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ORIGINAL RESEARCH

A New Risk Prediction Tool for Bleeding and Adverse Cardiovascular Events in Patients with Pre-Existing Coronary Stents Undergoing Gastrointestinal Cancer Surgery

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Background: Aged patients with coronary stents facing gastrointestinal cancer surgery are encountered more and more frequently in clinical practice, and such patients are at high risk of both bleeding and ischemia, requiring effective risk assessment. Therefore, this study will establish a prediction tool that can predict both bleeding events and major adverse cardiovascular events (MACEs).

Methods: Multicenter clinical data from 3127 gastrointestinal cancer surgery patients with a history of coronary stent implantation were utilized to establish and validate our prediction tool. We introduced the revised cardiac risk index (RCRI) score and the subsequent dual antiplatelet therapy (PRECISE-DAPT) score to be contrast. Net reclassification index (NRI) and integrated discrimination improvement (IDI) were used to interpret the strengths. Within 30 days post-surgery, we compared the bleeding events and MACEs.

Results: Among 3127 patients, 437 (13.9%) developed MACEs and 565 (18.1%) developed bleeding events. The MACEs model achieved good prediction performance both in the internal set (AUC: 0.924, 95% CI: 0.910–0.939) and the external set (AUC: 0.908, 95% CI: 0.880–0.937). The bleeding model also achieved good prediction performance both in the internal set (AUC: 0.862, 95% CI: 0.843–0.882) and the external set (AUC: 0.852, 95% CI: 0.818–0.886). The nomogram score greater than 131 indicates a high risk, with a postoperative MACEs incidence exceeding 23%. Similarly, the score exceeding 124 signifies a high risk, with a postoperative bleeding incidence above 21%.

Conclusion: The novel predictive instrument provides the online risk calculator, which could accurately quantify the risk of bleeding and ischemia in patients with coronary stent undergoing gastrointestinal cancer surgery.

Keywords: gastrointestinal cancer, bleeding, major adverse cardiovascular events, coronary stents, aged

Introduction

Neoplasms remain the main killer worldwide.[1–5] Gastrointestinal cancer[6–10] accounts for more than a quarter of all diagnosed malignant tumors in the world, accounting for 35% of cancer-related mortality, mainly including esophageal carcinoma, gastric cancer, colorectal cancer, pancreatic cancer, and hepatoma.[11] Foremost among the therapeutic modalities against gastrointestinal cancer is surgical intervention.[12] In the context of an aging global population, there

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is a rising number of elderly patients needing surgical intervention, many of whom have received percutaneous coronary intervention (PCI) and drug-eluting stents (DES).[13] The clinical work often involves cases where elective or emergent gastrointestinal cancer surgeries coincide with patients who have a history of PCI. Cardio-cerebrovascular diseases also pose significant threats to human health.[14] This confluence of circumstances often results in major adverse cardiovascular events (MACEs) in the postoperative period, encompassing non-fatal myocardial infarction (MI), ischemic stroke (IS), heart failure (HF) and cardiac death.[15] Previous investigations have underscored a marked elevation in the incidence of perioperative cardiovascular events among patients with prior stent implantations undergoing gastrointestinal cancer surgeries.[16] This phenomenon is believed to result from the combined effects of temporary discontinuation of antiplatelet therapy due to surgery, angiographic characteristics related to PCI, and the close timing between stent implantation and surgical intervention.[17] The management of these perioperative complexities remains a subject of ongoing debate and deliberation among the medical community. Significantly, apart from the inherent hemorrhagic risks posed by the gastrointestinal tumor itself, gastrointestinal cancer procedures is more prone to bleeding events, owing to diminished platelet function stemming from antiplatelet drug administration and the erosive impact of aspirin on gastric mucosal integrity.[18] The assessment of ischemic and hemorrhagic risks in patients with a history of coronary stent implantation undergoing gastrointestinal cancer surgery has become a significant concern for physicians and surgeons.

Present guidelines advocate the utilization of prognostic models for the evaluation of perioperative MACEs and the bleeding events, which encompass distinguished indices like the Revised Cardiac Risk Index (RCRI) and predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score.[19] While the RCRI has been a standard for over two decades, its clinical utility is limited by certain shortcomings. These include a tendency to underestimate cardiac risk and insufficient representation of high-risk subpopulations. At present, the PRECISE-DAPT score after stent implantation has been verified in many studies, but the bleeding risk assessment of non cardiac surgery after stent surgery lacks consideration.[20] Notably, the risk of bleeding complications in non-cardiac surgery varies significantly, especially in gastrointestinal cancer surgeries that involve lymph node dissections, vascular dissections, and digestive tract reconstructions. Additionally, the exigencies of diverse tumor stages may necessitate combined organ resections. It follows that assessing hemorrhagic risk requires careful consideration, necessitating detailed surgical evaluations to enhance the accuracy of treatment strategies. Existing predictive tools inadequately assess both ischemic and hemorrhagic risks in patients with a history of coronary stent placement undergoing gastrointestinal cancer surgery.

Consequently, we have crafted predictive models for MACEs and the bleeding events within the identical cohort, subsequently subjecting these models to rigorous validation within an external cohort. We aim to furnish a foundational point of reference for the perioperative therapeutic stratagems, custom-tailored to patients facing gastrointestinal cancer surgery subsequent to coronary stent implantation.

Methods

Patients and Design

We utilized multicenter data to form two independent cohorts. The first cohort comprised 2227 patients sourced from the First Medical Center of Chinese PLA General Hospital, where patients enrollment spanned from January 2017 to December 2021. The other cohort, numbering 900 patients, was culled from the Sixth Medical Center of Chinese PLA General Hospital and Hainan Hospital of PLA General Hospital from January 2017 to December 2021, which was deployed as an external validation cohort.

This study received approval from the Research Ethics Committee of the People's Liberation Army General Hospital, denoted by approval No. S2023-630-01.

