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# The predictive role of the nomogram based on clinical characteristics and thromboelastography markers for rebleeding after hypertensive intracerebral hemorrhage

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ABSTRACT

*Objectives:* Rebleeding after hypertensive intracerebral hemorrhage is a common and serious postoperative complication in neurosurgery, with high mortality and mental disability rates. The aim of this study was to establish a nomogram to analyze the role of thromboelastography in predicting rebleeding after hypertensive intracerebral hemorrhage.
*Basic methods:* We selected 375 patients with hypertensive intracerebral hemorrhage who underwent surgical treatment in Yuebei People's Hospital of Shaoguan City, Guangdong Province from May 2018 to August 2022, and retrospectively analyzed the relevant data of hypertensive intracerebral hemorrhage patients (including general data and clinical thromboelastography data), and analyzed the factors and thromboelastography parameters that affect rebleeding after surgery (45 cases, defined as re-examination of head CT within 72 h after surgery showed that the hematoma in the surgical area exceeded 20 ml).
*Main results:* Time from symptom onset to surgery, taking antiplatelet drugs, taking anticoagulant drugs, diabetes mellitus, difficulty in hemostasis during surgery, R value and EPL value in thromboelastography were risk factors for rebleeding after hypertensive intracerebral hemorrhage ($P < 0.05$). Logistic regression was used to determine the independent risk factors, and based on these risk factors, a nomogram was established and internally validated using a bootstrap method. ROC curve analysis showed that the nomogram model had high diagnostic value for rebleeding after hypertensive intracerebral hemorrhage, with AUC of 0.7314. The calibration curve of the nomogram showed good consistency between the predicted probabilities and the observed values. The decision curve analysis and clinical impact curve also revealed the potential clinical usefulness of the nomogram.
*Conclusions:* The nomogram based on clinical characteristics and thromboelastography markers may be useful for predicting rebleeding after hypertensive intracerebral hemorrhage.

## 1. Introduction

Intracerebral hemorrhage accounts for 10 %–20 % of all strokes [1], and surgical removal of hematoma can prevent further expansion of hematoma and prevent damage to brain tissue by hematoma decomposition products [2,3]. Rebleeding after hematoma removal indicates poor prognosis [4,5], and the rebleeding rates after minimally invasive and craniotomy surgery in patients with hypertensive intracerebral hemorrhage were 10.0 % and 15.4 %, respectively [6]. Most patients with hypertensive intracerebral hemorrhage who have surgical indications improve after surgery, but some patients will have rebleeding after surgery, and the disability and mortality rates after rebleeding are much higher than the first onset [7], and the reported rebleeding rates of minimally invasive surgery (MIS) and conventional craniotomy patients were 10.0 % and 15.4 %, respectively [8]. Therefore, understanding the risk factors for rebleeding after surgery is of great clinical significance for preventing rebleeding after surgery.

Research shows that the specific mechanism of hematoma

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enlargement after intracerebral hemorrhage is not fully understood, but it is closely related to platelet count and coagulation function abnormalities [9]. Thromboelastography (TEG) is a graph formed by the thromboelastograph recording the coagulation process, which is widely used in coagulation dysfunction. It can dynamically analyze the whole coagulation process, and at the same time dynamically monitor platelets and the whole coagulation process, accurately reflect the fibrinolysis of coagulation factors and fibrinogen, etc. It is one of the means to effectively detect blood hypercoagulability, hypocoagulability, and fibrinolysis phenomena [10].

There are many studies on the risk factors for predicting rebleeding after intracerebral hemorrhage surgery, but little is known about the relationship between thromboelastography and rebleeding after intracerebral hemorrhage surgery. This study aimed to determine the clinical value of thromboelastography in predicting rebleeding after surgical treatment of hypertensive intracerebral hemorrhage patients.

## 2. Materials and methods

### 2.1. Study population

The data source was 375 patients with intracerebral hemorrhage who underwent surgical treatment in Yuebei People's Hospital of Shaoguan City, Guangdong Province from May 2018 to August 2022 (Fig. 1). Use of the data was approved by Yuebei People's Hospital Medical Ethics Committee (YBEC-KY(2023)-101). Patients included in this study met the following criteria: Patients with a clear history of hypertension, who suddenly developed intracerebral hemorrhage in the basal ganglia, thalamus, ventricles, cerebellum and brainstem, and excluded secondary intracerebral hemorrhage caused by trauma, vascular structural abnormalities, coagulation dysfunction, hematological diseases, systemic diseases and tumor diseases, and reached the surgical treatment indications, underwent surgical treatment. Patients with the following diseases are excluded: 1. Patients with severe liver and kidney dysfunction; hyperthyroidism or hypothyroidism; malignant tumors; oral contraceptives; folic acid and vitamin B12; 2. Hypertensive intracerebral hemorrhage patients with hematological diseases. All patients had complete baseline clinical information and follow-up data.

