1.498, 95% CI=1.134-1.979,  $P = 0.004$ ), and MPV (HR=1.52, 95% CI=1.006-2.296,  $P = 0.047$ ) were risk factors; while craniotomy for hematoma evacuation (HR=0.092, 95% CI=0.016-0.524,  $P = 0.007$ ), FIB, PLT, and GCS score were protective factors. Specifically, compared to burr hole drainage, craniotomy for hematoma evacuation reduced the risk of postoperative rebleeding by 90.8% (1-0.092), as detailed in **Table 3**. It should be noted that univariate comparisons in **Table 2** demonstrated that the proportion of patients undergoing craniotomy was lower in the re-

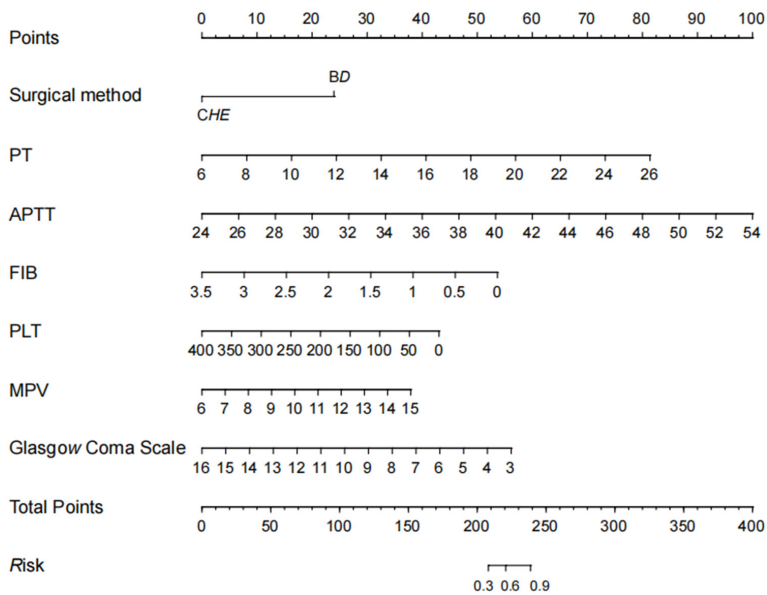
bleeding group (64.13%) than of the non-rebleeding group (75.23%), a difference attributable to the confounding effect of baseline disease severity between the two cohorts. Specifically, the rebleeding group presented with more severe injury, as evidenced by lower GCS scores (7 vs. 9 points) as well as marked abnormalities in coagulation and platelet indices. Despite the fact that craniotomy was preferentially performed in certain critically ill patients, its utilization rate remained lower than that in the non-rebleeding group with relatively mild baseline conditions. After adjusting for confounding variables via multivariate regression analysis, the therapeutic superiority of craniotomy was accurately elucidated: this approach allows direct visualization for hematoma evacuation and precise hemostasis, thus outperforming burr hole drainage. Craniotomy was there-

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**Table 3.** Independent influencing factors for rebleeding within 48 hours after surgery in patients by multivariate logistic regression analysis

| Variable        | B       | S.E.  | P value | HR    | Cutoff value                | 95% CI      |             |
|-----------------|---------|-------|---------|-------|-----------------------------|-------------|-------------|
|                 |         |       |         |       |                             | Lower bound | Upper bound |
| Surgical method | -2.381  | 0.885 | 0.007   | 0.092 | -                           | 0.016       | 0.524       |
| PT              | 0.404   | 0.142 | 0.004   | 1.498 | >15.975 s                   | 1.134       | 1.979       |
| APTT            | 0.331   | 0.07  | <0.001  | 1.393 | >43.70 s                    | 1.214       | 1.598       |
| FIB             | -1.523  | 0.553 | 0.006   | 0.218 | <1.535 g/L                  | 0.074       | 0.644       |
| PLT             | -0.011  | 0.005 | 0.028   | 0.989 | <147.655×10 <sup>9</sup> /L | 0.98        | 0.999       |
| MPV             | 0.419   | 0.21  | 0.047   | 1.52  | >12.29 fL                   | 1.006       | 2.296       |
| GCS             | -0.429  | 0.1   | <0.001  | 0.651 | <8 points                   | 0.536       | 0.792       |
| Constant        | -15.543 | 5.425 | 0.004   | 0     | -                           |             |             |

