International Journal of General Medicine

Dovepress
Taylor & Francis Group

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ORIGINAL RESEARCH

Development and External Validation of a Nomogram for Predicting Upper Gastrointestinal Bleeding in Patients After Percutaneous Coronary Intervention: A Retrospective Multicenter Cohort Study

Jingyi Yang[1,*], Qifeng Liu[2,*], Songnan Wang[3], Yanling Jv[3], Bing Pan[1], Shengxiang Feng[1], Jiani Li[1], Lida Zhang[1], Xuqi Li[2], Hongwei Yu[3]

[1]Department of Cardiovascular Medicine, Graduate Training Base, Jinzhou Central Hospital, Jinzhou Medical University, Jinzhou, People's Republic of China; [2]Department of Cardiology, The First Affiliated Hospital of Jinzhou Medical University, Jinzhou, People's Republic of China; [3]Department of Cardiology, Jinzhou Central Hospital, Jinzhou, People's Republic of China

*These authors contributed equally to this work

Correspondence: Hongwei Yu, Department of Cardiology, Jinzhou Central Hospital, Jinzhou, Liaoning, 121000, People's Republic of China, Email phyhw@163.com

Background: Dual antiplatelet therapy (DAPT) after percutaneous coronary intervention (PCI) increases the risk of upper gastrointestinal bleeding (UGIB) in patients with the acute coronary syndrome (ACS). As UGIB leads to a poor prognosis, it is essential to predict its occurrence early and effectively.

Objective: The study aimed to develop and validate a nomogram for predicting UGIB in patients with ACS undergoing DAPT after PCI.

Methods: This study was conducted on 1820 patients with ACS receiving DAPT after PCI in Jinzhou Central Hospital from January 2019 to September 2022. A logistic regression analysis was conducted to identify the risk factors of UGIB, which were utilized to develop a model for predicting the probability of UGIB in patients receiving DAPT. A validation cohort was used for verification. The discrimination, calibration, and clinical practicability of the nomogram were verified using receiver operating characteristic (ROC) curve analysis, Hosmer–Lemeshow (H–L) test, and decision curve analysis (DCA), respectively.

Results: Age, history of gastrointestinal ulcer/bleeding, heart failure, drinking status, and creatinine were independent risk factors for UGIB and included in our nomogram. The nomogram demonstrated good discriminative ability, with Area under the curve (AUC) values of 0.829, 0.848, and 0.838, respectively. The calibration curve and H–L test indicate that the model has good consistency ($P = 0.948$, $P = 0.777$, and $P = 0.913$, respectively). The nomograms can be clinically beneficial when the threshold probability is >0.02 in both the training and validation cohorts.

Conclusion: Our prediction model can guides clinical physicians in risk stratification of undergoing DAPT patients after PCI by calculating the probability of UGIB. Our study may help clinicians in the early identification of patients at a high risk of UGIB and in providing a personalized treatment and management strategies to reduce the associated adverse outcomes.

Keywords: percutaneous coronary intervention, upper gastrointestinal bleeding, risk factor, prediction model, dual antiplatelet therapy

Introduction

Acute coronary syndrome (ACS) is a life-threatening arteriosclerosis disease.[1] At present, it is typically treated with percutaneous coronary intervention (PCI). PCI improves myocardial perfusion, increases the survival rates after myocardial infarction, and diminishes the probability of recurrent infarction.[2] To reduce the recurrence of ischemic

https://doi.org/10.2147/IJGM.S575300
Received: 5 November 2025
Accepted: 4 February 2026
Published: 11 February 2026

events, the current guidelines recommend the use of the dual antiplatelet therapy (DAPT), which usually involves the use of aspirin and a P2Y12 receptor antagonist during and after PCI.[3]

The balance between bleeding and ischemia has always been a major challenge while deciding the optimum antiplatelet therapy for patients with atherosclerotic cardiovascular diseases.[4] Extensive use of antiplatelet drugs significantly increases the risk of bleeding. Upper gastrointestinal bleeding (UGIB) is the most common bleeding event, accounting for 48.7% of total bleeding events.[5] The prognosis for patients experiencing UGIB is unfavorable, with severely affected cases staring at life-threatening outcomes.[6,7] Therefore, it is crucial to analyze the clinical characteristics of patients with UGIB who received DAPT after PCI and explore the risk factors for UGIB.

Although some risk factors for UGIB have been identified,[8,9] the predictive power of individual factors for UGIB during DAPT after PCI is relatively low. At present, clinical doctors commonly use DAPT and PRECISE-DAPT scores to evaluate the risk of bleeding during DAPT after PCI.[10,11] However, DAPT and PRECISE-DAPT scoring systems are mainly used to predict composite bleeding events and may not be suitable for predicting the occurrence of UGIB. In addition, it has also been found that the PRECISE-DAPT scoring system may not be entirely suitable for Asian populations.[12] A suitable UGIB scoring system and risk-prediction model for patients undergoing DAPT after PCI have still not been developed. After all, UGIB can comprise about half of total bleeding events observed after DAPT. This study aims to explore independent risk factors for UGIB in patients with ACS undergoing DAPT within one year after PCI and construct a scoring system that may be suitable for Asian populations to predict UGIB. For patients at high risk of bleeding, clinical doctors use personalized antithrombotic strategies such as shortening the DAPT course, combining gastric mucosal protectants, and closer follow-up to reduce bleeding events.

Methods

Study Design and Patients

This study enrolled 2708 patients with ACS who received DAPT after PCI and their clinical data and basic information were collected from their medical records. Of these 2708 patients, 1820 patients treated at Jinzhou Central Hospital in China between January 2019 and September 2022 were randomized in a 7:3 ratio into a training cohort (n = 1276) and an internal validation cohort (n = 544). Additionally, data on 810 patients diagnosed with ACS and undergoing PCI at the First Affiliated Hospital of Jinzhou Medical University from October 2022 to June 2023 were collected. Among these 810 patients, 260 met the exclusion criteria. The remaining 550 patients were used as an external validation cohort.

The patients were enrolled based on the following inclusion criteria: (1) complete clinical data; (2) diagnosed with ACS and underwent PCI, ACS was defined as any one of the following: unstable angina pectoris, ST-segment elevation myocardial infarction, or non-ST-segment elevation myocardial infarction; and (3) continuously received DAPT (aspirin + clopidogrel/ticagrelor) post-operation. The exclusion criteria were as follows: (1) unknown or missed data on survival; (2) history of gastrointestinal tumors or cirrhosis, esophageal, and gastric varices; (3) a history of hemorrhagic diseases, such as allergic purpura or coagulation factor abnormalities; and (4) patients requiring anticoagulant therapy, such as atrial fibrillation, ventricular thrombi, pulmonary embolism, or deep vein thrombosis. The patient selection process and the study design are shown in Figure 1.