Clinical baseline data of each patient was collected as follows: General data collection: including gender, age, time interval from symptom onset to surgery, systolic and diastolic blood pressure at admission, use of antiplatelet and anticoagulant drugs; Clinical data: GCS score at admission; irritability or not; hematoma volume; degree of midline shift; whether combined with diabetes; whether there is difficulty in hemostasis during surgery, etc. Also includes the R time (the time it takes for the blood to start clotting),α angle (the angle formed by the tangent line to the curve at the point where the clot reaches 20 mm in amplitude), maximum amplitude (MA) value (This is the maximum strength of the clot) and elasticity of the clot after lysis (EPL) value in the thromboelastogram.

### 2.2. Statistical analyses

We used SPSS software 26.0 (SPSS Inc., Chicago, IL, USA) and R (version 4.0.2) for Windows to analyze the data. Measurement data were expressed as $x \pm s$, and intergroup comparison was performed by *t*-test. Count data were expressed as percentage (%), and intergroup comparison was performed by $\chi 2$ test. We compared the demographic characteristics and clinical relevant indicators, screened the related risk factors, and performed multivariate logistic regression analysis on the risk factors with $P < 0.1$ in univariate analysis. Based on the results of multivariate analysis, we used R language to make forest plot and nomogram for the independent risk factors, and evaluated the predictive ability of the model by ROC curve. The ROC curve was drawn using

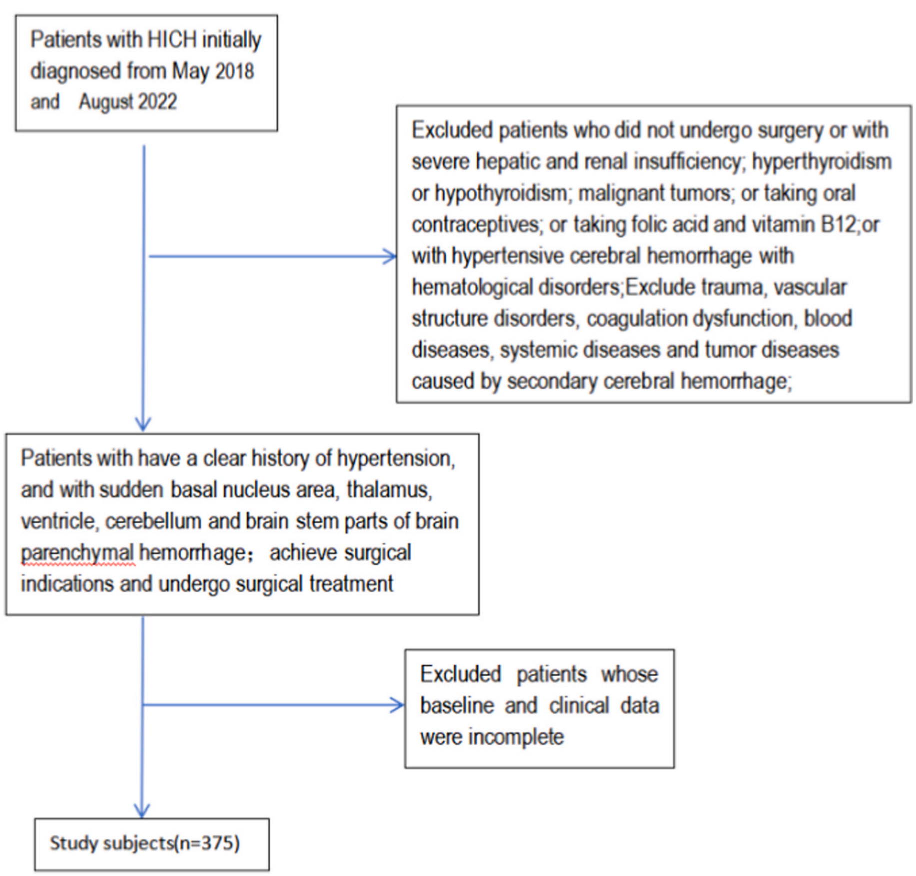



**Fig. 1.** The fowchart for selection procedure of patients with intracerebral hemorrhage who underwent surgical treatment.