Note: 1. PT, Prothrombin Time; APTT, Activated Partial Thromboplastin Time; FIB, Fibrinogen; PLT, Platelet Count; MPV, Mean Platelet Volume; GCS, Glasgow Coma Scale. 2. Explanation of categorical variable: Surgical method is a categorical variable, with burr hole drainage as the reference. HR=0.092 indicates that craniotomy for hematoma evacuation can reduce the risk of postoperative rebleeding by 90.8%, with no cutoff value (marked as “-” in the table). 3. Correlation between HR and cutoff value of continuous variables: ① PT: HR=1.498, the risk of rebleeding increases by 49.8% for each 1 s prolongation, cutoff value >15.975 s, and the risk-increasing effect becomes more pronounced beyond this value; ② APTT: HR=1.393, the risk increases by 39.3% for each 1 s prolongation, cutoff value >43.70 s, and the risk-regulating effect is enhanced beyond this value; ③ FIB: HR=0.218, the risk decreases by 78.2% for each 1 g/L increase, cutoff value <1.535 g/L, and its protective effect is significantly weakened with increased rebleeding risk below this value; ④ PLT: HR=0.989, the risk decreases by 0.11% for each 1×10<sup>9</sup>/L increase, cutoff value <147.655×10<sup>9</sup>/L, and the protective effect is weakened with increased rebleeding risk below this value; ⑤ MPV: HR=1.52, the risk increases by 52% for each 1 fL increase, cutoff value >12.29 fL, and the risk-increasing effect is more obvious beyond this value; ⑥ GCS score: HR=0.651, the risk decreases by 34.9% for each 1-point increase, cutoff value <8 points, and the risk-reducing effect is weakened with increased rebleeding risk below this value.



**Figure 1.** Nomogram for evaluating the predictive ability of clinical factors for rebleeding risk. Note: PT, Prothrombin Time; APTT, Activated Partial Thromboplastin Time; FIB, Fibrinogen; PLT, Platelet Count; MPV, Mean Platelet Volume.

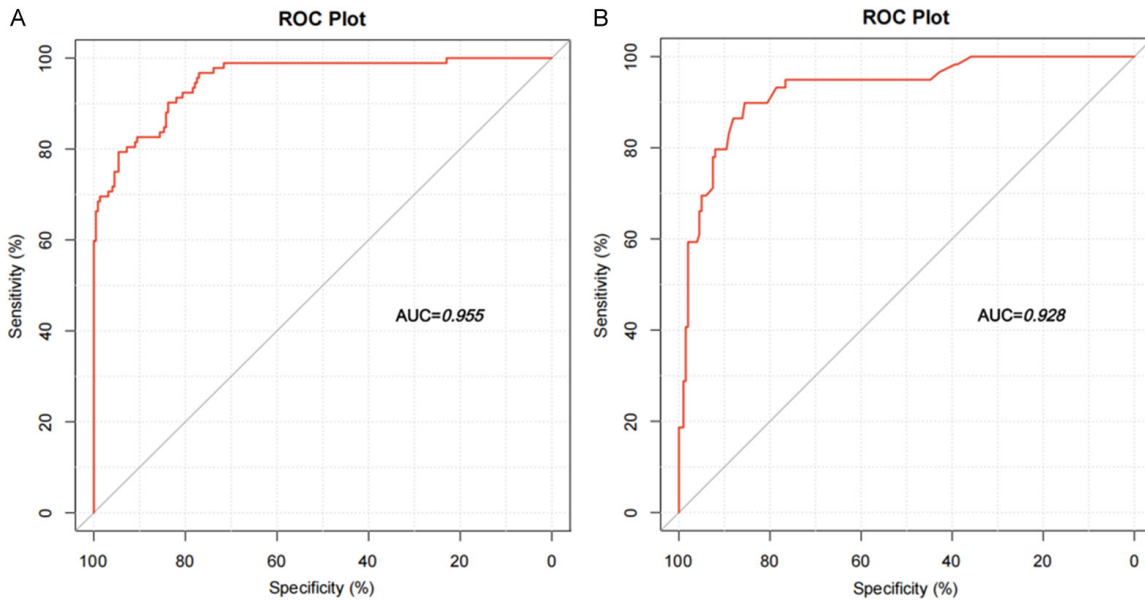
fore identified as a protective factor, an association that could not be reflected by simple univariate comparisons of procedural proportions.

