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Original Article

Risk factors and prediction model for rebleeding in grade IIb peptic ulcer patients after endoscopy

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Abstract: Objective: To investigate the risk factors for rebleeding in patients with IIb peptic ulcer bleeding (PUB) treated endoscopically and to develop a nomogram model. Method: A retrospective analysis was conducted on 287 patients with grade IIb PUB who underwent endoscopic treatment at Beijing Pinggu Hospital from January 2019 to December 2023. The patients were divided into a modelling cohort (n=201) and a validation cohort (n=86) in a 7:3 ratio. The modelling cohort consisted of a non-bleeding (NB) group (n=176) and a re-bleeding (RB) group (n=25), while the validation cohort included an NB group (n=75) and an RB group (n=11). Logistic regression was used to analyze and identify the risk factors for rebleeding after endoscopic treatment in class IIb PUB patients. Based on the results of Logistic regression, a nomogram model was developed, and receiver operating characteristic (ROC) curve and calibration curve were performed to evaluate its accuracy. Results: Ulcer site, ulcer diameter, Helicobacter pylori (Hp) infection, D-dimer (D-D), prothrombin time (PT), albumin (ALB), and prostaglandin E2 (PGE2) were associated with rebleeding after endoscopic treatment in grade IIb PUB patients (all P<0.05). Logistic regression analysis identified Hp infection (OR=9.723, P=0.007), D-D (OR=1.013, P=0.047), PT (OR=2.242, P=0.013), ALB (OR=0.899, P=0.036), and PGE2 (OR=0.987, P=0.042) as independent risk factors for rebleeding. The area under the ROC curve for the nomogram model constructed based on these factors was 0.875 (95% CI: 0.788-0.962). Conclusion: This study successfully identified key independent risk factors for rebleeding after endoscopic treatment in grade IIb PUB patients, providing clinicians with a scientific decision-making tool to reduce rebleeding risk and improve treatment outcomes.

Keywords: Peptic ulcer bleeding, endoscope, prediction model

Introduction

Peptic ulcer disease (PUD) is a common gastrointestinal disorder, occurring when the mucosal layer of the gastrointestinal tract is eroded by gastric acid and pepsin. It is a disease characterized by periodic epigastric pain, acid reflux, and other symptoms [1, 2]. According to epidemiological surveys, PUD affects 1 in 10 adults worldwide, with a prevalence of approximately 5-10% of the population [3]. Peptic ulcer bleeding (PUB) is one of the most common and severe complications of PUD, accounting for 40% to 60% of all cases of acute upper gastrointestinal bleeding [4]. Patients often present with symptoms such as melena, hematemesis, and, in severe cases, shock and death [4]. Forrest grading is used to classify patients with PUB based on endoscopic signs of bleeding, with Forrest grades I and II typically indicating high-risk ulcers that require prompt intervention. Current clinical management for PUB involves proton pump inhibitors, hemostatic drugs, gastroscopic injection therapy, and the use of titanium clips, which offer effective hemostasis in many cases [5]. Nevertheless, research has indicated that despite most patients experiencing cessation of bleeding following active medical intervention, the risk of rebleeding within 30 days remains significant, increasing the likelihood of unfavorable outcomes and mortality [6].

In recent years, advancements in endoscopic treatment technology have led to its widespread application in managing PUB, offering several advantages, including ease of operation, effective hemostasis, and rapid postoper-

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ative recovery [7, 8]. Despite the significant efficacy of endoscopic treatment, patients with Forrest grade IIb PUB are at an increased risk of rebleeding. This is due to the presence of coagulated blood on the ulcer surface, which can become dislodged during the procedure, posing a serious threat to the patient's health and quality of life. Therefore, a thorough analysis of the risk factors for rebleeding after endoscopic treatment in grade IIb PUB patients, and the development of an effective prediction model, are crucial for guiding clinical decision-making and reducing rebleeding risk. Several studies have investigated the risk factors for rebleeding in PUB patients, but most have focused on general PUB cases, with limited research on the specific risks for Forrest type IIb PUB. Some studies have suggested that factors such as hemodynamic instability, high shock index, and duodenal ulcers may be associated with rebleeding [9, 10], but these have not provided detailed analyses specific to grade IIb PUB. In addition, there is a lack of accurate and reliable prediction models based on disease characteristics and clinical indicators to assess rebleeding risk after endoscopic treatment in Forrest class IIb PUB patients. Therefore, it is essential to further investigate these risk factors and develop an effective prediction model to guide treatment and reduce rebleeding risks.

Based on the above information, this study focused on patients with grade IIb PUB undergoing endoscopic treatment. Clinical and laboratory data were collected and analyzed using statistical methods to identify the risk factors for rebleeding after endoscopic treatment. A monogram prediction model was developed using the risk factors screened, aiming to provide a more accurate and effective tool for clinical evaluation and decision-making.

Materials and methods

Selection of patient population

This study conducted a retrospective analysis of 287 patients with grade IIb PUB who underwent endoscopic treatment between January 2019 and December 2023. Patients were divided into a modelling cohort (n=201) and a validation cohort (n=86) in a 7:3 ratio. The modelling cohort was further divided into a non-bleeding (NB) group (n=176) and a re-bleeding (RB) group (n=25), while the internal validation cohort was similarly divided into an NB group (n=75) and an RB group (n=11). Additionally, 168 patients who visited our hospital at other times were included as an external validation cohort. A detailed flowchart of the study is shown in **Figure 1**.