pROC package, and the decision analysis curve and calibration curve were drawn by rms package. $P < 0.05$ was considered statistically significant. By comparing the independent factors, we used ROC curve and AUC value to test the frequency superiority and discrimination ability of the nomogram. We applied calibration curve to calibrate the nomogram, and performed decision curve analysis to evaluate the clinical utility of the nomogram. We used 1000 times repeated sampling method for internal validation, and clinical impact curve to evaluate the positive results of the model in clinical application.

## 3. Results

The results of the univariate analysis are shown in Table 1. The time from symptom onset to surgery, the use of antiplatelet drugs, the use of anticoagulant drugs, the presence of diabetes, the difficulty of hemostasis during surgery, and the R and EPL values in the thromboelastography were statistically significant ($P < 0.1$) in patients with and without postoperative rebleeding. These seven clinical characteristics were included in the multivariate logistic regression analysis and presented as a forest plot in Fig. 2.

The time from symptom onset to surgery, the use of antiplatelet drugs, the use of anticoagulant drugs, the presence of diabetes, the difficulty of hemostasis during surgery, and the R and EPL values in the thromboelastography were used to construct a nomogram, as shown in Fig. 3.

The performance of the nomogram was tested by ROC curve and AUC value, as shown in Fig. 4. The AUC value was 0.7314 (95%CI 0.684–0.821). The calibration curve of the nomogram showed good consistency (Fig. 5), indicating that the nomogram had a good predictive effect on the risk of rebleeding after intracerebral hemorrhage. In addition, the Hosmer-Lemeshow test gave a non-significant P value of 0.2969, indicating that it had good calibration ability.

The decision curve analysis of the nomogram is shown in Fig. 6. It can be seen that when predicting the risk of rebleeding after intracerebral hemorrhage, the nomogram had higher accuracy than the traditional prediction of intracranial rebleeding at 43%–98 %. The clinical impact curve in Fig. 7 also proved that the nomogram could well predict intracranial rebleeding after surgery. In summary, these results indicate that our nomogram performed better in predicting the risk of rebleeding after intracerebral hemorrhage.

**Table 1**
Demographics and clinical characteristics of patients with intracerebral hemorrhage who underwent surgical treatment.

| Characteristics | postoperative rebleeding | | P/χ2 value |
|---|---|---|---|
| | Y (n = 45),n (%) | N (n = 330),n (%) | |
| Gender (male) | 25 (55.6) | 170 (51.7) | 0.61 |
| Age (years) | 57.47 ± 14.42 | 55.95 ± 13.64 | 0.49 |
| The time from symptom onset to surgery (hours) | 6 (4.5,8) | 5 (3,7) | 0.08 |
| The systolic blood pressure on admission (mmHg) | 190.08 ± 7.94 | 189.06 ± 8.88 | 0.46 |
| The diastolic blood pressure on admission (mmHg) | 108.31 ± 9.21 | 109.93 ± 11.66 | 0.37 |
| The use of antiplatelet drugs (yes) | 5 (11.1) | 11 (3.3) | 0.04 |
| The use of anticoagulant drugs (yes) | 5 (11.1) | 13 (3.9) | 0.08 |
| GCS score on admission | 6.33 (5,8) | 6.66 (5,8) | 0.92 |
| irritable on admission (yes) | 16 (35.6) | 83 (25.2) | 0.14 |
| The volume of hematoma on admission (ml) | 46.62 ± 9.14 | 46.71 ± 8.02 | 0.95 |
| The degree of midline shift (cm) | 1.49 ± 0.35 | 1.44 ± 0.36 | 0.33 |
| Combined with diabetes (yes) | 13 (28.9) | 39 (11.8) | 0.002 |
| Difficulty of hemostasis during surgery (yes) | 9 (20) | 28 (8.5) | 0.031 |
| The R time in the thromboelastogram (minute) | 13.27 ± 5.89 | 11.16 ± 6.68 | 0.045 |
| The α angle in thromboelastography (degree) | 49.87 ± 10.43 | 52.40 ± 13.21 | 0.145 |
| The MA value in thromboelastography (mm) | 58.89 ± 8.43 | 59.44 ± 6.28 | 0.676 |
| The EPL value in thromboelastography (%) | 17.04 ± 5.49 | 14.50 ± 7.79 | 0.035 |