### Nomogram-based risk prediction analysis using multivariate logistic regression

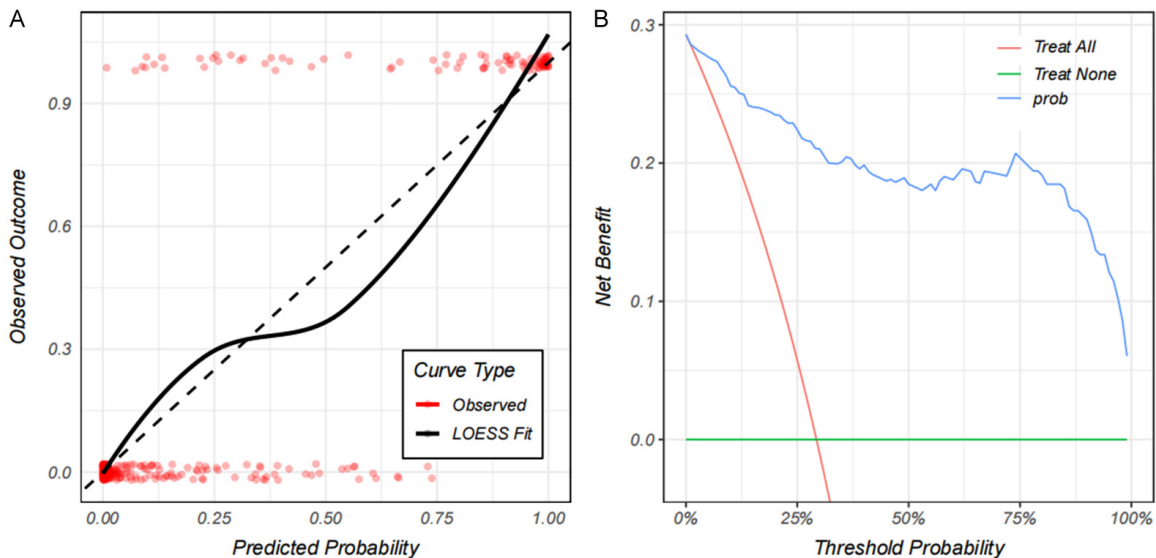
A nomogram was constructed based on multivariate logistic regression to assess the predictive efficacy of multiple clinical factors for rebleeding risk. By analyzing the score distribution of each variable in the nomogram and its correlation with the total score, we identified indicators with strong or weak associations with the risk of rebleeding. The results indicated that PT and APTT were strongly correlated indicators, as reflected by their wide score ranges and substantial contributions to risk prediction. FIB, PLT, and GCS score were also correlated with rebleeding risk. In contrast,

indicators such as surgical modality and MPV exhibited narrow score ranges, suggesting weak correlations with rebleeding risk (Figure 1).

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**Figure 2.** ROC curve for validating model performance. A. ROC curve of the training set. B. ROC curve of the validation set.

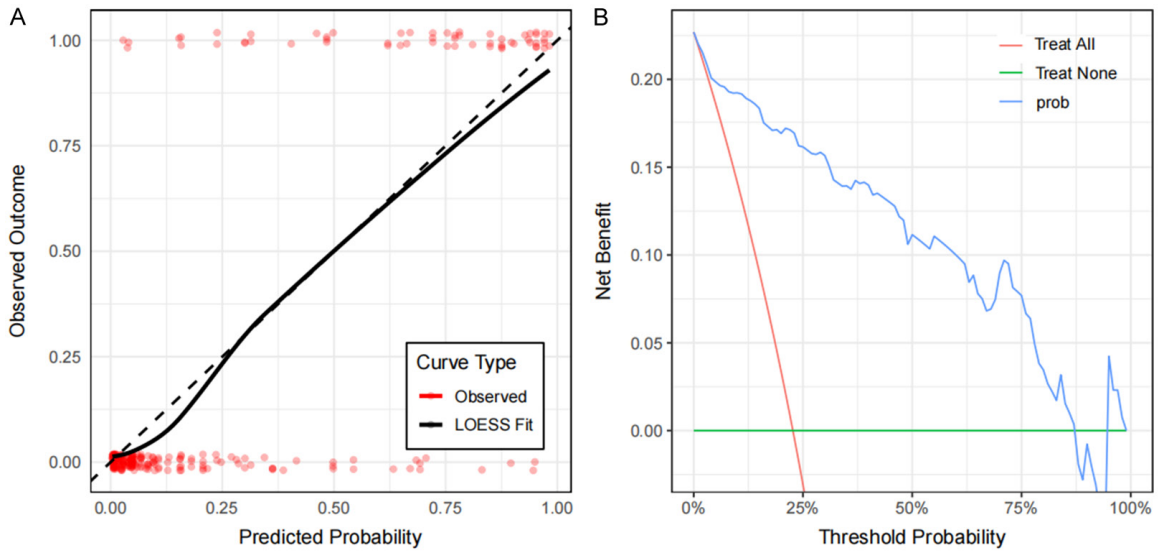


**Figure 3.** DCA and calibration curves of the training set for model performance validation. A. Calibration curve of the model. B. DCA curve of the model.