Data Collection

Clinical data of patients, including their hospital ID, name, gender, age, body mass index, blood pressure, smoking status, and drinking status, as well as their medical history, such as hypertension, diabetes, gastrointestinal ulcers/bleeding, and heart failure (HF), were collected from their hospital records. Data related to the following laboratory results were also collected: white blood cell count, platelet count, fasting blood glucose, C-reactive protein, albumin (ALB), creatinine (Cr), low-density lipoprotein cholesterol, plasma D-dimer (D–D), and amino-terminal pro b-type natriuretic peptide. In addition, information related to the patient's use of treatments, such as proton pump inhibitor and nonsteroidal anti-inflammatory drugs other than aspirin, as well as echocardiography indicators, such as ejection fraction, was obtained. The collected data were imported into an EXCEL spreadsheet to create a database.

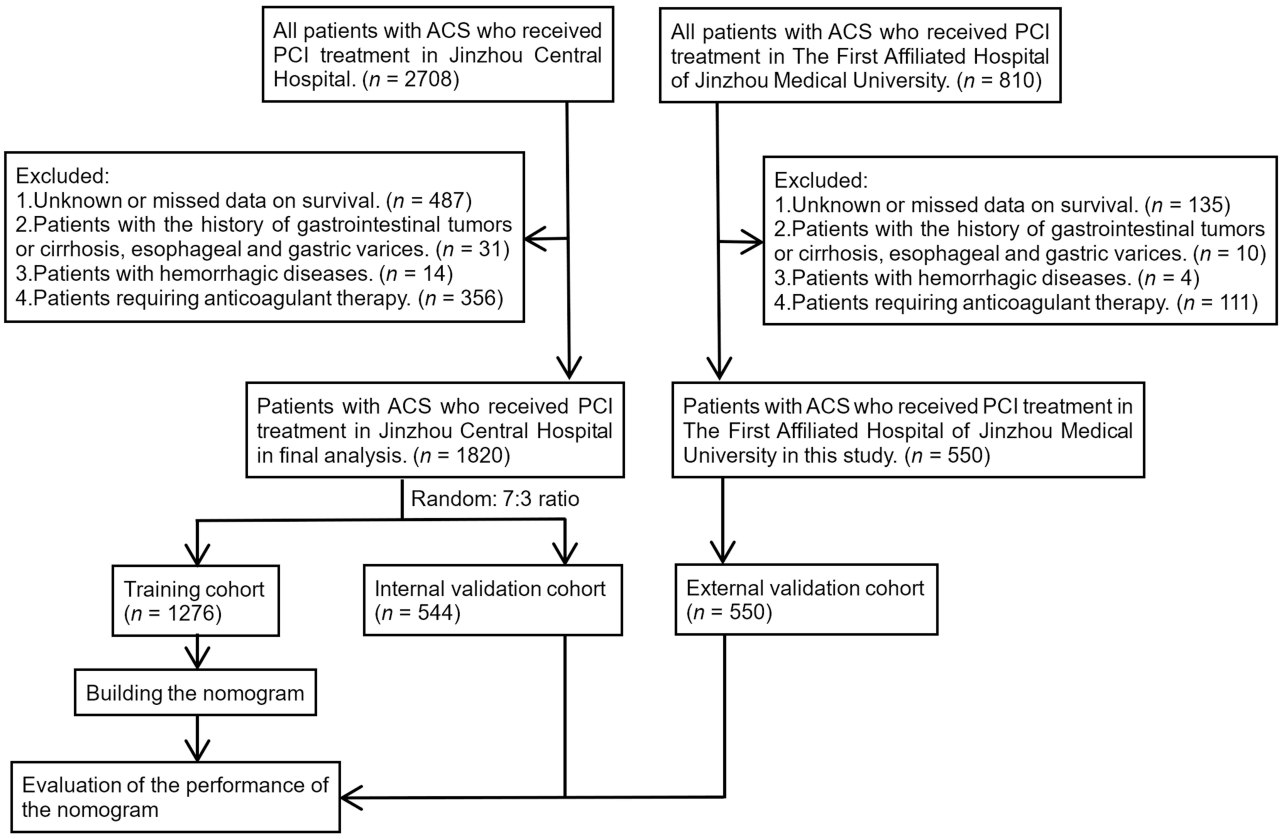

Figure 1 Study flow.
Abbreviations: ACS, acute coronary syndromes; PCI, percutaneous coronary intervention.

Definition of Important Variables and Outcome

The important variables were defined as follows. Smoking status was defined as smoking at least once per day for at least 6 months, and subjects maintained this status during the follow-up period. Drinking status was defined as subjects who consumed alcohol at least once per week regularly in the past 6 months and maintaining this status during the follow-up period. Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or previously diagnosed with hypertension and currently taking antihypertensive drugs. Diabetes was defined according to the World Health Organization criteria as follows: random blood glucose ≥ 11.1 mmol/L or fasting blood glucose ≥ 7.0 mmol/L. Anemia was defined according to the World Health Organization diagnostic criteria, serum hemoglobin < 13 g/dL in male adults and < 12 g/dL in female adults were identified as anemia patients. According to the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, the diagnosis of HF was primarily based on patients' clinical symptoms, signs, and relevant examinations.

The diagnostic criteria for UGIB described in the Guidelines for the diagnosis and treatment of acute non-variceal upper gastrointestinal bleeding (2015, Nanchang, China).[13] UGIB was diagnosed if the following symptoms were present: hematemesis, melena, hematochezia with or without the symptoms of peripheral circulatory failure (such as dizziness, palpitations, pallor, tachycardia, and hypotension), and/or positive fecal occult blood, endoscopy with no esophageal or gastric variceal bleeding, and the presence of bleeding lesions in the digestive tract. The definition of UGIB was based on the diagnostic results from the gastroenterology department of our hospital or other tertiary first-class hospitals.

Follow up all selected patients for one year and record the occurrence of adverse events. The occurrence of UGIB during DAPT within one year after PCI was defined as the outcome event. If UGIB events occur repeatedly during the follow-up process, regardless of whether DAPT is restarted, only the first event will be analyzed.