Inclusion criteria: (1) Presence of typical gastrointestinal bleeding symptoms such as melena or hematemesis, with a diagnosis of grade IIb PUB confirmed by endoscopy; (2) Patients who agreed to endoscopic treatment and received endoscopic hemostasis; (3) Availability of complete and accurate clinical data; and (4) age ≥18 years. Exclusion criteria: (1) Recent use of proton pump inhibitors; (2) Failure of the first endoscopic treatment and requiring intermediate surgery; (3) Severe cardiac, hepatic, renal, or other major organ dysfunction; (4) Co-existing immune or coagulation dysfunction; (5) Gastrointestinal bleeding due to other causes; (6) Food-related black stool. This study was approved by the Ethics Committee of Beijing Pinggu Hospital.

Sample size calculation

The sample size for this study was determined based on the primary objective of identifying risk factors for rebleeding in patients with grade IIb PUB after endoscopic treatment. The calculation was performed using the following considerations:

Primary endpoint: The primary endpoint of the study was the occurrence of rebleeding within 30 days after endoscopic treatment.

Expected event rate: Based on previous studies and clinical experience, the expected rebleeding rate in patients with grade IIb PUB was estimated to be 15%. This rate was used as the reference for the NB group.

Effect size and power analysis: To detect a clinically significant difference in rebleeding rates between the NB group and RB group, we assumed a relative risk (RR) of 2.0 for the occurrence of rebleeding. This assumption was based on the effect size observed in similar studies and the clinical relevance of identifying significant risk factors.

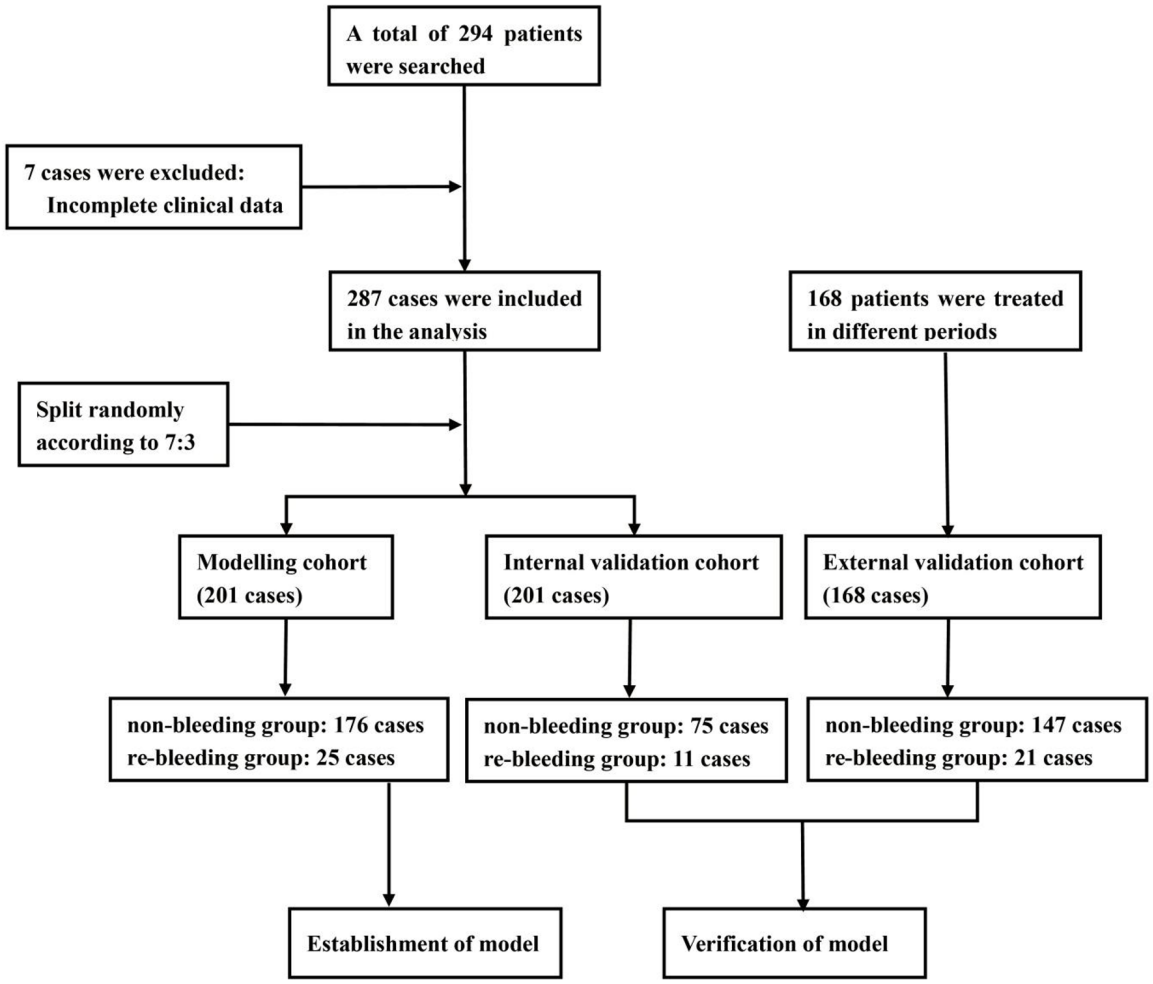

Figure 1. Study flow chart.