Inclusion and Exclusion Criteria

The inclusion criteria were any patients undergoing gastrointestinal cancer surgery within 1 year after coronary stent implantation whose postoperative pathological stage was T1~4N1~3M0, according to the 8th edition of the American Joint Committee on Cancer (AJCC) TNM staging criteria for malignant tumors. The exclusion criteria were as follows: (1) Concomitance with additional malignant neoplasms. (2) Independent presence of other organic cardiac ailments

(Valvular Heart Disease, Myocardial Disease, Congenital Heart Disease, Congenital Heart Disease, Cardiac Tumor, Disease of Great Vessels, Dysautonomia, Disease of Pulmonary System). (3) Prior history of cardiac vascular bypass grafting. (4) Received neoadjuvant chemotherapy. (5) Incomplete clinical data.

Outcomes

The primary endpoints encompassed MACEs and bleeding events within a 30-day window subsequent to gastrointestinal cancer surgery. MACEs encompassed MI, IS, HF and cardiac death.[15] The bleeding events were characterized in accordance with the exacting criteria articulated by the Bleeding Academic Research Consortium (BARC).[21] The comprehensive definitions of these bleeding categories are conveniently delineated within S Table 1.

All clinical occurrences were ascertained through a meticulous process of extracting the pertinent data from the corpus of medical system. To extract data factors from this medical system, we utilized a universally recognized medical system for storing and retrieving data. This expert application of the system enabled the identification of distinct instances across various data fields. MACEs were diagnosed by retrieving the patient's blood test results, electrocardiogram (ECG), and descriptions in the course record. We extracted the patient's postoperative medical records, surgical records, imaging data and endoscopic records to diagnose the bleeding events. The Medical Centers enlisted three senior medical doctors to collaboratively diagnose complications and resolve contentious matters through debate and consultation.

We adopted the most common definition of MI:[22] patients had both acute clinical cardiac symptoms and increased values of myocardial protein detected in blood, and at a minimum threshold one value is over the reference upper limit × 99%. The diagnosis could be confirmed by including one of the following details: (a) symptoms of chest tightness or angina pectoris; (b) The ECG showed an emerging ischemic signal; (c) emerging pathological Q waves; and (d) thrombus in coronary artery found during PCI or postmortem dissection. IS was defined as thrombosis or embolism caused by various reasons, with or without various neurological symptoms.[23] We diagnosed HF by dyspnea, fatigue, edema and other symptoms, as well as examination methods that suggested impaired cardiac pumping function.[24] When a patient died due to cardiac causes within 30 days after gastrointestinal cancer surgery, it could be diagnosed as cardiac death.[25] The antiplatelet therapy in this study followed the consensus of Chinese experts on dual antiplatelet therapy for coronary heart disease.[26]

Features Screening

We collected variables that may be related to MACEs and bleeding events according to clinical consensus as follows: (1) general information: [age, gender, body mass index (BMI), and smoking history]. Former smokers was defined as those who had not smoked for at least one year; (2) chronic medical history: cerebrovascular disease, heart failure, hypertension, diabetes mellitus, chronic kidney diseases, previous bleed; (3) preoperative medications (4) clinicopathology (5) cardiac factors: angiographic features, overlapping stents, multiple stents, bifurcation lesions, small stents [<2.5 mm], stents number, left anterior descending artery (LAD), right coronary artery (RCA), left circumflex artery (LCX), obtuse marginal branch (OM), stent diameter, ejection fraction (EF), only second generation drug-eluting stents were used in this study;[14](6) preoperative blood test indicators; (7) surgery-related variables.

Statistical Analysis

Categorical variables were presented as numbers and percentages. Continuous variables of normal distribution were represented by mean and standard deviation, while non-normal distribution variables were represented by median and interquartile range (IQR). We used the Kolmogorov–Smirnov test to test the normality of the data to determine whether the data conformed to a normal distribution. For continuous variables, we used *t*-test or ANOVA to determine if the data were normally distributed. Otherwise, we used Whitney *U*-test or Kruskal Wallis test. Similarly, for the data processing of categorical variables, we used chi-square test or fisher's exact test to compare the correlation and significance of categorical variables between different groups.

Methodologically, we used univariate logistic regression to initially screen variables that may be associated with outcomes. All variables with P values <0.05 were included in the multivariate regression equation, and then irrelevant

variables were removed step by step. Subsequently, a nomogram was constructed according to the multivariate regression equation to realize the visualization of the prediction model. In this study, bootstrap resampling was used as internal validation method to evaluate the performance of the model. More than two-thirds of the samples were randomly selected from the training data set to build a bootstrap sample set, process of which was repeated 1000 times.[27] We demonstrated the trade-off between sensitivity and specificity of the model at different thresholds by constructing ROC curves and compared the predictive ability of the model by comparing the area under the curve. The significance of differences between AUCs was achieved through the DeLong test. The calibration curve showed the relationship between the predicted probability of the model and the observed actual event rate. We used Decision curve analysis (DCA) to evaluate the actual utility of the model in clinical decision-making, which took into account the predicted results of the model and the costs and benefits of decision-making. Net reclassification index (NRI) was used to evaluate the improvement of classification performance of new models. Integrated discrimination improvement (IDI) was used to evaluate the improvement of continuous risk prediction performance of new models.

Data were statistically analyzed using R statistical software (R version 4.2.3, R Foundation for Statistical Computing) and GraphPad Prism 9. Statistical significance was accepted at the 0.05 level, and all tests were two-tailed.

Results

Baseline of Clinical Data

Two thousand two hundred and twenty-seven patients were recruited from the First Medical Center of Chinese PLA General Hospital, of whom 307 developed MACEs and 403 developed bleeding events. 900 patients were enrolled in the Sixth Medical Center of PLA General Hospital and Hainan Hospital of PLA General Hospital as external validation set, comprising 130 MACEs and 162 bleeding events. The screening process of patients according to the acceptance criteria was shown in Figure 1.

In Table 1, the clinical characteristics of training set were stratified according to the delineations of MACEs, among which the prevalence of heart failure, hypertension, emergency, angiographic features, time of surgery, Scr, NT-proBNP, surgery duration and premature cessation, etc, were significantly higher in MACEs group, whereas HGB and EF levels were significantly lower. Likewise, in Table 2, the clinical characteristics of training set were stratified according to the delineations of bleeding events, among which the prevalence of aspirin, chronic kidney disease, enlarged lymph node dissection, TNM stage, vessel invasion, CRP, Anti Xa and blood Loss, etc, were significantly higher in the bleeding group. The clinical characteristics of external validation set were shown in S Tables 2 and 3, respectively.