Statistical Analysis

Variables with more than 20% missing data were excluded from study, and variables with less than 20% missing data were filled with multiple imputation. Statistical analysis was performed using SPSS 26.0 and R 4.3.2 software programs. Continuous data were expressed as the mean ± standard deviation or median. The interquartile range and the categorical variables were described using n (%). Using the autoReg package, univariate logistic regression analysis was conducted on the training set with UGIB as the dependent variable and risk factors as independent variables. The independent variables with single factor $P < 0.01$ were included in the multivariate logistic regression analysis. A stepwise backward elimination procedure was performed to minimize the Akaike information criterion in the multiple factor logistic regression analysis. The factors were identified for constructing the prediction model of UGIB in patients receiving DAPT after PCI. Subsequently, these factors were incorporated into the risk-prediction model and a nomogram was plotted using the regplot package to visualize the model. The internal and external validation cohorts were used for model validation. The performance of the model was evaluated by plotting receiver operating characteristic (ROC) curves, calibration graphs, and decision curve analysis (DCA) using a pROC package, an rms package, a ggDCA package, and a ggprism package to assess its discrimination, calibration, and clinical applicability. $P < 0.05$ was considered statistically significant. All tests were 2-tailed. Throughout these processes, we complied with TRIPOD (transparent reporting of a multivariable prediction model for individual prognosis or diagnosis) guidance for performing the prediction model.

Results

Baseline Clinical Characteristics

The flowchart for selecting the patients is shown in Figure 1. This study was performed on 2370 patients. Of these, 1276 patients were placed in the training cohort with 49 cases of UGIB, 544 in the internal validation cohort with 23 cases of UGIB, and 550 in the external validation cohort with 21 cases of UGIB. Compared with the baseline clinical data of patients in the training cohort, no statistically significant difference was noted in each variable in the internal validation cohort ($P > 0.05$). In contrast, the external validation cohort showed statistically significant differences for age, previous cases of hypertension, stroke history, proton pump inhibitor treatment, white blood cell count, fasting blood glucose, low-density lipoprotein cholesterol, ALB, alanine transaminase, and ejection fraction values ($P < 0.05$, Table 1).

Variable Selection and Model Construction

The univariate logistic regression analysis showed statistically significant differences between the age, drinking status, diabetes, hypertension, anemia, gastrointestinal ulcer/bleeding history, HF, Cr, and ALB of patients with and without UGIB ($P < 0.05$). Independent variables with a P-value of <0.01 in the univariate analysis were included in the multivariate logistic regression analysis. A stepwise backward elimination procedure was performed to minimize the Akaike information criterion in the multiple factor logistic regression analysis. Finally, age (OR = 1.06, 95% CI: 1.03–1.09, $P < 0.001$), history of gastrointestinal ulcer/bleeding (OR = 3.77, 95% CI: 1.94–7.32, $P < 0.001$), HF (OR = 3.97, 95% CI: 2.13–7.40, $P < 0.001$), drinking (OR = 2.47, 95% CI: 1.32–4.64, $P = 0.005$), and Cr (OR = 1.02, 95% CI: 1.01–1.04, $P < 0.001$) were identified as the factors necessary for constructing the prediction model of UGIB in patients receiving DAPT after PCI (Table 2).

We developed a new scoring system using the multivariate analysis results for predicting the probability (P) of UGIB in patients who received DAPT after PCI: $\ln\left(\frac{P}{1-P}\right) = 0.0594 \times$ age (years) + 0.905 × (drinking status: yes = 1, no = 0) + 1.379 × (HF: yes = 1, no = 0) + 1.326 × (history of digestive ulcer/bleeding: yes = 1, no = 0) + 0.0243 × Cr (μmol/L) - 10.472.

Performance and Validation of the Prediction Model

We used Area under the curve (AUC) and the H–L test to evaluate the discriminative ability and calibration of our constructed prediction model, respectively, and plotted an ROC curve and a calibration curve. In the training cohort, the predictive model demonstrated good discriminative ability for predicting the probability of UGIB in patients after PCI, achieving an AUC value of 0.829 (95% CI, 0.776–0.882; $P < 0.001$; Figure 2A). The predictive

Table 1 Baseline Characteristics of the Training and Validation Cohort

Characteristics	Total (n = 1820)	Training Cohort (n = 1276)	Internal Validation Cohort (n = 544)	External Validation Cohort (n = 550)	T vs IV *P*-value	T vs EV *P*-value
Age [mean (SD), years]	60.45(12.08)	60.23(11.87)	60.96(12.53)	58.09(10.96)	0.243	0.000
Sex (male, n,%)	936(51.43%)	660(51.72%)	276(50.74%)	274(49.82%)	0.699	0.455
BMI (IQR, kg/m^2)	24.00(21.96, 26.10)	23.99(22.00, 26.18)	24.01(21.91, 25.94)	23.83(21.43, 26.33)	0.416	0.600
Smoking status (n,%)	772(42.42%)	535(41.93%)	237(43.57%)	250(45.45%)	0.517	0.163
Drinking status (n,%)	746(40.99%)	537(42.08%)	209(38.42%)	245(44.55%)	0.146	0.330
Diabetes (n,%)	773(42.47%)	544(42.63%)	229(42.10%)	245(44.55%)	0.832	0.449
Hypertension (n,%)	871(47.86%)	612(47.96%)	259(47.61%)	310(56.36%)	0.891	0.001
HF (n,%)	594(32.64%)	418(32.76%)	176(32.35%)	180(32.73%)	0.866	0.990
History of stroke (n,%)	673(36.98%)	486(38.09%)	187(34.38%)	253(46.00%)	0.133	0.002
History of digestive ulcer/bleeding (n,%)	226(12.42%)	161(12.62%)	65(11.95%)	65(11.82%)	0.692	0.634
History of anemia (n,%)	205(11.26%)	149(11.68%)	56(10.29%)	60(10.91%)	0.393	0.636
Treatment of oral PPI (n,%)	856(47.03%)	593(46.47%)	263(48.35%)	224(40.73%)	0.464	0.023
Treatment of other NSAIDs (n,%)	153(8.41%)	109(8.54%)	44(8.09%)	58(10.55%)	0.749	0.173
Treatment of ticagrelor (n,%)	1152(63.30%)	792(62.07%)	360(66.18%)	350(63.64%)	0.096	0.526
WBC (IQR,$\times 10^9$/L)	6.23(5.31, 7.13)	6.26(5.34, 7.13)	6.19(5.25, 7.11)	6.48(4.92, 8.41)	0.426	0.004
PLT (IQR,$\times 10^9$/L)	193(168, 218)	192(168, 217)	196(170, 218)	191(151, 233)	0.344	0.730
FBG (IQR, mmol/L)	5.75(4.89, 6.61)	5.73(4.85, 6.61)	5.83(4.93, 6.62)	5.89(4.54, 7.18)	0.325	0.030
Cr (IQR, μmol/L)	75(59, 93)	75(58, 93)	77(61, 93)	75(57, 102)	0.136	0.146
LDLC [mean (SD), mmol/L]	3.39(0.70)	3.40(0.70)	3.38(0.68)	3.21(0.63)	0.641	0.000
ALB (IQR, g/L)	45(42, 49)	45(42, 49)	45(42, 48)	44(38, 51)	0.552	0.018

(*Continued*)

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Table 1 (Continued).