Power and significance level: The study was designed to have a power of 80% (β=0.20) to detect a difference at a two-sided significance level of 0.05 (α=0.05).

Calculation result: Based on the above assumptions, the calculated sample size required for each group was approximately 100 patients. To account for potential dropouts or incomplete data, we aimed to enroll a total of 287 patients, with 201 patients in the modelling cohort and 86 patients in the validation cohort.

Data collection

General data of all patients were collected, including gender, age, ulcer site, ulcer diameter, history of smoking, history of alcohol consumption, Helicobacter pylori (Hp) infection, comorbidities (diabetes mellitus, hypertension, coronary artery disease), history of previous surgical procedures, history of previous gastric hemorrhage, use of non-steroidal anti-inflammatory drugs (NSIADS), admission to endoscopic treatment, endoscopic disposition, hemoglobin (HB) level at admission, platelet count (PLT), D-dimer (D-D), activated partial thromboplastin time (APTT), prothrombin time (PT), serum creatinine (Scr), blood urea nitrogen (BUN), albumin (ALB), AND prostaglandin E_2 (PGE_2).

Outcome measures

The diagnostic criteria for rebleeding in this study were as follows: (1) increased frequency of bloody vomiting and black stools, with bright red vomitus or discharge of dark red bloody stools within 7-30 d after hemostasis by endoscopic treatment; (2) a drop in HB of ≥20 g/L

Table 1. Comparison of baseline data between modeling and internal validation cohorts

Factors		Total (n=287)	Modeling cohort (n=201)	Internal validation cohort (n=86)	x^2/t	*P* value
Rebleeding (n, %)	Yes	36 (12.54)	25 (12.44)	11 (12.79)	0.007	0.934
	No	251 (87.46)	176 (87.56)	75 (87.21)		
Gender (n, %)	Male	170 (59.23)	118 (58.71)	52 (60.47)	0.077	0.781
	Female	117 (40.77)	83 (41.29)	34 (39.53)		
Age (Mean ± SD)		54.71±12.71	54.97±12.99	54.10±12.07	0.531	0.596
Ulcer site (n, %)	Stomach	153 (53.31)	107 (53.23)	46 (53.49)	0.002	0.968
	Duodenum	134 (46.69)	94 (46.77)	40 (46.51)		
Ulcer diameter (n, %)	<2 cm	180 (62.72)	126 (62.69)	54 (62.79)	0.001	0.986
	≥2 cm	107 (37.28)	75 (37.31)	32 (37.91)		
Smoking (n, %)	Yes	79 (27.53)	55 (27.36)	24 (27.91)	0.009	0.925
	No	208 (72.47)	146 (72.64)	62 (72.09)		
Drinking (n, %)	Yes	99 (34.49)	69 (34.33)	30 (34.88)	0.008	0.928
	No	188 (65.51)	132 (65.67)	56 (65.12)		
Hp infection (n, %)	Yes	116 (40.42)	81 (40.30)	35 (40.70)	0.004	0.950
	No	171 (59.58)	120 (59.70)	51 (59.30)		
Complication (n, %)	Diabetes	52 (18.12)	36 (17.91)	16 (18.60)	0.020	0.889
	Hypertension	128 (44.60)	90 (44.78)	38 (44.19)	0.009	0.927
	Coronary heart disease	28 (9.76)	19 (9.45)	9 (10.47)	0.070	0.791
Surgical history (n, %)	Yes	42 (14.63)	30 (14.93)	12 (13.95)	0.046	0.831
	No	245 (85.37)	171 (85.07)	74 (86.05)		
History of gastric bleeding (n, %)	Yes	32 (11.15)	22 (10.93)	10 (11.63)	0.028	0.866
	No	255 (88.37)	179 (89.07)	76 (88.37)		
Taking NSIADs (n, %)	Yes	71 (24.74)	49 (24.38)	22 (25.58)	0.047	0.829
	No	216 (75.74)	152 (75.62)	64 (74.42)		
APTT (Mean ± SD)		17.86±3.48	17.79±3.42	18.03±3.64	0.534	0.594
Endoscopic disposal (n, %)	Mechanical hemostasis	143 (49.83)	101 (50.25)	42 (48.84)	0.150	0.881
	Electric coagulation hemostasis	18 (6.27)	12 (5.97	6 (6.98)		
	Local injection hemostasis	126 (43.90)	88 (43.78)	38 (44.19)		
HB (Mean ± SD)		111.40±17.39	111.63±17.65	110.88±16.83	0.334	0.738
PLT (Mean ± SD)		210.27±23.83	210.41±23.85	209.95±23.89	0.150	0.881
D-D (Mean ± SD)		300.21±49.91	297.11±50.91	307.45±46.97	1.612	0.108
APTT (Mean ± SD)		28.08±2.54	28.06±2.55	28.13±2.52	0.214	0.831
PT (Mean ± SD)		13.01±0.99	12.94±0.99	13.18±0.98	1.887	0.060
Scr (Mean ± SD)		84.29±15.22	84.31±15.23	84.22±15.29	0.046	0.964
BUN (Mean ± SD)		10.44±2.86	10.43±2.89	10.45±2.79	0.054	0.957
ALB (Mean ± SD)		29.70±7.12	30.24±7.08	28.45±7.09	1.961	0.051
PGE_2 (Mean ± SD)		283.14±52.81	284.15±53.30	280.79±51.86	0.493	0.622

Abbreviations: SD, standard error; Hp, Helicobacter pylori; NSIADs, non-steroidal anti-inflammatory drugs; APTT, activated partial thromboplastin time; HB, hemoglobin; PLT, platelet count; D-D, D-dimer; APTT, activated partial thromboplastin time; PT, prothrombin time; Scr, serum creatinine; BUN, blood urea nitrogen; ALB, albumin; PGE_2, prostaglandin E_2.

within 24 h; (3) bright red bloody gastric contents aspirated from the stomach; and (4) gastrointestinal decompression tubes draining haemorrhagic fluids or active bleeding visible on endoscopy.