MACEs were observed in 13.8% of them, comprising 113 cases of non-fatal heart attacks, 65 cases of IS, 135 cases of HF, and 11 cardiac deaths (Figure 2A). The incidence of bleeding events was 18.1%, including 189 cases of BARC bleeding type 1 events, 80 cases of type 2 events, 100 cases of type 3a events, 69 cases of type 3b events, and 6 cases of type 3c events (Figure 2B).

Establishment and Validation of the MACEs Model

We used univariate logistic regression analysis to preliminarily screen variables related to MACEs. Thirty-two factors such as heart failure, hypertension, emergency, angiographic feature and time of surgery were correlated with MACEs. All the above variables were included in the multivariate logistic regression equation, and then irrelevant variables were removed step by step. Ten factors including heart failure, hypertension, emergency, angiographic features, time of surgery, Scr, NT-proBNP, surgery duration, EF and premature cessation of DAPT were selected as the indicators of the prediction model (Table 3).

A Nomogram was constructed according to the results of multivariate logistic regression (Figure 3A). A total score could be obtained by summing the scores corresponding to each indicator, which represented the risk of MACEs. The threshold for risk change was 131, and exceeding this score was considered high hazard. The MACEs model achieved good prediction performance both in the internal set (AUC: 0.924, 95% CI: 0.910–0.939) and the external set (AUC: 0.908, 95% CI: 0.880–0.937) (Figure 4A). Bootstrap resampling was used for internal validation, and the average AUC after 1000 replicates was 0.918 (0.908–0.939). The calibration curve fitted the diagonal very well (HL test, $p = 0.656$, Figure 4B). The decision curve of the MACEs model suggested that patients can obtain benefits in most of the threshold range. (Figure 4C).

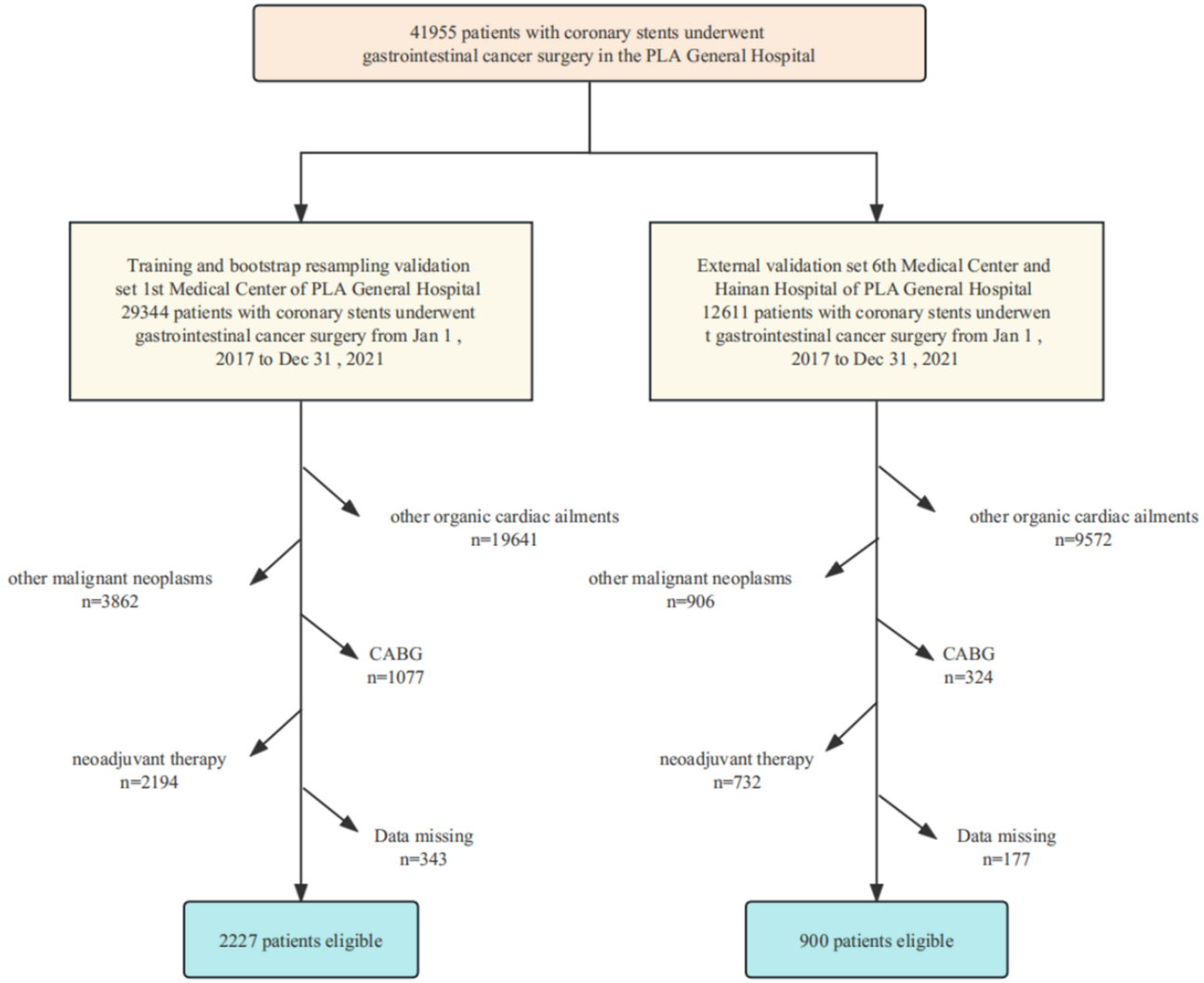

Figure 1 Flowchart of the study.
Abbreviation: CABG, coronary artery bypass grafting.