Characteristics	Total (n = 1820)	Training Cohort (n = 1276)	Internal Validation Cohort (n = 544)	External Validation Cohort (n = 550)	T vs IV *P*-value	T vs EV *P*-value
ALT (IQR, U/L)	45(36, 55)	45(36, 55)	46(37, 55)	57(40, 76)	0.675	0.000
CRP (IQR, mg/dl)	6(5, 7)	6(5, 7)	6(5, 7)	6(5, 8)	0.326	0.288
D-D (IQR, mg/L)	0.472(0.394, 0.570)	0.477(0.399, 0.571)	0.464(0.386, 0.561)	0.479(0.345, 0.627)	0.093	0.328
NT-proBNP (IQR, pg/mL)	641(521, 793)	639(515, 784)	651(534, 810)	624(502, 778)	0.121	0.206
EF (IQR, %)	55(50, 60)	55(50, 60)	55(50, 60)	53(47, 60)	0.951	0.000

Notes: Continuous variables are shown as mean ± standard deviation (SD) or median and (interquartile range) (IQR). Categorical variables are presented as numbers and percentages (%).
Abbreviations: BMI, body mass index; HF, heart failure; WBC, white blood cell count; PLT, platelets; FBG, fasting blood glucose; Cr, serum creatinine; LDLC, low-density lipoprotein cholesterol; ALB, albumin; CRP, C-reactive protein; D-D, D-dimer; NT-proBNP, N-terminal pro b-type natriuretic peptide; EF, ejection fraction.

https://doi.org/10.2147/IJGM.S575300

Table 2 Results of Univariate and Multivariate Logistic Regression Analyses on the Influencing Factors of UGIB in the Training Cohort

Variables	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age	1.05 (1.03–1.08)	<0.001	1.06 (1.03–1.09)	<0.001
Sex	0.82 (0.46–1.45)	0.495	–	–
BMI	0.95 (0.86–1.05)	0.288	–	–
Smoking status	1.35 (0.76–2.38)	0.309	–	–
Drinking status	2.45 (1.36–4.44)	0.003	2.47 (1.32–4.64)	0.005
Diabetes	2.00 (1.12–3.58)	0.019	–	–
Hypertension	1.91 (1.06–3.46)	0.031	–	–
HF	3.74 (2.07–6.76)	<0.001	3.97 (2.13–7.40)	<0.001
History of stroke	1.59 (0.90–2.82)	0.112	–	–
History of digestive ulcer/bleeding	4.00 (2.16–7.38)	<0.001	3.77 (1.94–7.32)	<0.001
History of anemia	2.28 (1.14–4.57)	0.020	–	–
Treatment of oral PPI	0.94 (0.53–1.66)	0.822	–	–
Treatment of other NSAIDs	1.52 (0.63–3.66)	0.348		
Treatment of ticagrelor	1.40 (0.76–2.60)	0.284		
WBC	1.20 (0.99–1.46)	0.067		
PLT	1.00 (0.99–1.00)	0.297	–	–
FBG	1.10 (0.92–1.32)	0.274	–	–
Cr	1.03 (1.02–1.04)	<0.001	1.02 (1.01–1.04)	<0.001
LDLC	1.48 (0.98–2.22)	0.060	–	–
ALB	0.94 (0.89–0.99)	0.028	–	–
ALT	1.02 (1.00–1.04)	0.069		
CRP	1.03 (0.98–1.08)	0.214	–	–
D-D	1.26 (0.98–1.62)	0.076	–	–
NT-proBNP	1.00 (1.00–1.00)	0.484	–	–
EF	0.99 (0.95–1.03)	0.507	–	–

Abbreviations: BMI, body mass index; HF, heart failure; WBC, white blood cell count; PLT, platelets; FBG, fasting blood glucose; Cr, serum creatinine; LDLC, low-density lipoprotein cholesterol; ALB, albumin; CRP, C-reactive protein; D-D, D-dimer; NT-proBNP, N-terminal pro b-type natriuretic peptide; EF, ejection fraction.

model also exhibited excellent discriminatory power in both the internal and external validation cohorts, with the AUC values of 0.848 (95% CI, 0.768–0.927; $P < 0.001$) and 0.838 (95% CI, 0.755–0.921; $P < 0.001$), respectively (Figure 2B and C). In the training cohort, both the calibration curve and the H–L test indicated good consistency between the predicted probability and the actual probability in this model, suggesting a high degree of fit ($x^2 = 2.772$, $P = 0.948$; Figure 3A). In the validation cohort, both the calibration curve and the H–L

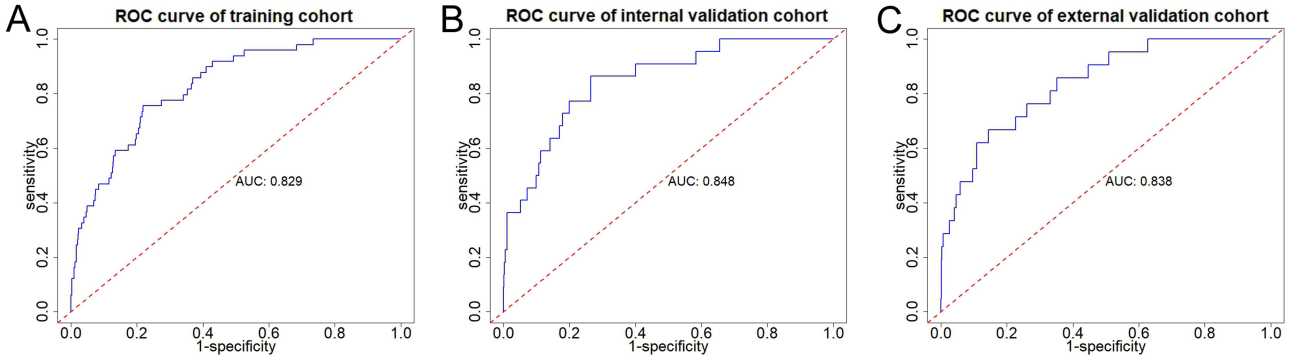

Figure 2 Receiver operating characteristic (ROC) curve of the prediction model. (**A**) Training cohort, (**B**) internal validation cohort, and (**C**) external validation cohort.