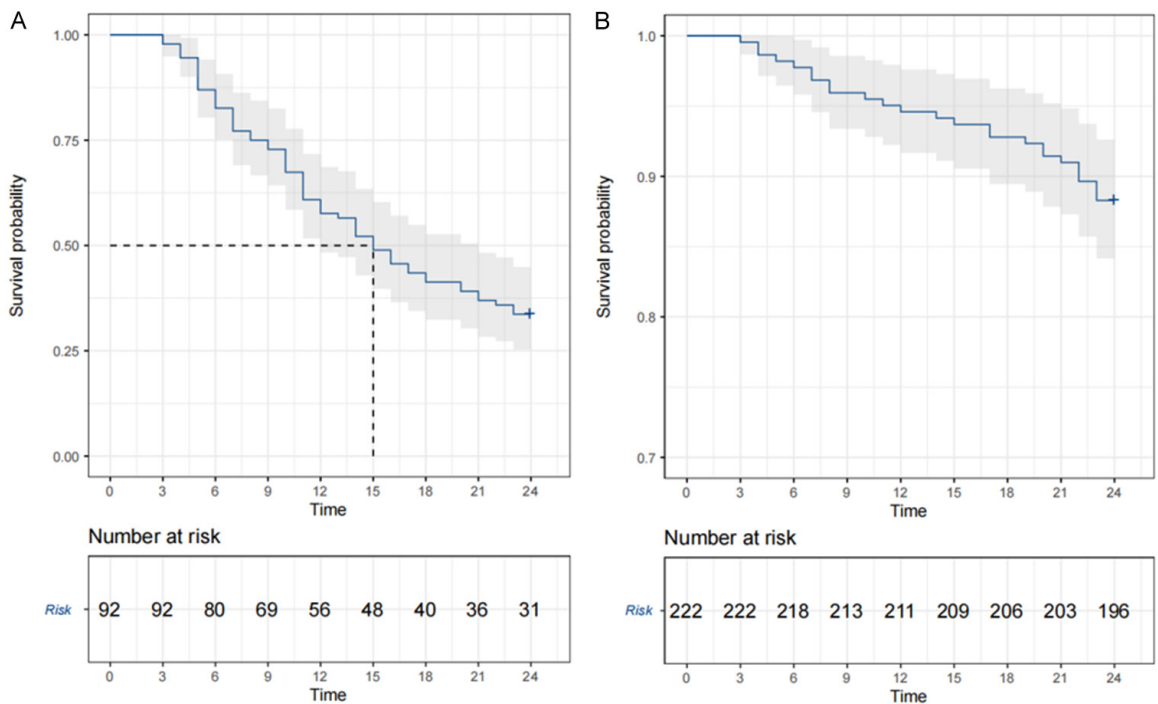
The ROC curves showed that the AUC for the training set was 0.955 (95% CI: 0.902-0.985,  $P < 0.001$ ), and the AUC for the validation set was 0.928 (95% CI: 0.884-0.960,  $P < 0.001$ ), indicating that the model had excellent discriminative ability (Figure 2). Meanwhile, calibration curves for the training and validation sets show a high degree of consistency between predicted and actual probabilities (training set:  $\chi^2 = 2.4127$ ,  $P = 0.42$ ; validation

set:  $\chi^2 = 3.7756$ ,  $P = 0.69$ ), suggesting that the model is overall significant and has outstanding calibration performance (Figures 3 and 4A). Furthermore, decision curve analysis (DCA) shows positive net benefits for both the training and validation sets within a risk threshold range of 0-80%, confirming the model's high clinical applicability across a wide range of decision-making scenarios (Figures 3 and 4B).

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**Figure 4.** DCA and calibration curves of the validation set for verification of model performance. A. Calibration curve of the model. B. DCA curve of the model.