Statistical analysis

SPSS 26.0 was used to analyze the data. The measurement data were expressed as mean ± standard deviation, and comparisons were made using t-tests (for two groups) or F-tests (for multiple groups). Categorical data were expressed as frequencies and percentages, with comparisons made using the chi-square (x^2) test. Multivariate Logistic regression analysis was performed to identify the influencing factors for rebleeding in patients with grade IIb PUB after endoscopic treatment. R language and rms program package were used to establish a nomogram prediction model. The model's discriminative ability and calibration were assessed through the calibration diagram and area under the receiver operating characteristic (ROC) curve (AUC). The Hosmer-Lemeshow test was used to verify model fit,

Table 2. Influencing factors of rebleeding after endoscopic therapy in IIb PUB patients

Factors	Univariate analysis		Multivariate analysis				
	x^2/t	*P* value	*B*	*SE*	*P* value	*OR*	*95% CI*
Gender	0.530	0.467					
Age	1.357	0.176					
Ulcer site	12.667	0.000	0.471	1.430	0.742	1.602	0.907-26.414
Ulcer diameter	18.269	0.000	2.286	1.310	0.081	9.836	0.754-128.244
Smoking	1.855	0.173					
Drinking	0.407	0.523					
Hp infection	11.926	0.001	2.275	0.836	0.007	9.723	1.889-50.058
Diabetes	0.001	0.989					
Hypertension	0.007	0.933					
Coronary heart disease	0.010	0.920					
Surgical history	0.213	0.645					
History of gastric bleeding	0.026	0.871					
Taking NSIADs	0.297	0.586					
APTT	1.149	0.252					
Endoscopic disposal	0.298	0.766					
HB	0.217	0.828					
ALT	0.711	0.478					
D-D	5.353	0.000	0.012	0.006	0.047	1.013	1.000-1.025
APTT	1.504	0.134					
PT	4.592	0.000	0.807	0.326	0.013	2.242	1.184-4.244
Scr	1.115	0.266					
BUN	1.067	0.287					
ALB	2.629	0.009	-0.106	0.051	0.036	0.899	0.814-0.933
PGE_2	3.024	0.003	-0.014	0.007	0.042	0.987	0.974-1.000
Constant			-12.419	4.946	0.012	0.000	

Abbreviations: SD, standard error; Hp, Helicobacter pylori; NSIADs, non-steroidal anti-inflammatory drugs; APTT, activated partial thromboplastin time; HB, hemoglobin; PLT, platelet count; D-D, D-dimer; APTT, activated partial thromboplastin time; PT, prothrombin time; Scr, serum creatinine; BUN, blood urea nitrogen; ALB, albumin; PGE_2, prostaglandin E_2.

and the decision curve analysis (DCA) was conducted to evaluate the model's clinical utility. A *P*-value of <0.05 was considered statistically significant.

Results

Comparison of baseline information between modelling and validation cohorts

There were no significant differences in basic characteristics and laboratory data between the modelling cohort and the validation cohort (all P>0.05). There were 25 (12.44%) patients who experienced postoperative rebleeding in the modelling cohort, and 11 (12.79%) in the validation cohort (P>0.05), supporting the validity of the comparison (**Table 1**).

Analysis of factors associated with rebleeding

Univariate analysis identified that, in the modelling cohort, patients' ulcer site, ulcer diameter, Hp infection, D-D, PT, ALB, and PGE_2 were associated with rebleeding after endoscopic treatment. Multivariate Logistic regression analysis further identified Hp infection, D-D, PT, ALB and PGE2 were independent risk factors for rebleeding in patients with grade IIb PUB after endoscopic therapy (all P<0.05) (**Table 2**).

Establishment of a nomogram model

A prediction model equation was established using R4.2.1 software based on the five influencing factors obtained: Log (P) =2.275×Hp infection +0.012×D-D+0.807×PT-0.106×ALB-0.014×PGE2-12.419. A neomorph model was