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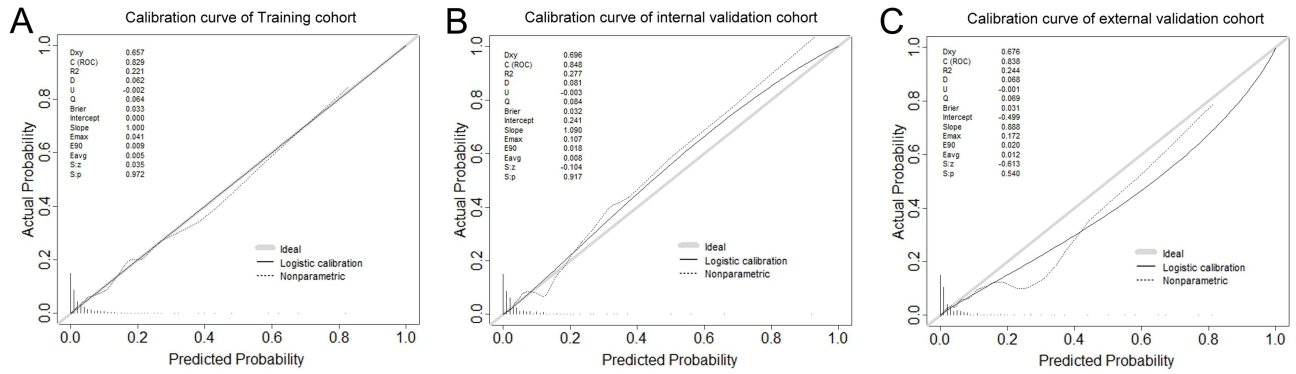

Figure 3 Calibration curves of the prediction model. (**A**) Training cohort, (**B**) internal validation cohort, and (**C**) external validation cohort.

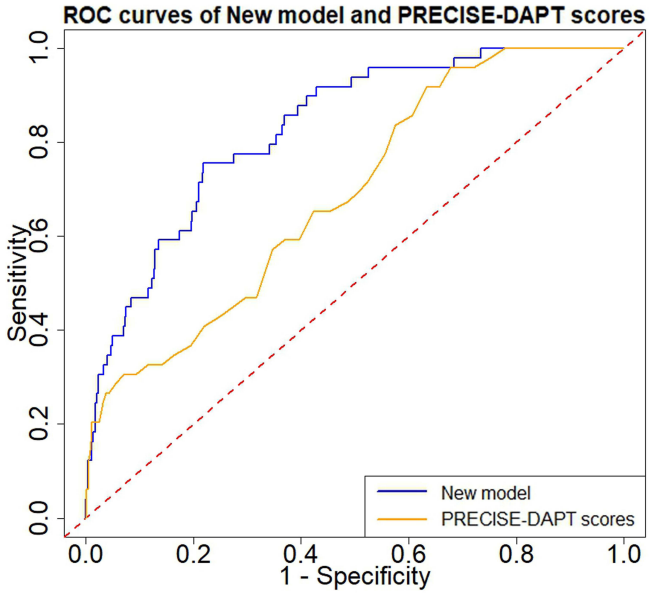

Figure 4 Receiver operating characteristic (ROC) curve of the PRECISE-DAPT scores.

test indicate that the predicted probabilities of the model are quite close to the observed actual probabilities, showing high consistency (x^2 = 4.818, P = 0.777; x^2 = 3.318, P = 0.913) (Figure 3B and C).

We applied the PRECISE-DAPT scores to predict UGIB occurrence in our subjects and plotted the ROC curve, with an AUC of 0.690 (95% CI: 0.620–0.760; $P < 0.001$). The predictive value of the PRECISE-DPAPT scores is lower than the model we constructed (95% CI: 0.055–0.223, Z = 3.233, P = 0.001; Figure 4).

Clinical Application of the Prediction Model

To avoid complex calculation processes and facilitate the clinical application of our prediction model, we developed a nomogram that can intuitively predict results using the regression coefficients for five predictive variables employed in the multivariate analysis and the intercept of the prediction model. The total points were obtained by summing up the points of the respective predictive factors. The probability corresponding to the total points represents the predicted risk of UGIB after PCI (Figure 5). For example, if a 78-year-old patient receiving PCI has a history of gastrointestinal ulcer/bleeding, drinking, and HF, with a creatinine level of 49, the corresponding scores will be 66, 74, 64, 75, and 27, respectively, and the total score will be 306, which turns into an estimated risk of 26.3% for UGIB during DAPT (Figure 5). Using this method, clinicians can rapidly assess the risk of UGIB during DAPT after PCI.

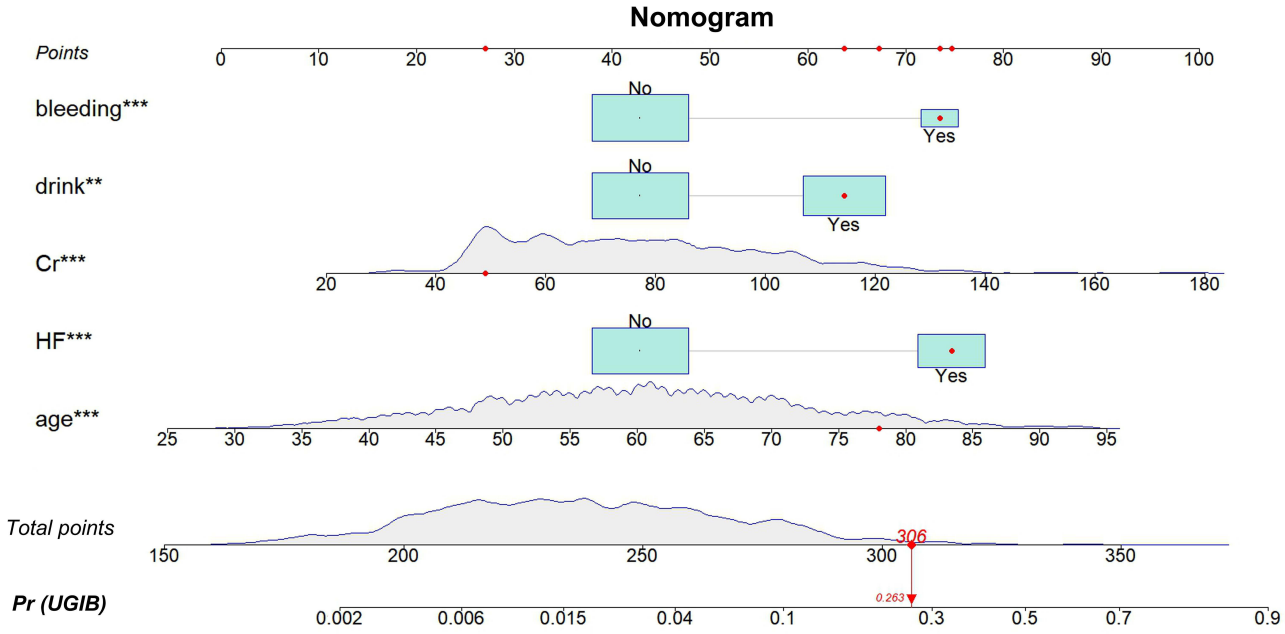

Figure 5 Nomogram for predicting postoperative upper gastrointestinal bleeding (UGIB) in patients with dual antiplatelet therapy after percutaneous coronary intervention (PCI). $^{**}P < 0.01$, $^{***}P < 0.001$. Red dot: the assignment and score of variables in the model for selected patients. Red value: the total score and the corresponding risk in the model for selected patients.