Contrast of the MACEs Nomogram and RCRI

We compared the predictive ability of RCRI and MACEs models using AUC, and the results showed that RCRI (AUC: 0.723, 95% CI: 0.676–0.771) was inferior to our nomogram in the same datasets ($p < 0.001$, Figure 4A). In terms of the

Table 1 Baseline Characteristics of the Patients with and Without MACEs in the Training Cohort

Variable	Overall (n=2227)	Non-MACEs (n=1920)	MACEs (n=307)	P Value
Demographic characteristics				
Male, n (%)	812 (36.5)	693 (36.1)	119 (38.8)	0.402
Age (yr), median [IQR]	67.00 (64.00, 71.00)	67.00 (63.00, 70.00)	68.00 (64.00, 71.00)	0.019
BMI (kg/m^2), median [IQR]	24.35 (22.03, 26.93)	24.00 (21.72, 26.34)	27.11 (24.82, 28.70)	**< 0.001**
Smoking_status (%)				0.722
Never smoker	1082 (48.6)	928 (48.3)	154 (50.2)	
Current smoker	600 (26.9)	523 (27.2)	77 (25.1)	
Former smoker	545 (24.5)	469 (24.4)	76 (24.8)	

(*Continued*)

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Table 1 (Continued).

Variable	Overall (n=2227)	Non-MACEs (n=1920)	MACEs (n=307)	P Value
Previous history, n (%)				
Acute coronary syndrome	1756 (78.9)	1497 (78.0)	259 (84.4)	0.013
Hypertension	1259 (56.5)	1123 (58.5)	246 (44.3)	0.052
Diabetes mellitus	764 (34.3)	642 (33.4)	122 (39.7)	0.036
Cerebrovascular disease	1139 (51.1)	964 (50.2)	175 (57.0)	0.032
Heart failure	1194 (53.6)	993 (51.7)	201 (65.5)	**< 0.001**
Chronic kidney disease	260 (11.7)	157 (8.2)	103 (33.6)	**< 0.001**
Previous bleed	346 (15.5)	247 (12.9)	99 (32.2)	**< 0.001**
Preoperative medication, n (%)				
Aspirin	1743 (78.3)	1452 (75.6)	291 (94.8)	**< 0.001**
Clopidogrel	1312 (58.9)	1025 (53.4)	287 (93.5)	**< 0.001**
Ticagrelor	618 (27.6)	512 (26.7)	106 (34.5)	0.274
Cessation	1261 (56.6)	1044 (54.4)	217 (70.7)	**< 0.001**
Beta blockers	331 (14.9)	281 (14.6)	50 (16.3)	0.504
Insulin	798 (35.8)	671 (34.9)	127 (41.4)	0.035
Oral anticoagulants	327 (14.7)	260 (13.5)	67 (21.8)	**< 0.001**
Clinicopathology				
TNM stage, n (%)				0.081
I	450 (20.2)	405 (21.1)	45 (14.7)	
IIa	591 (26.5)	511 (26.6)	80 (26.1)	
Iib	444 (19.9)	383 (19.9)	61 (19.9)	
IIIa	350 (15.7)	294 (15.3)	56 (18.2)	
IIIb	270 (12.1)	227 (11.8)	43 (14.0)	
IIIc	122 (5.5)	100 (5.2)	22 (7.2)	
Enlarged lymph node dissection, n (%)	282 (12.7)	236 (12.3)	46 (15.0)	0.221
Vascular thrombus, n (%)	339 (15.2)	262 (13.6)	77 (25.1)	**< 0.001**
Tumor diameter, median [IQR]	3.50 (2.30, 5.00)	3.50 (2.20, 5.00)	3.50 (2.50, 5.00)	0.076
Cardiac factors				
Angiographic features, n (%)	871 (39.1)	720 (37.5)	151 (49.2)	**< 0.001**
Overlapping	92 (4.1)	56 (2.9)	36 (11.7)	**< 0.001**
Multiple stents	431 (19.4)	295 (15.4)	136 (44.3)	**< 0.001**
Bifurcation lesions	243 (10.9)	137 (7.1)	106 (34.5)	**< 0.001**
Small stents	51 (2.3)	41 (2.1)	10 (3.3)	0.310
Stent number, n (%)				**< 0.001**
1	1183 (53.1)	1023 (53.3)	160 (52.1)	
2	496 (22.3)	461 (24.0)	35 (11.4)	
3	548 (24.6)	436 (22.7)	112 (36.5)	
LAD, n (%)	1549 (69.6)	1329 (69.2)	220 (71.7)	0.426
RCA, n (%)	1212 (54.4)	1031 (53.7)	181 (59.0)	0.098
LCX, n (%)	1053 (47.3)	890 (46.4)	163 (53.1)	0.033
OM, n (%)	4 (0.2)	3 (0.2)	1 (0.3)	0.448
Stent diameter(mm), median [IQR]	3.00 (2.50, 3.50)	3.00 (2.50, 3.50)	3.00 (2.50, 3.50)	0.644
EF(%), median [IQR]	58.00 (54.00, 62.00)	58.00 (54.00, 62.00)	55.00 (50.50, 59.00)	**< 0.001**
Preoperative laboratory data				
RBC(10^{12}), mean (SD)	4.22 (0.62)	4.24 (0.60)	4.15 (0.68)	0.019
WBC(10^{12}), median [IQR]	5.91 (4.84, 7.10)	5.89 (4.84, 7.06)	6.05 (4.91, 7.36)	0.195
HGB(g/L), median [IQR]	126.00 (110.00, 140.00)	127.00 (110.00, 140.00)	122.70 (107.70, 137.20)	0.020
Leukocyte(10^9), median [IQR]	0.29 (0.22, 0.35)	0.29 (0.23, 0.35)	0.27 (0.20, 0.33)	**< 0.001**
PLT(10^9), median [IQR]	209.00 (171.00, 253.00)	208.00 (171.00, 251.00)	213.00 (170.00, 256.00)	0.477
ALT(U/L), median [IQR]	13.90 (10.20, 20.10)	14.10 (10.30, 20.80)	13.00 (9.70, 17.65)	**< 0.001**

(*Continued*)

Table 1 (Continued).