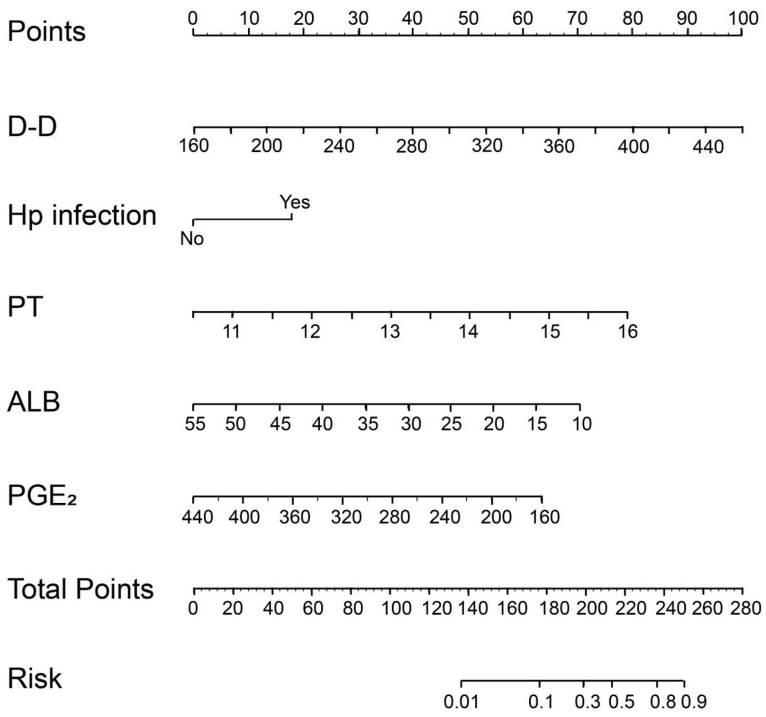

Figure 2. The nomogram prediction model. Abbreviations: Hp, Helicobacter pylori; D-D, D-dimer; PT, prothrombin time; ALB, albumin; PGE_2, prostaglandin E_2.

constructed (**Figure 2**). The calibration curve for the prediction model is shown in **Figure 3A**. The AUC under the ROC curve for the model was 0.875 (95% CI: 0.788-0.962) (**Figure 3B**) in the modeling cohort. The decision analysis curve is shown in **Figure 3C**, confirming the model's validity with a high yield.

Internal verification of the nomogram model

In the validation cohort, the probability of rebleeding was predicted using the nomogram, and the ROC curve was plotted. The predicted values from the calibration curve were close to the actual value (Hosmer-Lemeshow: x^2=6.672, P=0.572) (**Figure 4A**). The AUC of the nomogram model was 0.907 (95% CI: 0.833-0.981) (**Figure 4B**). The decision curve showed a high net benefit, indicating that the nomogram model has good calibration ability in the verification group (**Figure 4C**).

External verification of the nomogram model

A total of 168 patients were included in the external validation cohort, of which 21 (12.50%) had rebleeding. The characteristics of patients in the external validation cohort are shown in **Table 3**. The data of patients in the external validation cohort were brought into the nomogram prediction model, and the ROC curve obtained is shown in **Figure 5**. The AUC reached 0.902 (95% CI: 0.843-0.961) for the external validation cohort, demonstrating that the nomogram prediction model has good generalizability.

Discussion

In recent years, the advancement and widespread application of endoscopy, interventional therapy, and other technologies have significantly improved the diagnosis and treatment of gastrointestinal hemorrhage in China. However, the occurrence of rebleeding remains a significant challenge for clinicians [11]. PUB patients with Forrest grade Ia-IIb often experience active bleeding that is difficult to control. Additionally, studies have shown that the clinical mortality rate for PUB patients is approximately 11.1%, with a high risk of hypohemolytic shock, peripheral circulatory failure, and other complications, which pose a significant threat to patient survival [12]. Therefore, it is of great significance to identify the factors affecting rebleeding in Forrest IIb PUB patients and formulate targeted intervention programs to reduce the risk of rebleeding and improve the prognosis of patients.

Hp infection is a significant pathogenic factor in the development of peptic ulcer, chronic gastritis and even gastric cancer, inducing gastric tissue lesions through the release of protease and cytotoxin [13]. In this study, differences in Hp infection rates were observed between the NB group and the RB group. Multivariate Logistic regression analysis showed that Hp infection was an influential factor for rebleeding in patients with Forrest IIb PUB. This is possibly due to Hp entering the mucus layer on the surface of the gastric mucosa through the flagellum and use the urease function to change