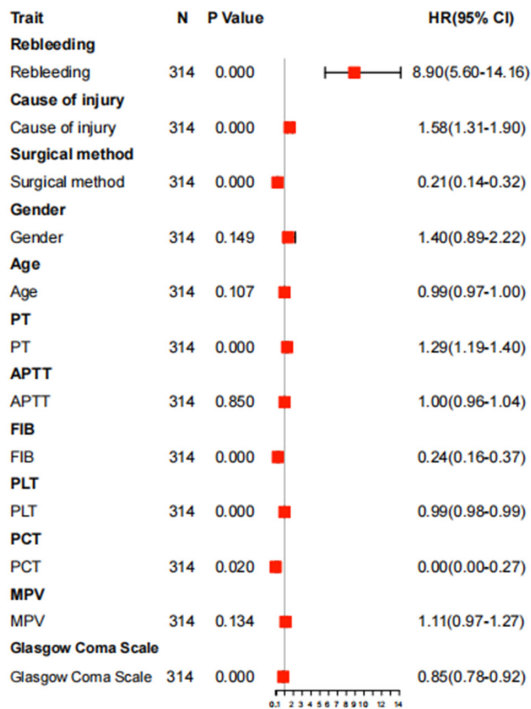
**Figure 5.** Survival curves of the rebleeding group and non-bleeding group at 2 years postoperatively. A. Kaplan-Meier survival curve of the rebleeding group. B. Kaplan-Meier survival curve of the non-bleeding group.

*2-year postoperative survival status of the rebleeding group versus the non-rebleeding group*

As shown in **Figure 5**, the survival rate of the rebleeding group decreased more significantly over time compared to the non-bleeding group

( $P < 0.001$ ). At 1 year, 56 patients survived in the rebleeding group, with a survival rate of 60.87%, significantly lower than the 90.09% survival rate of the non-bleeding group. At 2 years, 31 patients survived in the rebleeding group, with a survival rate of 33.70%, also significantly lower than the 88.29% survival rate

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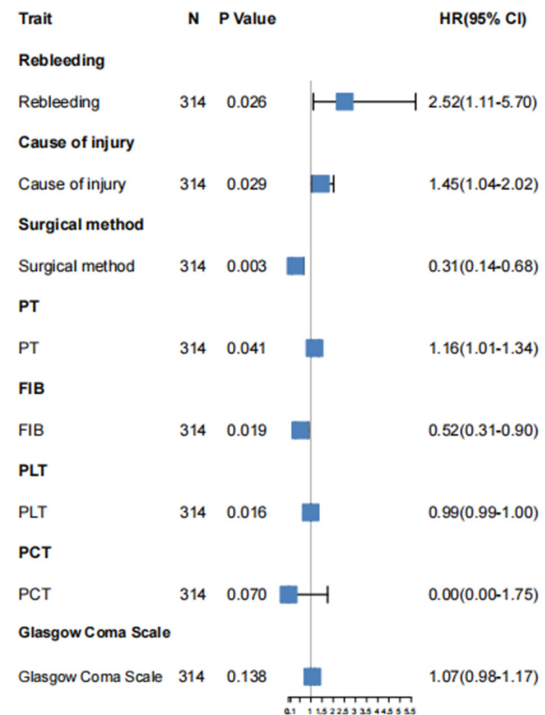
**Figure 6.** Forest plot of independent influencing factors for 2-year mortality in patients by univariate Cox regression analysis. Note: PT, Prothrombin Time; APTT, Activated Partial Thromboplastin Time; FIB, Fibrinogen; PLT, Platelet Count; PCT, Plateletcrit; MPV, Mean Platelet Volume.

of the non-bleeding group. These results indicate that rebleeding had a significant impact on patients' 2-year survival after surgery, and the survival prognosis of the non-bleeding group is relatively better.

### Independent factors influencing 2-year mortality

Univariate Cox regression analysis showed that rebleeding (HR=8.90, 95% CI=5.60-14.16,  $P<0.001$ ), cause of injury (HR=1.58, 95% CI=1.31-1.90,  $P<0.001$ ), surgical procedure (HR=0.21, 95% CI=0.14-0.32,  $P<0.001$ ), PT (HR=1.29, 95% CI=1.19-1.40,  $P<0.001$ ), FIB (HR=0.24, 95% CI=0.16-0.37,  $P<0.001$ ), PLT (HR=0.99, 95% CI=0.98-0.99,  $P<0.001$ ), PCT (HR=0.00, 95% CI=0.00-0.27,  $P=0.020$ ), and GCS score (HR=0.85, 95% CI=0.78-0.92,  $P<0.001$ ) were likely independent influencing factors for 2-year mortality; sex, age, activated APTT, and MPV had no significant effect ( $P>0.05$ ), as shown in **Figure 6**.