Variable	Overall (n=2227)	Non-MACEs (n=1920)	MACEs (n=307)	P Value
Scr(μmol/L), median [IQR]	72.00 (51.00, 92.00)	70.00 (50.00, 91.00)	78.00 (59.00, 96.00)	**< 0.001**
NT-proBNP(pg/mL), median [IQR]	344.30 (173.30, 592.20)	308.95 (154.02, 527.30)	650.00 (438.50, 891.85)	**< 0.001**
CRP(mg/L), median [IQR]	11.00 (3.70, 16.40)	11.00 (3.70, 16.40)	11.70 (3.85, 17.50)	0.294
Anti-Xa(IU/mL), median [IQR]	1.04 (0.69, 1.35)	1.03 (0.68, 1.34)	1.09 (0.72, 1.58)	0.107
TT(s), median [IQR]	16.50 (15.70, 17.30)	16.50 (15.70, 17.30)	16.30 (15.60, 17.15)	0.010
APTT(s), median [IQR]	34.80 (31.50, 38.20)	34.90 (31.50, 38.20)	34.45 (31.00, 37.85)	0.427
FIB(g/L), median [IQR]	3.31 (2.81, 3.92)	3.30 (2.80, 3.90)	3.45 (2.90, 4.10)	0.025
PT(s), median [IQR]	13.30 (12.70, 14.00)	13.30 (12.70, 14.00)	13.30 (12.70, 14.00)	0.574
D-Dimer(μg/mL), median [IQR]	0.80 (0.42, 1.70)	0.80 (0.41, 1.70)	1.00 (0.50, 1.90)	0.013
Surgery-related factors				
Type of surgery, n (%)				0.053
Esophageal cancer	176 (7.9)	153 (8.0)	23 (7.5)	
Gastric cancer	624 (28.0)	528 (27.5)	96 (31.3)	
Colon cancer	523 (23.5)	443 (23.1)	80 (26.1)	
Rectal cancer	414 (18.6)	355 (18.5)	59 (19.2)	
Liver cancer	213 (9.6)	199 (10.4)	14 (4.6)	
Cholangiocarcinoma	170 (7.6)	147 (7.7)	23 (7.5)	
Pancreatic cancer	107 (4.8)	95 (4.9)	12 (3.9)	
Emergency, n (%)	736 (33.0)	485 (25.3)	251 (81.8)	**< 0.001**
ASA physical status, n (%)				0.004
I	89 (4.0)	81 (4.2)	8 (2.6)	
II	948 (42.6)	842 (43.9)	106 (34.5)	
III	919 (41.3)	771 (40.2)	148 (48.2)	
IV	271 (12.2)	226 (11.8)	45 (14.7)	
Transfusion, n (%)	273 (12.3)	221 (11.5)	52 (16.9)	0.009
Time of surgery, n (%)				**< 0.001**
≤6 months	910 (40.9)	642 (33.4)	268 (87.3)	
> 6 months	1317 (59.1)	1278 (66.6)	39 (12.7)	
Surgery duration, median [IQR]	148.00 (100.50, 200.00)	145.00 (100.00, 200.00)	158.10 (111.10, 206.10)	0.045
Blood loss, median [IQR]	650.00 (450.00, 850.00)	650.00 (450.00, 850.00)	650.00 (450.00, 850.00)	0.994
Urine volume, median [IQR]	400.00 (200.00, 700.00)	400.00 (200.00, 700.00)	300.00 (150.00, 625.00)	0.005

Note: Bold font represented P value < 0.001.

Abbreviations: BMI, body mass index; TNM, the American Joint Committee on Cancer tumor nodes metastasis stage; LAD, left anterior descending artery; RCA, right coronary artery; LCX, left circumflex artery; OM, obtuse marginal branch; EF, ejection fraction; RBC, red blood cell; WBC, white blood cell; HGB, hemoglobin; PLT, platelet; ALT, alanine transaminase; Scr, serum creatinine; NT-proBNP, N-terminal pro-brain natriuretic peptide; CRP, C-reactive protein; Anti-Xa, Anti-factor Xa; PT, prothrombin time; APTT, activated partial thromboplastin time; FIB, fibrinogen; TT, thrombin time; ASA, American Society of Anesthesiologists; Cessation, premature cessation of dual antiplatelet therapy; IQR, interquartile range.

Table 2 Baseline Characteristics of the Patients with and Without Bleeding Events in the Training Cohort

Variable	Overall (n=2227)	Non-Bleeding (n=1824)	Bleeding (n=403)	P Value
Demographic characteristics				
Male, n (%)	812 (36.5)	662 (36.3)	150 (37.2)	0.770
Age (yr), median [IQR]	67 (64, 71)	67 (63, 71)	67 (64, 70)	0.714
BMI (kg/m^2), median [IQR]	24.35 (22.03, 26.93)	24.22 (21.82, 26.67)	25.46 (23.03, 27.74)	**< 0.001**
Smoking_status (%)				0.609
Never smoker	1082 (48.6)	878 (48.1)	204 (50.6)	
Current smoker	600 (26.9)	493 (27.0)	107 (26.6)	
Former smoker	545 (24.5)	453 (24.8)	92 (22.8)	

(*Continued*)

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Table 2 (Continued).