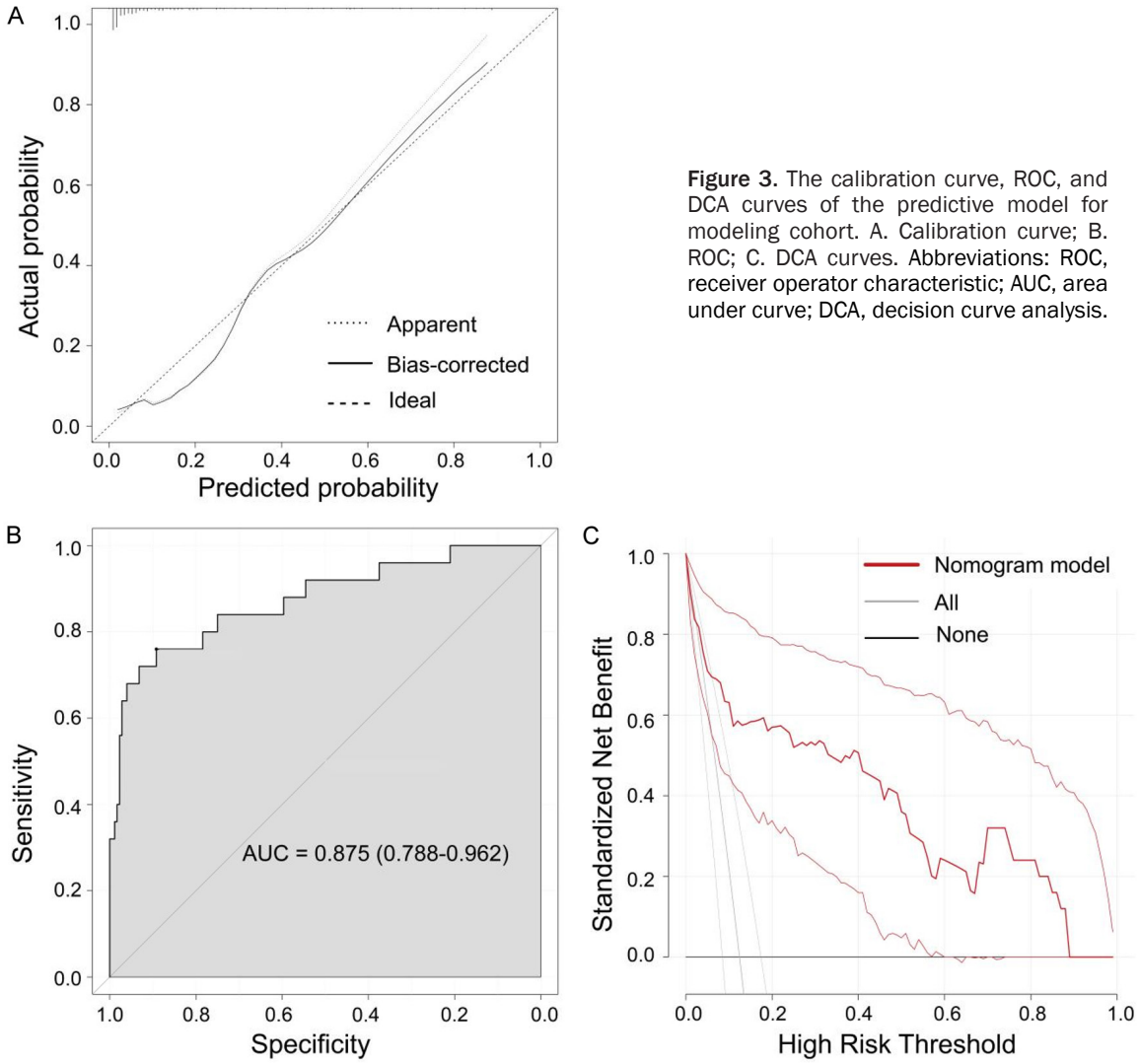

Figure 3. The calibration curve, ROC, and DCA curves of the predictive model for modeling cohort. A. Calibration curve; B. ROC; C. DCA curves. Abbreviations: ROC, receiver operator characteristic; AUC, area under curve; DCA, decision curve analysis.

its surroundings into an alkaline environment, leading to damage to the gastric mucosa [14]. Additionally, Hp induces a range of immune-mediated inflammatory responses, both through its antigens and the toxins it secretes, leading to chronic inflammation and in turn resulting in damage and apoptosis of mucosal cells, atrophy of the gastric mucosa, and instanced risk of rebleeding in Forrest IIb PUB patients. Ojetti V et al. [15] highlighted that Hp infection stimulates increased gastrin production, which promotes gastric acid secretion, destroys the mucus-bicarbonate barrier, and impairs gastric mucosa function. Furthermore, the coexistence of NSAID use and Hp infection has been identified as a significant risk factor for upper gastrointestinal hemorrhage, with the two conditions acting synergistically to exacerbate the damage to the gastric mucosa [15]. In addition, a study by Gong L et al. [16] found that Hp infection was a risk factor for hemorrhage in elderly PUD patients, and was positively correlated with the severity of hemorrhage, which is similar to the results of this study.

This study identified serum D-D as a risk factor for rebleeding in Forrest class IIb PUB patients. D-D is the final product of fibrinogen degradation and reflects alterations in the coagulation-fibrinolytic system [17, 18]. In patients with Forrest class IIb PUB, the fibrinolytic system is activated to remove the clot attached to the ulcer base, leading to increased serum D-D levels. This indicates a state of secondary fibrinolysis, reducing the stability of the clot and increasing the risk of rebleeding. Yue W et al. [19] demonstrated that elevated serum D-D levels are indicative of a hypercoagulable state