Multivariate Cox regression analysis showed that rebleeding (HR=2.52, 95% CI=1.11-5.70,



**Figure 7.** Forest plot of independent influencing factors for 2-year mortality in patients by multivariate Cox regression analysis. Note: PT, Prothrombin Time; FIB, Fibrinogen; PLT, Platelet Count; PCT, Plateletcrit.

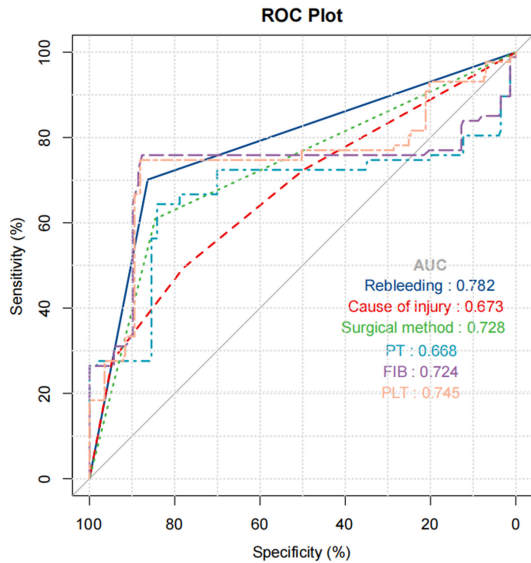
$P=0.026$ ), traffic accident (HR=1.45, 95% CI=1.04-2.02,  $P=0.029$ ), and higher PT (HR=1.16, 95% CI=1.01-1.34,  $P=0.041$ ) were independent risk factors for 2-year mortality. Hematoma evacuation craniotomy (HR=0.31, 95% CI=0.14-0.68,  $P=0.003$ ), lower FIB (HR=0.52, 95% CI=0.31-0.90,  $P=0.019$ ), and lower PLT (HR=0.99, 95% CI=0.99-1.00,  $P=0.016$ ) were independent protective factors. The PCT and GCS scores had no significant impact ( $P>0.05$ ), as shown in **Figure 7**.

As shown in **Figure 8** and **Table 4**, ROC curve analysis of the predictive efficacy of independent factors influencing 2-year mortality revealed that rebleeding (AUC=0.782), surgical procedure (AUC=0.728), FIB (AUC=0.724), and PLT (AUC=0.745) had strong predictive value. Among these, rebleeding had the highest AUC, suggesting that its relatively better ability to identify 2-year mortality risk.

### Discussion

Acute subdural hematoma (aSDH) is a highly challenging subtype of TBI, and its rebleeding and long-term survival prognosis are influenced

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**Figure 8.** ROC curves of independent influencing factors for 2-year mortality in patients. Note: PT, Prothrombin Time; FIB, Fibrinogen; PLT, Platelet Count; PCT, Plateletcrit.

by the interaction of multiple factors. This study analyzed indicators such as coagulation function and platelet indices, and explored the value of these indices in clinical decision-making for aSDH patients, providing a basis for optimizing treatment strategies.

Coagulation indices (PT, APTT, FIB) play a key role in aSDH rebleeding. Prolonged PT and APTT are associated with impaired extrinsic and intrinsic coagulation pathways, reflecting the disturbance of the coagulation cascade after trauma, which is consistent with the pathologic mechanism of TC [23]. TC, characterized by coagulation factor consumption and hyperfibrinolysis, can exacerbate the risk of bleeding. In this study, both served as risk factors for rebleeding, confirming that abnormal coagulation pathways promote the progression of aSDH. The study by Wang et al. demonstrated that patients with prolonged PT and APTT after burr hole drainage had a significantly higher rebleeding rate, which is consistent with the results of this study [24]. As a coagulation substrate, a decrease in FIB levels indicates insufficient reserves of clotting materials, making it difficult to effectively form thrombi to close damaged vessels, which is contrary to protective factors (i.e., low FIB increases the risk of rebleeding). This is consistent with the conclusions of previous studies on TC that low fibrino-

genemia promotes bleeding progression [25], highlighting the potential value of FIB supplementation in the treatment of aSDH. Existing literature has confirmed that the consumption of clotting factors and endothelial damage reflected by prolonged PT/APTT can disrupt the integrity of the BBB by activating inflammatory pathways and releasing pro-inflammatory cytokines such as tumor necrosis factor- $\alpha$  [26], and coagulation dysfunction caused by hypoperfusion can further aggravate endothelial glycocalyx shedding and expand BBB leakage [27]. Decreased FIB not only indicates insufficient clotting substrates but also impairs vascular wall stability. Patients with TBI and low fibrinogenemia have significantly increased cerebral edema volume, which is directly related to increased BBB permeability [28]. In TC, this process drives disease progression through a vicious cycle of coagulation abnormalities, inflammation activation, blood-brain barrier disruption, and exacerbated edema.