In order to further facilitate the application of the model by clinical physicians, an interactive web calculator was developed using the Shiny platform (Figure 6). The interface allows users to input patient-specific variables—such as age, Cr level, presence of HF and drinking, etc. Click "predict" to directly generate the probability of UGIB in patients with ACS under DAPT after PCI. The tool also provides a user-friendly visualization of both probability output and contributing factors. The application is publicly accessible at https://phyhw1978.shinyapps.io/UGIB/, reinforcing the feasibility of prediction model into bedside risk assessment.

A DCA was performed to evaluate the clinical utility of the prediction model. In the training cohort, the decision curve showed that if the risk threshold probability for UGIB was >0.02, PCI based on the prediction model may provide higher net benefits to patients than those afforded by treating all patients or not treating anyone. Hence, it can be suggested that nomograms are clinically more beneficial (Figure 7A). The nomogram model provided a higher net clinical benefit to both internal and external validation cohorts too, although not as significantly as it did in the training cohort (Figure 7B and C).

Risk Stratification

To facilitate clinicians in identifying high-risk patients, patients are grouped based on the optimal cutoff value for the risk of UGIB, with patients being divided into low-risk and high-risk groups. With this stratification, the incidence of UGIB in the high-risk group was 14.78%, whereas in the low-risk group, it was only 1.85%. The detection rate of UGIB in the high-risk group was 7.94 times higher than that in the low-risk group, indicating an enrichment of patients in the high-risk group who are likely to develop UGIB (Table 3).

Previously, when we employed multiple factor logistic regression analysis to identify independent influencing factors of UGIB, the results indicated that oral PPI usage was not a protective factor for UGIB. This result may be caused by confounding due to medication indications. To confirm this hypothesis, we employed regression analysis to separately examine the impact of oral PPI use on UGIB in the high-risk and low-risk groups. The results indicated that oral PPI use served as a protective factor for UGIB in the high-risk group (OR = 0.764, 95% CI: 0.641–0.887, $P = 0.021$), whereas this effect was not observed in the low-risk group (OR = 0.919, 95% CI: 0.586–1.252, $P = 0.136$).

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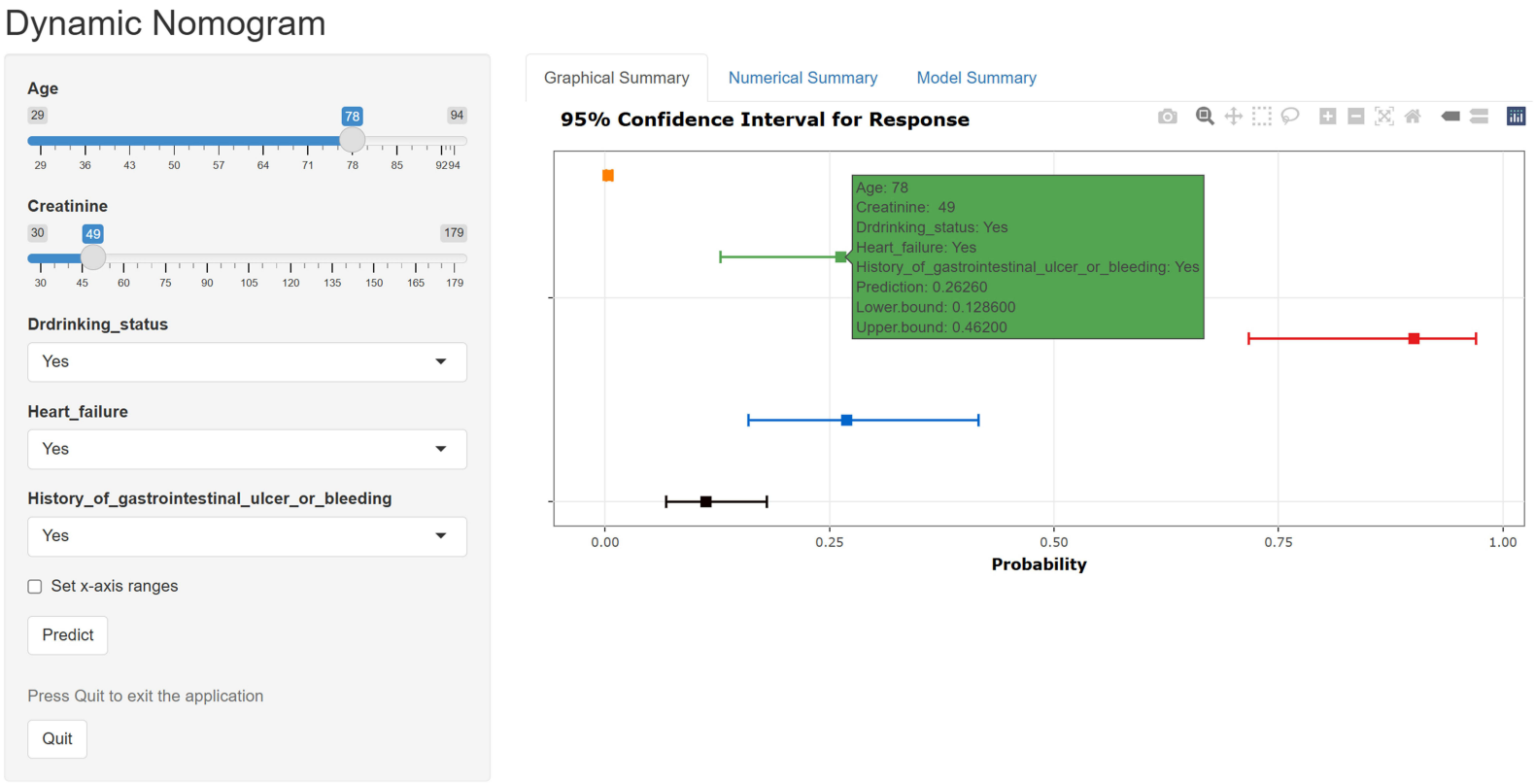

Figure 6 Web-based calculator for predicting postoperative upper gastrointestinal bleeding (UGIB) in patients with dual antiplatelet therapy after percutaneous coronary intervention (PCI).