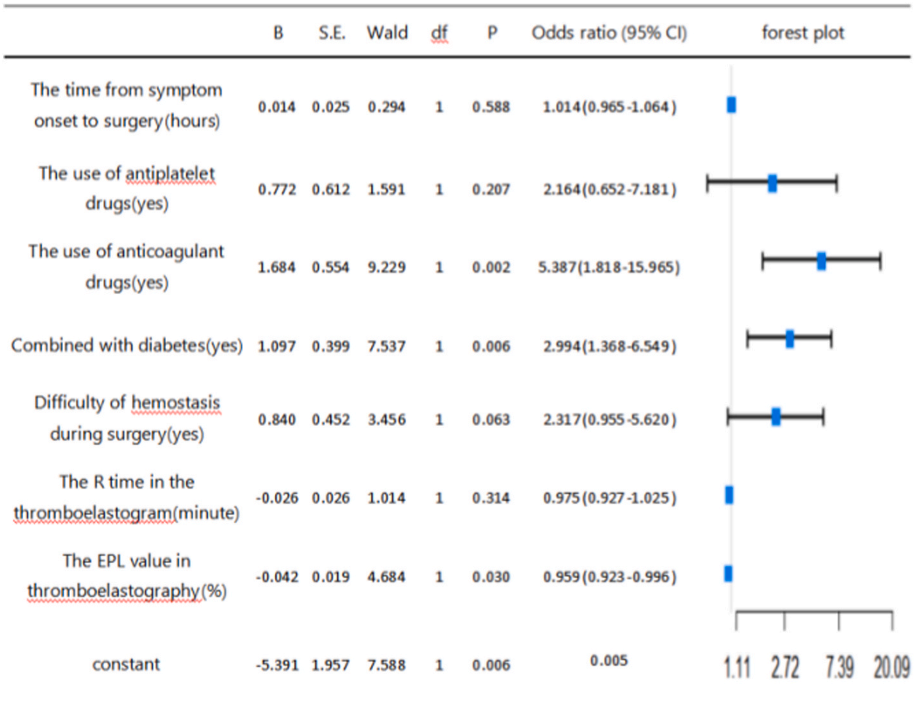
## 4. Discussion

Rebleeding after intracerebral hemorrhage (ICH) surgery is still a very tricky problem for many neurosurgeons [11], with a relatively poor prognosis. Postoperative rebleeding can bring disastrous consequences to patients, greatly increasing the disability and mortality rates, and aggravating the burden on family and society [12]. In order to better prevent the occurrence of postoperative rebleeding, we searched for other reliable risk factors to help predict whether rebleeding would occur after ICH surgery. We applied logistic regression to screen the time from onset to surgery, use of antiplatelet drugs, anticoagulant drugs, diabetes mellitus, difficulty in hemostasis during surgery, R value and EPL value in thromboelastography as independent risk factors for rebleeding after ICH surgery.

Kaneko et al. [13] reported as early as 1977 that they visualized and cauterized branches from the striate artery, which are usually 100–200 μm small. They later hypothesized in 1983 [14] that insufficient hemostasis or damage to the striate branches might cause rebleeding and adverse outcomes in 100 patients. Nearly 15 % of patients who underwent craniotomy and hematoma evacuation in the STICH trial had surgical rebleeding [15]. Morgenstern et al. [16] reported that the rebleeding rate of patients who underwent standard craniotomy was 40 % within 4 h after onset, but surgery after 12 h of symptom onset could reduce the rebleeding rate to 12 %. The authors attributed this performance to the difficulty of hemostasis in the ultra-early period, which is consistent with the conclusion of this article, considering the interval from symptom onset to surgery as a risk factor for postoperative rebleeding.