Platelet-related indices are complex. Decreased PLT impairs primary hemostasis and is associated with a higher risk of rebleeding, consistent with reports that thrombocytopenia exacerbates TBI [14, 29]. Elevated MPV indicates larger, more reactive platelets - typically younger ones. While these cells have greater procoagulant potential, overactivation can contribute to microvascular thrombosis and unstable hemostasis, potentially inducing rebleeding. This supports the role of both platelet quantity and quality in controlling bleeding in aSDH. This study further clarifies that aSDH patients have a significantly increased risk of rebleeding when  $PLT < 147.655 \times 10^9/L$ . This threshold provides a quantitative basis for clinically identifying high-risk individuals with insufficient platelet counts. This finding is consistent with the conclusions of Nemecek et al., who demonstrated that  $PLT < 100 \times 10^9/L$  is an independent risk factor for hemorrhagic complications in the TBI population, but did not identify a specific threshold for the aSDH subtype [30]. The higher threshold of  $147.6 \times 10^9/L$  determined in this study may be related to the specific pathologic conditions of aSDH patients, such as the disruption of the BBB after brain parenchymal injury and the activation of the coagulation-inflammation crosstalk.

Although this study did not directly detect molecular or platelet activation markers asso-

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**Table 4.** ROC data

| Marker          | AUC   | CI_lower_upper | Specificity | Sensitivity | Youden_index | Cut_off | Accuracy | Precision | F1_Score |
|-----------------|-------|----------------|-------------|-------------|--------------|---------|----------|-----------|----------|
| Rebleeding      | 0.782 | 0.729-0.836    | 86.34%      | 70.11%      | 56.46%       | 0.5     | 81.85%   | 70.11%    | 68.16%   |
| Cause of injury | 0.673 | 0.605-0.740    | 77.97%      | 49.43%      | 27.40%       | 2.5     | 70.06%   | 49.43%    | 47.78%   |
| Surgical method | 0.728 | 0.671-0.784    | 84.58%      | 60.92%      | 45.50%       | 0.5     | 21.97%   | 39.08%    | 21.73%   |
| PT              | 0.668 | 0.585-0.751    | 84.14%      | 64.37%      | 48.51%       | 15.975  | 78.66%   | 64.37%    | 62.57%   |
| FIB             | 0.724 | 0.642-0.807    | 87.67%      | 75.86%      | 63.53%       | 1.535   | 15.61%   | 24.14%    | 13.68%   |
| PLT             | 0.745 | 0.672-0.818    | 88.11%      | 74.71%      | 62.82%       | 147.655 | 15.61%   | 25.29%    | 14.24%   |

Note: PT, Prothrombin Time; FIB, Fibrinogen; PLT, Platelet Count.

ciated with TC, the observed abnormalities in coagulation/platelet indices can be reasonably corroborated by established molecular pathways. In this study, prolonged PT and APTT were closely associated with the consumption of coagulation factors V/VIII and the downregulation of plasminogen activator inhibitor-1 (PAI-1). The release of tissue factors after trauma activates the extrinsic coagulation pathway, leading to rapid consumption of coagulation factors, while endothelial damage caused by hypoperfusion further exacerbates the dysfunction of the intrinsic coagulation pathway [8]. Decreased FIB levels reflect insufficient coagulation substrates, which is consistent with the increased fibrin degradation due to excessive fibrinolysis in TC [8]. Regarding platelet indices, decreased PLT and increased MPV indirectly indicate abnormal platelet activation. Previous studies have confirmed that upregulation of P-selectin and glycoprotein IIb/IIIa expression on platelet surface in patients with TBI leads to dysfunction of adhesion and aggregation. This not only impairs primary hemostasis but also increases the risk of unstable thrombus formation [31]. In summary, the abnormal clinical indicators observed in this study are highly consistent with the underlying molecular mechanisms, providing indirect support for the association between coagulation/platelet dysfunction and rebleeding.