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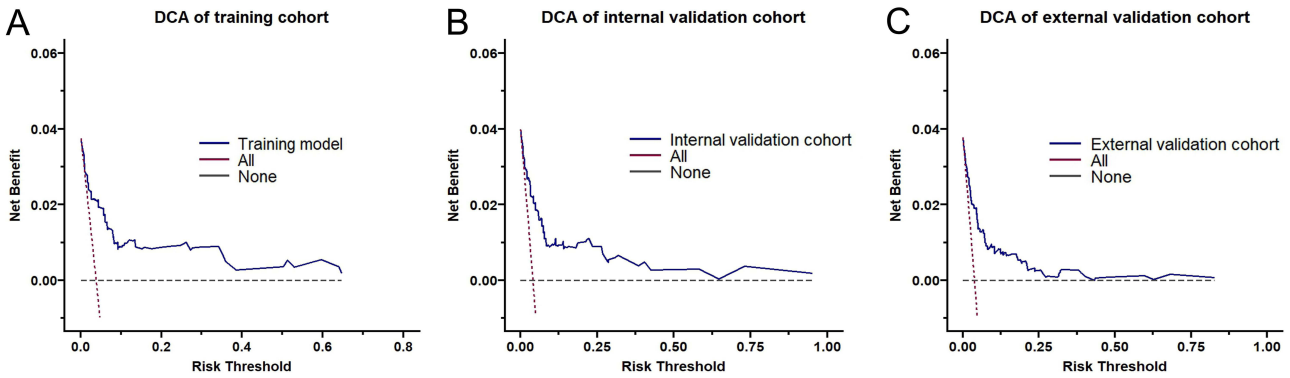

Figure 7 Decision curve analysis (DCA) of the prediction model. (**A**) Training cohort, (**B**) internal validation cohort, and (**C**) external validation cohort.

Sensitivity Analysis

To further evaluate the robustness and validity of the prediction model, we performed the sensitivity analysis by validating it in different patients, including those of different genders and with or without comorbidities such as diabetes and hypertension. The model demonstrated stable discrimination, achieving an AUC of 0.817 for male patients and 0.848 for female patients. The model's AUC values also remained consistent across various comorbidity groups: 0.823 for the diabetes group, 0.808 for the non-diabetes group, 0.825 for the hypertension group, and 0.852 for the non-hypertension group. Model performance remained stable with AUC values above 0.8 in all subgroups (Figure 8).

Discussion

Development of medicine and therapeutic equipment in recent years has made PCI the most important method to treat severe coronary heart diseases, such as ACS. To reduce the occurrence of ischemic adverse events, such as stent thrombosis, DAPT should also be performed on patients undergoing PCI. However, the increasing use of antiplatelet drugs increases the risk of bleeding complications in patients.[5,14] UGIB has been identified as the most common bleeding complication and leads to a poor prognosis for patients. The current CRUSADE and ACUITY bleeding scores are mainly used to evaluate the probability of composite bleeding in patients within 30 days of hospitalization or discharge.[15,16] These scores are not used for patients receiving DAPT after PCI. Multiple international guidelines recommend that the risk of bleeding should be assessed one year after PCI and guide the duration of DAPT. However, the data for constructing DAPT and PRECISE-DAPT scoring system comes from European and American populations, and some studies have found that PRECISE-DAPT scoring system may not be entirely suitable for Asian populations.[12,17] This study shows that the PRECISE-DAPT scores showed a predictive value for 5-year bleeding events with a C-statistic of 0.586 (95% CI: 0.538–0.634). However, the PRECISE-DAPT score has no predictive value for bleeding in the 1-2-year group with a C-statistic of 0.571 (95% CI: 0.526–0.616) and the 2-year group with a C-statistic of 0.520 (95% CI: 0.464–0.576). This study suggests that the predictive value of the PRECISE-DAPT scoring system is relatively limited in Asian populations. Of course, there are also different conclusions. A study from Korea showed that during a follow-up of 1 year, the risk of bleeding with a PRECISE-DAPT scores>24 points for 1-year BARC≥3a is 8.35 times higher than that

Table 3 Effectiveness of Risk Stratification Based on the Prediction Model in the Training Cohort

Risk Stratification	Cutoff Value	Number of Individuals Classified into Each Risk Group, n (%)	Number of Outcome Classified into Each Risk Group, n (%)	Identified Rate of UGIB in Each Risk Group (%)	The Ratio Compared with Low-Risk Group
High	0-0.066	197(15.44)	29(59.18)	14.78	7.94
Low	0.067–1	1079(84.56)	20(40.82)	1.85	1

Abbreviation: UGIB, upper gastrointestinal bleeding.

https://doi.org/10.2147/IJGM.S575300

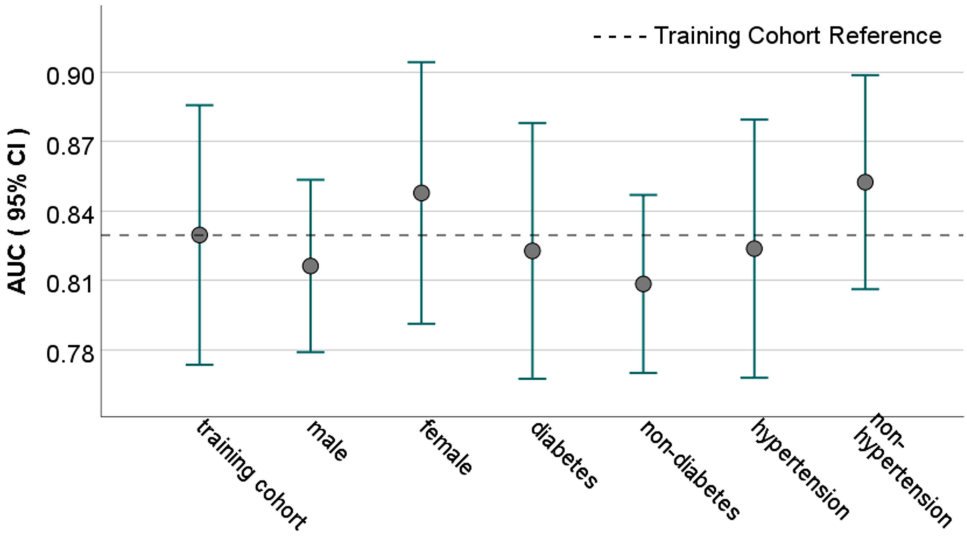

Figure 8 AUC comparisons across clinical subgroups.

of patients with a score of ≤17 (HR: 8.35, 95% CI: 5.86–11.90).[18] Therefore, whether the PRECISE-DAPT score can be equally applied to Asian populations is an interesting topic worthy of discussion.