Zhang et al. [12] also reported that blood pressure variability was associated with the occurrence of rebleeding after ICH surgery. This study did not find that blood pressure was a risk factor for rebleeding after ICH surgery, possibly because the patients started to lower their blood pressure early after admission and did not have severe hypertension. It may also be due to the small sample size of this study, and further confirmation is needed from multicenter controlled studies. Coagulation dysfunction is a common factor for rebleeding after intracerebral hemorrhage. A large amount of coagulation factors are consumed during the formation of intracerebral hematoma, leading to consumptive coagulation dysfunction; secondly, if the patient has underlying liver disease, long-term oral anticoagulant or antiplatelet drugs, it can affect coagulation function. This is similar to the results of this study, where the use of antiplatelet drugs, anticoagulant drugs and difficulty in hemostasis during surgery were all risk factors for rebleeding after ICH surgery. Regarding the use of thromboelastography to predict the risk of rebleeding after ICH surgery, no relevant literature has been reported. Thromboelastography (TEG) is a method of monitoring the coagulation status of whole blood, which has been widely used in clinical practice and has achieved rapid development since the 1980s. At present, TEG has been widely used to guide clinical component transfusion and related drug use, real-time coagulation monitoring in various situations, prediction of venous thrombosis risk and so on. This study used TEG-related data such as R value and EPL to predict the risk of rebleeding after surgery.

Taken together, based on the results of logistic regression analysis, Our nomogram includes 7 risk factors: time from symptom onset to surgery, use of antiplatelet drugs, anticoagulant drugs, diabetes mellitus, difficulty in hemostasis during surgery, R value and EPL value in thromboelastography; the data show that our nomogram has better discrimination for predicting the risk of rebleeding after ICH surgery; the decision curve and clinical impact curve show that our model has good



| | B | S.E. | Wald | df | P | Odds ratio (95% CI) | forest plot |
|---|---|---|---|---|---|---|---|
| The time from symptom onset to surgery(hours) | 0.014 | 0.025 | 0.294 | 1 | 0.588 | 1.014(0.965-1.064) | |
| The use of antiplatelet drugs(yes) | 0.772 | 0.612 | 1.591 | 1 | 0.207 | 2.164(0.652-7.181) | |
| The use of anticoagulant drugs(yes) | 1.684 | 0.554 | 9.229 | 1 | 0.002 | 5.387(1.818-15.965) | |
| Combined with diabetes(yes) | 1.097 | 0.399 | 7.537 | 1 | 0.006 | 2.994(1.368-6.549) | |
| Difficulty of hemostasis during surgery(yes) | 0.840 | 0.452 | 3.456 | 1 | 0.063 | 2.317(0.955-5.620) | |
| The R time in the thromboelastogram(minute) | -0.026 | 0.026 | 1.014 | 1 | 0.314 | 0.975(0.927-1.025) | |
| The EPL value in thromboelastography(%) | -0.042 | 0.019 | 4.684 | 1 | 0.030 | 0.959(0.923-0.996) | |
| constant | -5.391 | 1.957 | 7.588 | 1 | 0.006 | 0.005 | |



**Fig. 2.** Multivariate logistic regression analysis for patients with intracerebral hemorrhage who underwent surgical treatment.

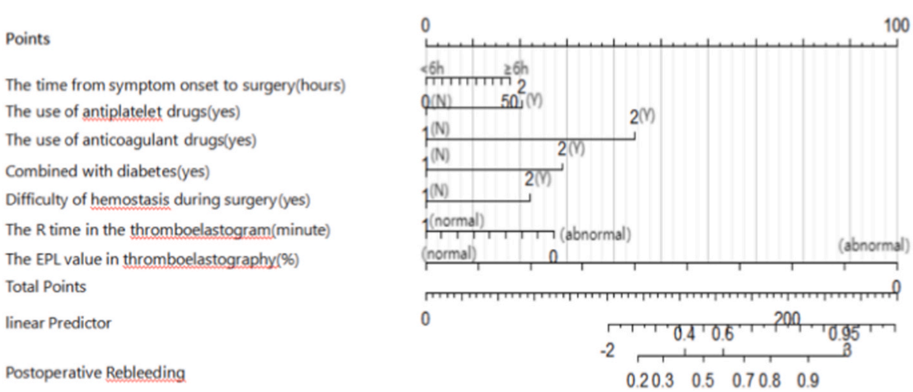



**Fig. 3.** Clinical nomogram for predicting the probability of rebleeding after surgical treatment of hypertensive intracerebral hemorrhage patients.