Variable	Overall (n=2227)	Non-Bleeding (n=1824)	Bleeding (n=403)	P Value
Previous history, n (%)				
Acute coronary syndrome	1756 (78.9)	1423 (78.0)	333 (82.6)	0.057
Hypertension	1844 (82.8)	1533 (84.0)	321 (79.7)	0.069
Diabetes mellitus	764 (34.3)	621 (34.0)	143 (35.5)	0.623
Cerebrovascular disease	1139 (51.1)	923 (50.6)	216 (53.6)	0.301
Heart failure	1194 (53.6)	986 (54.1)	208 (51.6)	0.404
Chronic kidney disease	260 (11.7)	140 (7.7)	120 (29.8)	**< 0.001**
Previous bleed	346 (15.5)	221 (12.1)	125 (31.0)	**< 0.001**
Preoperative medication, n (%)				
Aspirin	1743 (78.3)	1387 (76.0)	356 (88.3)	**< 0.001**
Clopidogrel	1312 (58.9)	1038 (56.9)	274 (68.0)	**< 0.001**
Ticagrelor	618 (27.6)	498 (27.3)	120 (29.8)	0.336
Cessation	1261 (56.6)	1041 (57.1)	220 (54.6)	0.393
Beta blockers	331 (14.9)	275 (15.1)	56 (13.9)	0.599
Insulin	798 (35.8)	667 (36.6)	131 (32.5)	0.138
Calcium channel blockers	327 (14.7)	260 (14.3)	67 (16.6)	0.255
Clinicopathology				
TNM stage, n (%)				**< 0.001**
I	450 (20.2)	433 (23.7)	17 (4.2)	
IIa	591 (26.5)	547 (30.0)	44 (10.9)	
IIb	444 (19.9)	356 (19.5)	88 (21.8)	
IIIa	350 (15.7)	250 (13.7)	100 (24.8)	
IIIb	270 (12.1)	181 (9.9)	89 (22.1)	
IIIc	122 (5.5)	57 (3.1)	65 (16.1)	
Enlarged lymph node dissection, n (%)	282 (12.7)	188 (10.3)	94 (23.3)	**< 0.001**
Vascular thrombus, n (%)	339 (15.2)	230 (12.6)	109 (27.0)	**< 0.001**
Tumor diameter, median [IQR]	3.50 (2.30, 5.00)	3.50 (2.20, 5.00)	4.00 (2.50, 5.50)	0.008
Cardiac factors				
Angiographic features, n (%)	871 (39.1)	710 (38.9)	161 (40.0)	0.745
Overlapping	92 (4.1)	74 (4.1)	18 (4.5)	0.814
Multiple stents	431 (19.4)	343 (18.8)	88 (21.8)	0.185
Bifurcation lesions	243 (10.9)	196 (10.7)	47 (11.7)	0.656
Small stents	51 (2.3)	45 (2.5)	6 (1.5)	0.315
Stent number, n (%)				0.326
1	1183 (53.1)	970 (53.2)	213 (52.9)	
2	496 (22.3)	415 (22.8)	81 (20.1)	
3	548 (24.6)	439 (24.1)	109 (27.0)	
LAD, n (%)	1549 (69.6)	1274 (69.8)	275 (68.2)	0.565
RCA, n (%)	1212 (54.4)	986 (54.1)	226 (56.1)	0.495
LCX, n (%)	1053 (47.3)	855 (46.9)	198 (49.1)	0.444
OM, n (%)	4 (0.2)	2 (0.1)	2 (0.5)	0.152
Stent diameter(mm), median [IQR]	3.00 (2.50, 3.50)	3.00 (2.50, 3.50)	3.00 (2.75, 3.50)	0.681
EF(%), median [IQR]	58.00 (54.00, 62.00)	58.00 (54.00, 62.00)	57.00 (53.00, 62.00)	0.431
Preoperative laboratory data				
RBC(10^{12}), mean (SD)	4.22 (0.62)	4.24 (0.61)	4.17 (0.66)	0.064
WBC(10^{12}), median [IQR]	5.91 (4.84, 7.10)	5.90 (4.85, 7.08)	5.97 (4.82, 7.24)	0.474
HGB(g/L), median [IQR]	126.00 (110.00, 140.00)	127.00 (110.00, 140.00)	124.00 (105.00, 138.50)	0.021
Leukocyte(10^9), median [IQR]	0.29 (0.22, 0.35)	0.29 (0.23, 0.35)	0.28 (0.20, 0.34)	0.024
PLT(10^9), median [IQR]	209.00 (171.00, 253.00)	207.00 (171.00, 252.00)	214.00 (170.00, 254.00)	0.489
ALT(U/L), median [IQR]	13.90 (10.20, 20.10)	14.10 (10.20, 20.40)	13.20 (9.85, 19.05)	0.019

(*Continued*)

Table 2 (Continued).

Variable	Overall (n=2227)	Non-Bleeding (n=1824)	Bleeding (n=403)	P Value
Scr(μmol/L), median [IQR]	72.00 (51.00, 92.00)	71.00 (51.00, 92.00)	75.00 (51.00, 93.00)	0.625
NT-proBNP(pg/mL), median [IQR]	344.30 (173.30, 592.20)	336.50 (172.12, 580.52)	400.50 (176.90, 681.25)	0.005
CRP(mg/L), median [IQR]	11.00 (3.70, 16.40)	10.90 (2.90, 15.70)	13.20 (6.35, 19.50)	**< 0.001**
Anti-Xa(IU/mL), median [IQR]	1.04 (0.69, 1.35)	1.01 (0.67, 1.30)	1.30 (0.91, 1.85)	**< 0.001**
TT(s), median [IQR]	16.50 (15.70, 17.30)	16.50 (15.70, 17.30)	16.40 (15.60, 17.30)	0.303
APTT(s), median [IQR]	34.80 (31.50, 38.20)	34.80 (31.40, 38.10)	35.15 (32.15, 39.00)	0.038
FIB(g/L), median [IQR]	3.31 (2.81, 3.92)	3.30 (2.80, 3.91)	3.36 (2.86, 3.99)	0.239
PT(s), median [IQR]	13.30 (12.70, 14.00)	13.30 (12.70, 14.00)	13.30 (12.75, 14.00)	0.180
D-Dimer(μg/mL), median [IQR]	0.80 (0.42, 1.70)	0.80 (0.40, 1.63)	1.20 (0.50, 2.18)	**< 0.001**
Surgery-related factors				
Type of surgery, n (%)				0.983
Esophageal cancer	176 (7.9)	147 (8.1)	29 (7.2)	
Gastric cancer	624 (28.0)	509 (27.9)	115 (28.5)	
Colon cancer	523 (23.5)	429 (23.5)	94 (23.3)	
Rectal cancer	414 (18.6)	338 (18.5)	76 (18.9)	
Liver cancer	213 (9.6)	171 (9.4)	42 (10.4)	
Cholangiocarcinoma	170 (7.6)	142 (7.8)	28 (6.9)	
Pancreatic cancer	107 (4.8)	88 (4.8)	19 (4.7)	
Emergency, n (%)	736 (33.0)	568 (31.1)	168 (41.7)	**< 0.001**
ASA physical status, n (%)				0.043
I	89 (4.0)	80 (4.4)	9 (2.2)	
II	948 (42.6)	782 (42.9)	166 (41.2)	
III	919 (41.3)	733 (40.2)	186 (46.2)	
IV	271 (12.2)	229 (12.6)	42 (10.4)	
Transfusion, n (%)	273 (12.3)	163 (8.9)	110 (27.3)	**< 0.001**
Time of surgery, n (%)				0.562
≤6 months	910 (40.9)	751 (41.2)	159 (39.5)	
> 6 months	1317 (59.1)	1073 (58.8)	244 (60.5)	
Surgery duration, median [IQR]	148.00 (100.50, 200.00)	145.00 (100.00, 200.00)	158.10 (107.00, 205.55)	0.010
Blood loss, median [IQR]	650.00 (450.00, 850.00)	600.00 (400.00, 800.00)	800.00 (600.00, 1000.00)	**< 0.001**
Urine volume, median [IQR]	400.00 (200.00, 700.00)	400.00 (172.50, 700.00)	400.00 (200.00, 700.00)	0.631

Note: Bold font represented P value < 0.001.