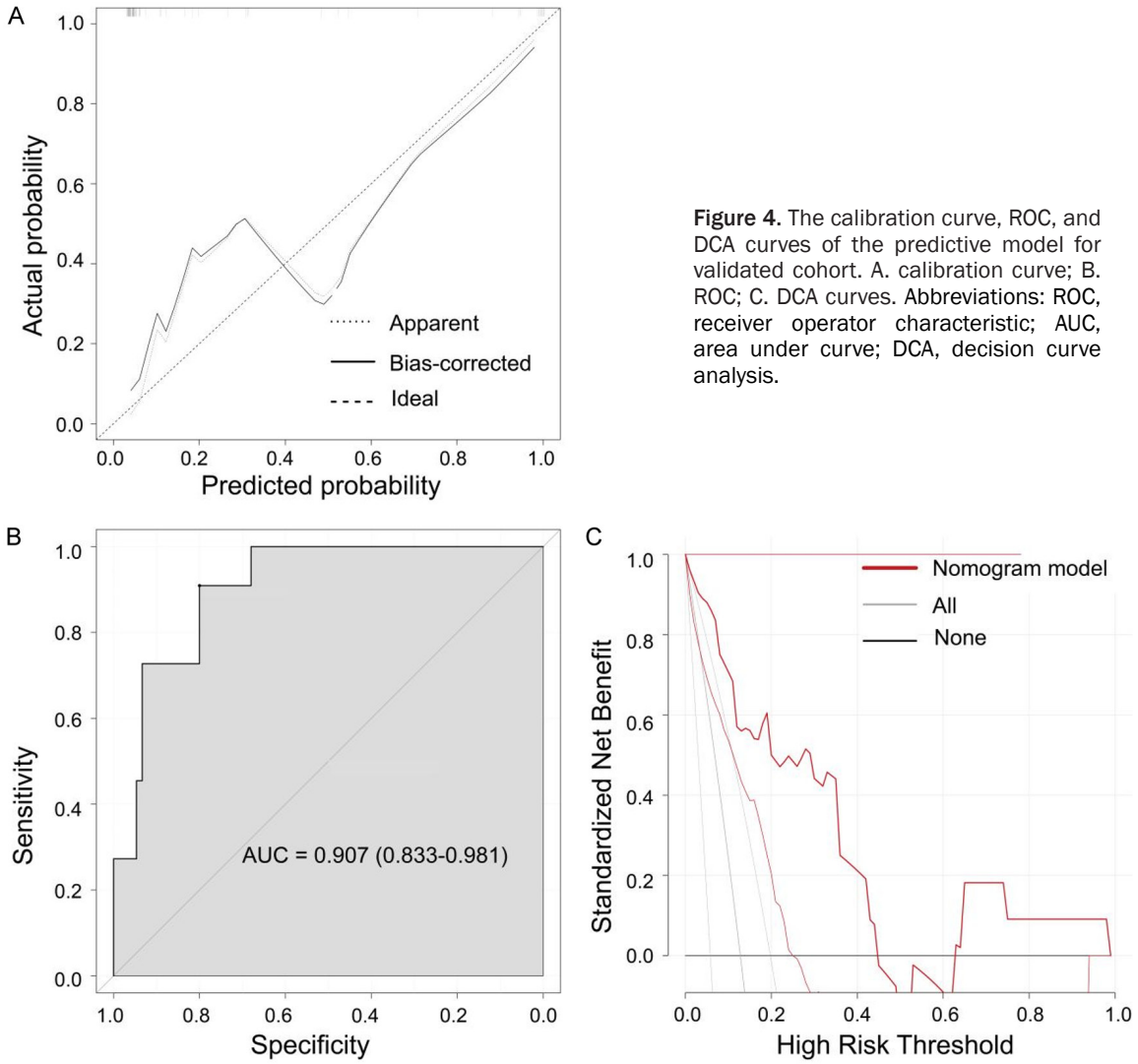

Figure 4. The calibration curve, ROC, and DCA curves of the predictive model for validated cohort. A. calibration curve; B. ROC; C. DCA curves. Abbreviations: ROC, receiver operator characteristic; AUC, area under curve; DCA, decision curve analysis.

and disruption of the integrity of the gastrointestinal mucosa, impairing the endothelial cells and ultimately leading to gastrointestinal bleeding. Furthermore, they established that this is an independent predictor of rebleeding in patients with non-variceal upper gastrointestinal bleeding. Typically, the coagulation and fibrinolytic systems are in a dynamic equilibrium [20]. This study also found PT to be a risk factor for rebleeding in Forrest class IIb PUB patients. PT is a valid indicator of exogenous coagulation status and a key test for disseminated vascular coagulation, and its prolongation indicates coagulation disorders [21]. Given that ulcer lesions in Forrest class IIb PUB patients are inherently bleeding, prolonged PT results in decreased coagulation factors, reduced fibrin production, and promotes clot shedding, thereby increasing the risk of rebleeding. Studies have found that prolonged PT increases the risk of bleeding and can predict rebleeding in PUB patients [22]. He S et al. [23] pointed out that prolonged PT in PUB patients would reduce the formation of thrombin and make blood clots easily dissolve and fall off, thereby increasing the risk of rebleeding after endoscopic treatment. These findings are consistent with the results of this study.

Finally, this study found that ALB and PGE2 were both influential factors for rebleeding in patients with Forrest IIb PUB after endoscopic treatment. ALB is a plasma protein that plays a crucial role in maintaining plasma colloid osmotic pressure and ensuring the integrity of vascular endothelium. A decrease in ALB level