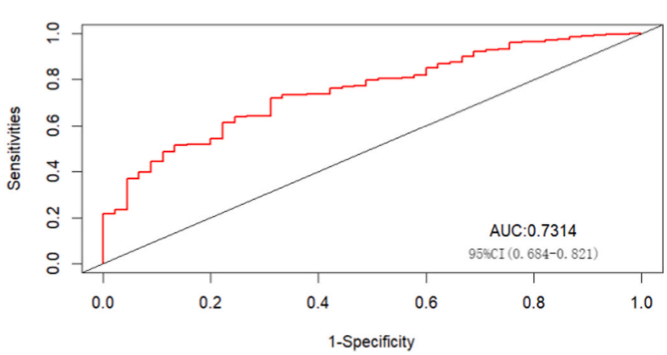



**Fig. 4.** Discrimination and calibration of the clinical nomogram for determining rebleeding after surgical treatment of hypertensive intracerebral hemorrhage patients. Receiver operator characteristic curve of the clinical nomogram in the set. AUC: area under the curve; CI: confidence interval.

predictive accuracy and overall net benefit. The nomogram can divide ICH patients into high and low risk groups for postoperative rebleeding. In summary, our nomogram seems to help predict the prognosis of ICH patients after surgery, as well as the treatment decision for ICH patients.

## 5. Conclusion

We found that The time from symptom onset to surgery, the use of antiplatelet drugs, the use of anticoagulant drugs, the presence of diabetes, the difficulty of hemostasis during surgery, and the R and EPL values in the thromboelastography were risk factors for rebleeding after hypertensive intracerebral hemorrhage. We developed a diagnostic model for preoperative risk of rebleeding in patients with hypertensive intracerebral hemorrhage. This model may provide a reliable preoperative diagnostic tool that can improve the accuracy of predicting rebleeding after hypertensive intracerebral hemorrhage, which may help in clinical decision-making for treatment selection. However, there are still some limitations in our study. First, our fndings were based on a retrospective design, and thus, this study cannot exclude all potential bias. Second, our data was obtained from a single cancer center, and the

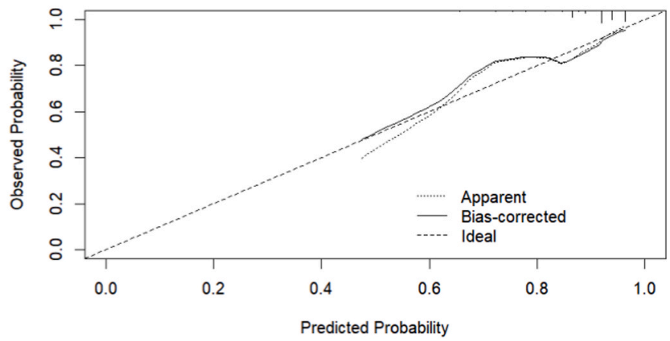



**Fig. 5.** Calibration curve of the clinical nomogram in the set. For the calibration curve, the y-axis represents the actual observed rebleeding probabilities, and the x-axis represents nomogram-predicted probabilities. The calibration curve shows how well the predicted probabilities agreed with the observed probabilities. The diagonal black dash line represents a perfect prediction by an ideal model, and the black solid line represents the predictive performance of the nomogram. The solid line has a closer fit to the dashed line, which indicates a better prediction.

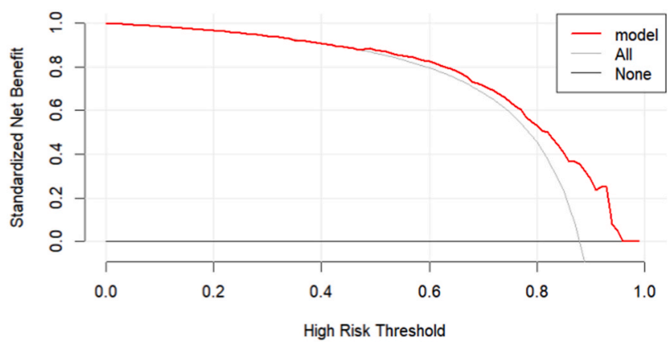



**Fig. 6.** Decision curve analyses depicting the clinical net benefit of the clinical nomogram. The x-axis shows the threshold probability. Threshold probability was defined as the minimum probability of disease at which further interventionwould be warranted. The y-axis represents the net benefit, which is calculated across a range of threshold probabilities. Net benefit = sensitivity × prevalence – (1 – specificity) × (1 – prevalence) × w, where w is the odds at the threshold probability. The horizontal solid black line represents the assumption that no patients with rebleeding were involved, and the solid gray line represents the assumption that all patients had rebleeding. The solid red line represents the clinical nomogram (model). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

sample size was small. A larger sample size from

Other institutions would be required to further validate our results. Finally, the endpoint of our study was rebleeding, and more research on the patients with hypertensive intracerebral hemorrhage should also be carried out in the future.