Abbreviations: BMI, body mass index; TNM, the American Joint Committee on Cancer tumor nodes metastasis stage; LAD, left anterior descending artery; RCA, right coronary artery; LCX, left circumflex artery; OM, obtuse marginal branch; EF, ejection fraction; RBC, red blood cell; WBC, white blood cell; HGB, hemoglobin; PLT, platelet; ALT, alanine transaminase; Scr, serum creatinine; NT-proBNP, N-terminal pro-brain natriuretic peptide; CRP, C-reactive protein; Anti-Xa, Anti-factor Xa; PT, prothrombin time; APTT, activated partial thromboplastin time; FIB, fibrinogen; TT, thrombin time; ASA, American Society of Anesthesiologists; Cessation, premature cessation of dual antiplatelet therapy; IQR, interquartile range.

improvement of risk prediction and reclassification, the NRI (0.358, 95% CI: 0.266–0.450) and IDI (0.352, 95% CI: 0.306–0.398) of the new model are greatly improved in contrast with RCRI.

Establishment and Validation of the Bleeding Nomogram

The factors associated with postoperative bleeding events were analyzed by univariate logistic regression. Thirty variables with significant differences screened by regression analysis were included in the multivariate logistic regression analysis. Finally, eight factors including Surgery duration, Anti-Xa, Blood loss, TNM, CRP, enlarged lymph node dissection, chronic kidney disease and previous bleed were selected as the indicators of the prediction model (Table 4).

According to the method of multivariate logistic regression analysis, we screened eight variables to construct the nomogram (Figure 3B). A total risk assessment score for bleeding events was obtained by calculating the score represented by each variable. In addition, we determined the cut-off point for scoring by fitting the data, and scored more than 124 as high-risk. We used AUC to show the predictive ability of the model, and the results showed that the

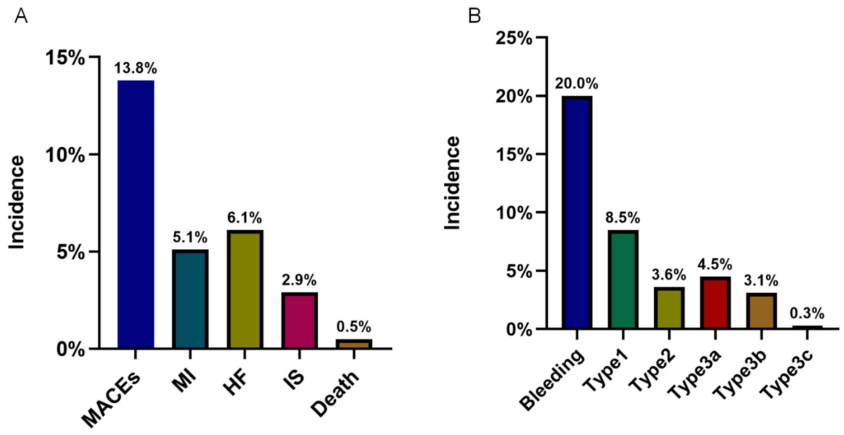

Figure 2 Comparison of the proportion of patients with different outcomes. (**A**) The histogram to show the proportions of MACEs subgroups. (**B**) The histogram to show the proportions of MBs subgroups.

Abbreviations: MACEs, major adverse cardiovascular events; MI, non-fatal myocardial infarction, IS, ischemic stroke, HF, heart failure; Bleeding type, Bleeding Academic Research Consortium type.

new model performed very well both in the training set (AUC: 0.862, 95% CI: 0.843–0.882) and in the validation set (AUC: 0.852, 95% CI: 0.818–0.886, Figure 5A). Bootstrap resampling was used for internal validation, and the average AUC after 1000 replicates was 0.863 (0.842–0.882). We used Hosmer and Lemeshow (HL) tests to calibrate the predictive ability and visualize the calibration process (MACEs, HL test, p = 0.656) and (Bleeding, HL test, p = 0.205, Figure 5B). The decision curve of the model suggested that patients can obtain benefits in most of the threshold range (Figure 5C).

Table 3 Univariate and Multivariate Logistic Regression Analysis for the Risk Factors Associated with MACEs

Variable	Univariate Analysis			Multivariate Analysis		
	B	OR (95% CI)	P value	B	OR (95% CI)	P value
Age (yr)	0.131	1.14 (0.929–1.393)	0.203			
BMI (kg/m^2)	0.069	1.071 (0.87–1.312)	0.511			
Diabetes mellitus	0.043	1.044 (0.826–1.308)	0.715			
Cerebrovascular disease	0.022	1.023 (0.87–1.202)	0.786			
Heart failure	0.228	1.247 (1.061–1.465)	**0.007**	0.734	1.729 (1.235–2.421)	**< 0.001**
Acute coronary syndrome	0.164	1.389 (1.142–1.537)	**0.003**	0.336	1.757 (1.147–2.692)	**0.01**
Chronic kidney disease	0.424	1.276 (0.711–1.317)	0.877			
Previous bleed	0.544	1.045 (0.569–1.801)	0.881			
Aspirin	0.012	1.012 (0.805–1.263)	0.917			
Clopidogrel	0.262	0.769 (0.634–0.928)	**0.007**	0.324	0.709 (0.342–1.435)	0.891
Cessation	0.244	0.784 (0.646–0.947)	**0.013**	0.411	2.132 (1.505–3.021)	**< 0.001**
Calcium channel blockers	1.261	1.283 (1.216–1.365)	**< 0.001**	1.432	1.311 (0.863–1.803)	0.921
Vascular thrombus	0.259	1.295 (0.098–1.526)	0.802			
Angiographic features	0.306	1.358 (1.136–1.621)	**0.002**	0.622	1.495 (1.074–2.081)	**0.017**
EF(%)	−0.435	0.459 (0.214–0.651)	**< 0.001**	−0.287	0.428 (0.334–0.593)	**< 0.001**
Leukocyte(10^9)	0.223	1.802 (0.605–2.051)	0.217			
ALT(U/L)	0.573	1.774 (1.507–2.088)	**< 0.001**	0.154	1.724 (0.989–4.141)	0.893
Scr(μmol/L)	0.059	1.261 (1.115–1.572)	**0.013**	0.327	1.008 (1.002–1.014)	**0.005**
NT-proBNP(pg/mL)	0.424	1.655 (1.337–2.163)	**0.006**	0.732	1.335 (1.212–1.474)	**< 0.001**
Emergency	0.506	1.603 (1.378–1.743)	**0.002**	0.893	3.743 (2.601–4.183)	**< 0.001**
Transfusion	0.265	1.304 (0.925–1.852)	0.148			

(*Continued*)

Table 3 (Continued).