Both surgical procedures and GCS scores at admission are associated with the risk of rebleeding and can provide guidance for treatment management. Craniotomy allows for direct visualization of the hematoma and meticulous hemostasis. In our study cohort, a univariate analysis indicated fewer rebleeding cases among patients treated with craniotomy for hematoma evacuation. Results from multivariate analysis with adjustment for confounding factors demonstrated that craniotomy served as a protective factor against postoperative

rebleeding. Burr hole drainage is suitable for liquefied hematomas but may leave behind organized blood clots and has limited hemostatic effect, which may increase the risk of rebleeding [32]. Lower GCS scores reflect more severe injury; patients with impaired consciousness are more prone to edema and cerebrovascular dysregulation, thus early GCS assessment is helpful for risk stratification [33, 34]. These findings are consistent with the results of Compagnone et al., who demonstrated that in patients with aSDH, craniotomy was associated with a lower risk of rebleeding-related adverse outcomes compared to other surgical approaches, attributed to precise hemostasis under direct vision [35]. Furthermore, another study showed that patients with traumatic SDH and a GCS score <8 had a significantly increased risk [36], which aligns with the understanding of the injury mechanism in this study, providing further evidence support.

In the 2-year analysis, coagulation and platelet markers remained independent predictors of outcomes. Longer PT, decreased fibrinogen, and decreased PLT - markers of persistent impaired hemostasis - were associated with higher rebleeding rate, subsequent clinical deterioration, and increased mortality. These findings support the prospective evaluation of early detection and correction of coagulopathy as a reasonable strategy to improve long-term outcome [37].

Rebleeding is an independent predictor of death and a major driver of long-term outcome. It can contribute to secondary brain injury - initiating inflammatory cascades, edema, and brain herniation - and its effects may outweigh the initial injury. This close link to survival is consistent with clinical practice: prevention and control of rebleeding are central to improving aSDH prognosis [38]. High-energy injury mechanisms such as traffic accidents have

higher mortality rates, likely due to multiple injuries and more severe contusions/lacerations, often accompanied by coagulopathy and neurologic deficits. The observed protective effect of craniotomy supports the value of precision surgical strategies - more thorough hematoma evacuation and direct hemostasis - when selecting surgical options.

We developed a prognostic nomogram for aSDH and evaluated it using ROC analysis [39]. This nomogram integrates multi-domain input information, visualizing the risk as a total score corresponding to the predicted outcome probability. In our model, coagulation indices such as PT and APTT have relatively large weightings, consistent with their role as direct readings of hemostasis. For transparency, we can report the score allocation and corresponding predicted risks (along with the AUC/C index with a 95% CI) if necessary. ROC curves validated the model's discriminative power, with high AUC values for indices such as rebleeding indicating their accurate ability to identify mortality risk. This supports early clinical screening of high-risk patients and the development of individualized interventions such as prophylactic coagulation correction and targeted neuroprotection. This study has certain limitations: the retrospective design may have introduced selection bias, and some potential confounding factors (such as pre-hospital emergency measures and refined postoperative patient management) were not fully included; the dynamic changes in platelet indices and coagulation indices (such as fluctuations at different time points after injury) were not analyzed in depth, making it impossible to accurately capture the impact of hemostatic function evolution on prognosis; although the sample size covers a certain number of cases, multicenter, large-sample studies can still improve the generalizability of the conclusions. In addition, this study lacked postoperative dynamic monitoring data (such as changes in indicators at 6 hours/24 hours), relying only on baseline admission data, which cannot guide real-time clinical adjustments to the treatment plan. Future research may focus on: (1) dynamically monitoring coagulation-platelet indices, analyzing their temporal changes and their association with rebleeding/prognosis, and clarifying the intervention window; (2) exploring the impact of genetic polymorphisms on TIC and uncovering the mechanisms of individualized coagulation dysfunction;

(3) constructing a more comprehensive prognostic prediction model by combining radiomics and biomarkers, providing a deeper theoretical basis for the precise diagnosis and treatment of aSDH; (4) future research will focus on the specific correlation between postoperative dynamic real-time monitoring indicators and real-time clinical adjustment guidance of treatment plans, thereby providing a basis for clinical treatment adjustments.

In summary, coagulation indices (PT, APTT, fibrinogen), platelet indices (PLT, MPV), and clinical factors (such as surgical method, GCS, and injury mechanism) are independently associated with rebleeding and 2-year survival in patients with aSDH. These findings support practical risk stratification and may provide guidance for the correction of perioperative coagulation dysfunction and surgical planning. Future work includes external validation of the model, mechanistic studies of the platelet/coagulation pathway, and prospective studies to verify whether targeted interventions can improve outcomes.

### Disclosure of conflict of interest

None.

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