## Ethics statements

Use of the data was approved by Yuebei People's Hospital Medical Ethics Committee (YBEC-KY(2023)-101). This article follows the ethical principles of the Helsinki Declaration, focuses on the dignity and rights of human subjects, and is committed to ensuring the scientific and standardized nature of the research process. We strictly abide by international ethical norms to ensure the reliability and feasibility of research results. This retrospective study was carried out using the opt-out method for the case series of our hospital. Informed consent was waived by our Institutional Review Board because of the retrospective nature of our study.

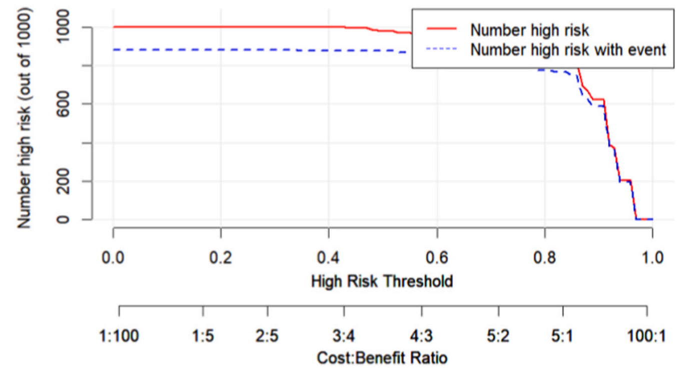



**Fig. 7.** The horizontal axis is the threshold probability value and the loss-benefit ratio, the vertical axis is the number of rebleeding, the red curve (number high risk) indicates the number of people who are classified as rebleeding by the model at each threshold probability, and the blue curve (number high risk with event) indicates the number of people who actually rebleed at each threshold probability. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.).

## Data avalability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Code availability statement

The code that supports the findings of this study is based on the R language, which is openly available at R Project for Statistical Computing. The code also includes some custom functions and scripts, which are partially written by Peng Wang. The full code is available from the corresponding author, Peng Wang, upon reasonable request.

## Authors' contributions and consent to participate and for publication

Peng Wang and Shasha Yang contributed equally to this manuscript. Peng Wang collected the data, analyzed the data, and drafted the manuscript. Shasha Yang and Jing Zhang conceived of the study, participated in its design and coordination, and helped to draft the manuscript. Muguo Guoji, Li Nan and Neng Zhang was responsible for the whole project, reviewed the manuscript, designed the study, and supervised the study. This work was done with the voluntary participation of all authors. All authors contributed to the article and approved the submitted version. All authors agree to publish this paper.

## Funding

None.

## CRediT authorship contribution statement

**Peng Wang:** Formal analysis, Methodology, Software, Writing – review & editing. **Shasha Yang:** Resources, Software. **Muguo Guoji:** Conceptualization, Data curation. **Li Nan:** Formal analysis, Methodology. **Neng Zhang:** Project administration, Software. **Jing Zhang:** Methodology, Writing – original draft.

## Declaration of competing interest

I declare that there is no conflict of interest in the writing and publication of this paper between the various authors.

Firstly, I must emphasize that my financial and economic status has no direct or indirect relationship with the writing and publication of this paper. My personal assets and liabilities have no conflict with the content or conclusion of this paper. Additionally, I have not engaged in any investment activities including stocks, bonds, and other financial products in the past five years. I have also not participated in any forms of commercial activities.

Furthermore, I must clearly state that I, as an author of this paper, have not been influenced by any potential conflicts of interest during the writing and publication process of this paper. I fully understand the concept of "conflict of interest" and must ensure that there is no conflict of interest in my activities related to this paper.

Finally, I emphasize again that my economic and financial status have no relationship with the writing and publication of this paper. I have also not participated in any activities that may cause a conflict of interest. I am willing to bear any responsibility related to this paper, including but not limited to any consequences caused by my negligence or error.

## Data availability

No data was used for the research described in the article.

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