Table 3. Characteristics of the external verification cohort

Factors		NB group (n=147)	RB group (n=21)	x^2/t	*P* value
Gender (n, %)	Male	99 (67.35)	12 (57.14)	0.854	0.356
	Female	48 (32.65)	9 (42.86)		
Age (Mean ± SD)		54.64±12.28	54.85±12.36	0.073	0.942
Ulcer site (n, %)	Stomach	86 (58.50)	6 (28.57)	6.645	0.001
	Duodenum	61 (41.50)	15 (71.43)		
Ulcer diameter (n, %)	<2 cm	101 (68.71)	7 (33.33)	10.015	0.002
	≥2 cm	46 (31.29)	14 (66.67)		
Smoking (n, %)	Yes	40 (27.21)	6 (28.57)	0.017	0.896
	No	107 (72.79)	15 (71.53)		
Alcohol consumption (n, %)	Yes	51 (34.69)	7 (33.33)	0.015	0.903
	No	96 (64.61)	14 (66.67)		
Hp infection (n, %)	Yes	52 (35.37)	15 (71.43)	9.963	0.002
	No	95 (64.63)	6 (28.57)		
Complication (n, %)	Diabetes	27 (18.37)	4 (19.05)	0.051	0.822
	Hypertension	66 (44.90)	9 (42.86)	0.031	0.860
	Coronary heart disease	14 (9.52)	2 (9.52)	0.112	0.738
Surgical history (n, %)	Yes	22 (14.97)	3 (14.29)	0.060	0.806
	No	125 (85.03)	18 (85.71)		
History of gastric bleeding (n, %)	Yes	20 (13.61)	2 (9.52)	0.030	0.863
	No	127 (86.39)	19 (90.47)		
Taking NSIADs (n, %)	Yes	37 (25.17)	5 (23.81)	0.018	0.893
	No	110 (74.83)	16 (76.19)		
APTT (Mean ± SD)		17.82±3.51	17.68±3.63	0.170	0.865
Endoscopic disposal (n, %)	Mechanical hemostasis	73 (49.66)	10 (47.61)	0.860	0.650
	Electric coagulation hemostasis	12 (8.16)	3 (14.29)		
	Local injection hemostasis	62 (42.18)	8 (38.10)		
HB (Mean ± SD)		111.63±17.57	110.87±17.85	0.185	0.853
PLT (Mean ± SD)		209.98±23.84	210.39±23.44	0.074	0.941
D-D (Mean ± SD)		290.55±44.65	313.02±63.60	2.035	0.044
APTT (Mean ± SD)		28.11±2.53	28.09±2.61	0.034	0.973
PT (Mean ± SD)		12.86±0.91	13.78±1.24	4.126	0.000
Scr (Mean ± SD)		84.33±15.18	84.29±14.95	0.011	0.991
BUN (Mean ± SD)		10.44±2.98	10.41±2.86	0.043	0.966
ALB (Mean ± SD)		31.61±7.35	24.69±5.91	4.125	0.000
PGE_2 (Mean ± SD)		286.79±54.32	248.51±41.11	3.102	0.002

Abbreviations: SD, standard error; Hp, Helicobacter pylori; NSIADs, non-steroidal anti-inflammatory drugs; APTT, activated partial thromboplastin time; HB, hemoglobin; PLT, platelet count; D-D, D-dimer; APTT, activated partial thromboplastin time; PT, prothrombin time; Scr, serum creatinine; BUN, blood urea nitrogen; ALB, albumin; PGE_2, prostaglandin E_2.

can weaken the function of vascular endothelial barrier, making blood vessels more vulnerable to damage and rupture. Zhuang et al. [24] noted that ALB can induce endothelial cell damage by increasing the level of oxidized low-density lipoprotein in vascular endothelial cells, further aggravating vascular damage and ulcer formation. In addition, ALB can reflect the nutritional status of the body, and significant ALB loss can impair ulcer healing, increasing the risk of rebleeding. Ito et al. [25] have demonstrated that reduced ALB level contributes to the formation of edema in mucosal tissue, creating an unfavorable environment for ulcer healing, thus elevating the risk of rebleeding. A number of studies have shown that PGE2 can protect the function of gastric mucosa and maintain its blood circulation, inhibit the secretion of gastric acid, and promote the regeneration of epithelial cells [26, 27]. For patients with Forrest IIb grade PUB, increased secretion of gastrin and gastric acid result in gastric muco-

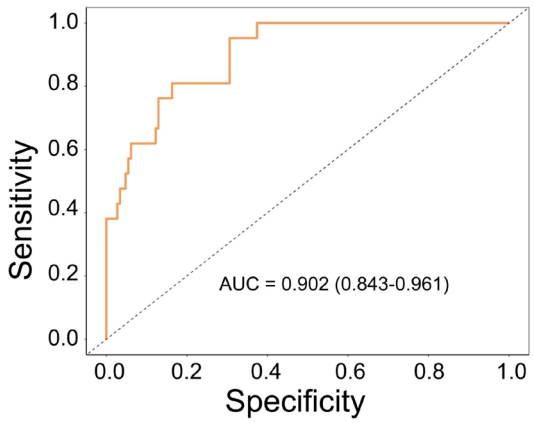

Figure 5. ROC curve analysis of the model in external validation cohort. Abbreviation: ROC, receiver operator characteristic.

sal damage, thereby reducing the level of PGE2 and further inducing intravascular coagulation. In addition, Li R et al. [28] found that PGE2 can inhibit gastric acid secretion, synthesize gastric mucosal protective substances, and maintain good blood circulation of gastric mucosa. This can play a protective role in peptic ulcer bleeding and is a protective factor for pediatric peptic ulcer recurrence and upper digestive tract bleeding, which aligns with the results of this study.

In summary, Hp infection, D-D, PT, ALB and PGE2 are significant risk factors for rebleeding after endoscopic treatment in Forrest IIb PUB patients. The predictive model based on these factors has certain predictive efficacy. However, the study's retrospective nature and limited clinical information on the subjects may have restricted the comprehensiveness of the analysis. Therefore, future research should focus on multicenter, large-scale studies that incorporate a wider range of factors to develop a more robust prediction model. Previous studies have also highlighted the relevance of factors such as patient age, shock, bleeding volume, and the Rockall risk score in predicting rebleeding. These factors should be considered in future research to enhance the prevention of rebleeding in Forrest IIb PUB patients.

Conclusion

Hp infection, D-D, PT, ALB and PGE2 are influential factors for rebleeding after endoscopic treatment in patients with Forrest IIb PUB. The nomogram model developed using these factors demonstrates excellent differentiation and calibration, making it a valuable tool for clinicians to identify high-risk patients and implement timely interventions.

Disclosure of conflict of interest

None.

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