We attempted to apply the PRECISE-DAPT scores to predict the UGIB in our subjects and plotted the ROC curve with an AUC of 0.690. It did not demonstrate ideal predictive value. A suitable UGIB scoring system and risk-prediction model for Asian patients undergoing DAPT after PCI have still not been developed. Therefore, it is essential to explore the risk factors for bleeding as well as identify the clinical features of UGIB in patients receiving DAPT after PCI to establish a rapid and highly applicable UGIB risk-prediction model.

Previous studies have shown that age, *Helicobacter pylori* infection, smoking, history of peptic ulcer(s), renal insufficiency, cardiac insufficiency, and prolonged activated partial thromboplastin time are risk factors for UGIB after PCI.[19–21] In our study, we found that age, history of diabetes, hypertension, gastrointestinal ulcers/bleeding, alcohol consumption, anemia, HF, ALB, and Cr in the UGIB group were higher than those in the non-UGIB group ($P < 0.05$). Further analysis identified age, history of gastrointestinal ulcers/bleeding, alcohol consumption, HF, and Cr as independent predictors of UGIB. UGIB mainly results from gastric mucosal ischemia and injury. Older patients often have more underlying diseases, slower gastric peristalsis, decreased blood flow to the gastrointestinal mucosa, and slower growth and repair rates. All these factors increase the chance of mucosal injury in older patients. Moreover, aging-induced reductions in organ reserve in older adults impair drug clearance and metabolism, which leads to the occurrence of UGIB events.[22] HF patients are prone to UGIB because of reduced cardiac output, which can lead to inadequate blood supply to the gastrointestinal mucosa, thereby increasing the likelihood of ulcers and subsequent bleeding.[23,24] Elevated Cr levels indicate decreased renal function, which leads to impaired drug clearance and increased damage to the gastric mucosa.[25–28] Patients with long-term alcohol consumption who also use antiplatelet medications are at a significantly high risk of developing UGIB, owing to alcohol-induced local mucosal irritation.[29] Additionally, studies have shown that long-term alcohol consumption can damage the gastrointestinal mucosa by inducing inflammatory responses, which can lower the platelet levels and cause coagulation disorders, thereby increasing the risk of UGIB.[30]

The use of certain drugs can also affect the occurrence of UGIB. The 12-month DAPT of aspirin combined with P2Y12 receptor inhibitors has gone through more than 20 years of history and has become the cornerstone treatment for preventing thrombotic complications in ACS patients, supported by multiple studies.[31] In the absence of contraindications, prasugrel and ticagrelor are generally considered superior choices to clopidogrel. PHILO trial and other studies have found that there is an "East Asian paradox" phenomenon in antiplatelet therapy among East Asian populations, which suggests that in the selection of P2Y12 receptor inhibitors, we need to comprehensively consider the balance between bleeding risk and ischemia risk, and if necessary, combine proton pump inhibitors (PPIs) to prevent

gastrointestinal bleeding. The P2Y12 inhibitors used in this study were clopidogrel or ticagrelor. The use of ticagrelor was not high in all groups (62.1% - 66.2%), indicating that we were cautious in our selection of P2Y12 receptor inhibitors. We included ticagrelor as an independent variable in our regression analysis. However, we did not find that ticagrelor was a significant risk factor for UGIB in our study. Although PPIs can prevent gastrointestinal bleeding, we did not identify PPIs application as a protective factor for UGIB in our previous statistical analysis. This could potentially be attributed to the fact that patients prescribed PPIs were more frequently assessed by clinicians as having a higher risk of bleeding. When we employed regression analysis to analyze different risk groups, we found that oral PPI use served as a protective factor for UGIB in the high-risk group. This also suggests that for high-risk patients undergoing DAPT, PPIs should be actively used in combination to prevent UGIB.

A nomogram can intuitively show the probability of the occurrence of a certain clinical outcome event. Based on the five risk factors identified in this study, we constructed a risk prediction model for UGIB and generated a nomogram. To further facilitate bedside application for clinicians, we have developed a web calculator based on the nomogram. This scoring system allows for rapid calculation of the risk of UGIB, enabling risk stratification and assisting clinicians in identifying patients with a higher risk of bleeding. For high-risk patients, we should strengthen the management of controllable factors, such as quitting alcohol, using gastric mucosal protectants, and shortening the duration of dual antibody treatment. At the same time, it is necessary to conduct a strong follow-up for such patients during treatment, dynamically assess the risk of thrombosis and bleeding, and formulate personalized diagnosis and treatment plans.

Limitations

Our study has several shortcomings. Its retrospective design limits the predictive value of the study findings. Information on H. pylori infection was not collected during the follow-up period. In addition, the decision curve shows that the predictive model is only likely to provide higher net returns when the risk probability of UGIB is greater than 0.02. Therefore, our model may not be suitable for patients with particularly low risk of bleeding. This model was developed within the Chinese population, and its global applicability may be limited. Although the retrospective cohort of 2370 patients may be considered relatively large for this population, it is still small compared to cohorts used in other established risk-prediction models. Therefore, the clinical application of the model needs to be validated by conducting larger, multicenter prospective studies.

Conclusions

We developed a novel clinical prediction model based on five risk factors: age, history of gastrointestinal ulcers/bleeding, alcohol use, HF, and Cr. The model may be applicable for the early prediction of UGIB during DAPT following PCI in Asian populations. It can serve as a simple and convenient bedside tool for clinical assessment of UGIB related to DAPT, facilitating risk stratification and thereby aiding clinicians in making individualized treatment and management decisions.

Data Sharing Statement

The data that support the study findings are available from the corresponding author upon reasonable request.

Ethical Approval and Informed Consent

The study was reviewed and approved by the Ethics Committee of Jinzhou Central Hospital (No. 2024-LW-018) and the Institutional Ethics Committee of the First Affiliated Hospital of Jinzhou Medical University (No. KYLL2024454). This investigation was conducted as per the principles of the Declaration of Helsinki. As this study was a retrospective study and used anonymized existing data without imposing additional risks on patients, the informed consent was waived.

Acknowledgments

We extend our gratitude to all the investigators who contributed to data collection and the development of this manuscript.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the National Natural Science Foundation of China Youth Fund Support Project (81300931) and Liaoning Provincial Natural Science Foundation Funded Project (201602300).

Disclosure

The authors report no conflicts of interest in this work.

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