Variable	Univariate Analysis			Multivariate Analysis		
	B	**OR (95% CI)**	**P value**	**B**	**OR (95% CI)**	**P value**
Time of surgery, > 6mon vs ≤6 mon	−0.376	0.351 (0.254–0.478)	**< 0.001**	−0.437	0.066 (0.045–0.098)	**< 0.001**
LAD	1.037	2.821 (2.288–3.473)	**< 0.001**	0.312	1.698 (0.973–3.134)	0.789
RCA	1.175	3.239 (2.603–4.019)	**< 0.001**	0.781	1.548 (0.568–2.424)	0.476
LCX	1.899	6.681 (4.805–9.316)	**< 0.001**	0.114	1.121 (0.875–1.431)	0.363
OM	0.344	1.411 (1.082–1.823)	**0.012**	0.257	1.847 (0.943–5.443)	0.893
RBC(10^{12})	−0.022	0.342 (0.173–5.368)	0.879			
HGB(g/L)	−0.541	0.716 (0.289–6.313)	0.281			
APTT(s)	0.011	1.011 (0.977–1.043)	0.487			
D-Dimer(μg/mL)	0.441	1.554 (1.152–2.072)	**0.003**	0.457	1.382 (0.998–1.752)	0.307
Surgery duration	0.043	1.303 (1.183–1.622)	**0.019**	0.416	1.202 (1.008–1.579)	**0.036**
Urine volume	0.213	1.021 (0.772–1.134)	0.698			

Note: Bold font represented P value < 0.05.

Abbreviations: BMI, body mass index; TNM, the American Joint Committee on Cancer tumor nodes metastasis stage; LAD, left anterior descending artery; RCA, right coronary artery; LCX, left circumflex artery; OM, obtuse marginal branch; EF, ejection fraction; RBC, red blood cell; WBC, white blood cell; HGB, hemoglobin; PLT, platelet; ALT, alanine transaminase; Scr, serum creatinine; NT-proBNP, N-terminal pro-brain natriuretic peptide; CRP, C-reactive protein; Anti-Xa, Anti-factor Xa; PT, prothrombin time; APTT, activated partial thromboplastin time; FIB, fibrinogen; TT, thrombin time; ASA, American Society of Anesthesiologists; Cessation, premature cessation of dual antiplatelet therapy; IQR, interquartile range.

Comparison of the Bleeding Model and PRECISE-DAPT

The external validation set analysis demonstrated a lower AUC value of 0.733 (0.686–0.779) for the PRECISE-DAPT, as depicted in Figure 5A, in contrast to the higher AUC values observed for the novel model in the identical datasets ($p < 0.001$). In contrast with PRECISE-DAPT, the bleeding prediction model we constructed has improved in reclassification, reflected in the increase of NRI and IDI by 0.230 (95% CI: 0.152–0.308), and 0.167 (95% CI: 0.138–0.196), respectively.

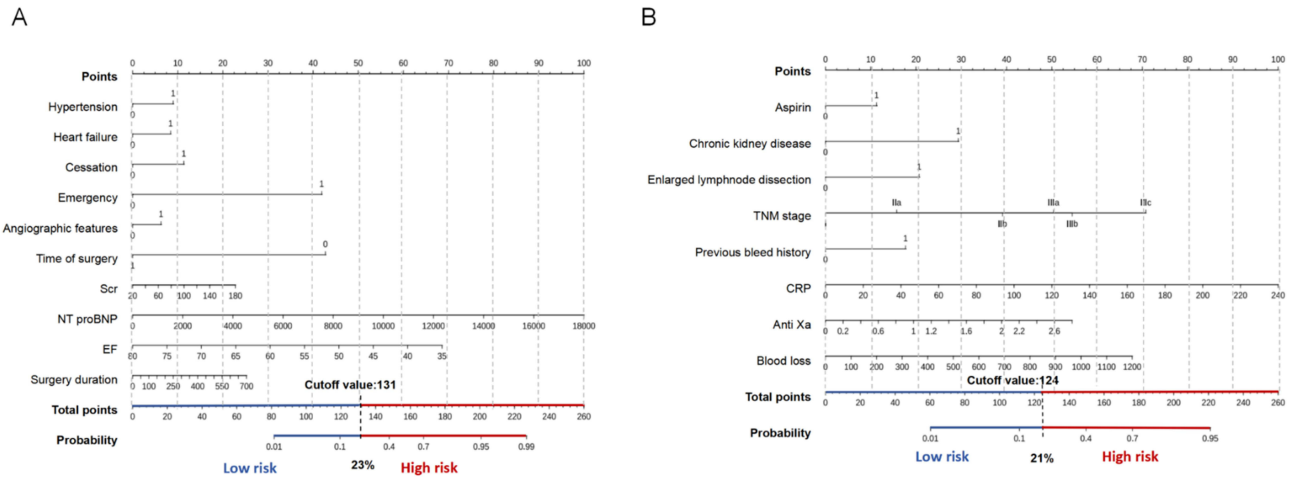

Figure 3 Nomogram of risk prediction for different outcomes. (**A**) The nomogram to predict the probability of MACEs. (**B**) The nomogram to predict the probability of MBs.

Abbreviations: MACEs, major adverse cardiovascular events; EF, ejection fraction; Scr, serum creatinine; NT-proBNP, N-terminal pro-brain natriuretic peptide; Cessation, premature cessation of dual antiplatelet therapy; TNM, the American Joint Committee on Cancer tumor nodes metastasis stage; CRP, C-reactive protein; Anti-Xa, Anti-factor Xa.

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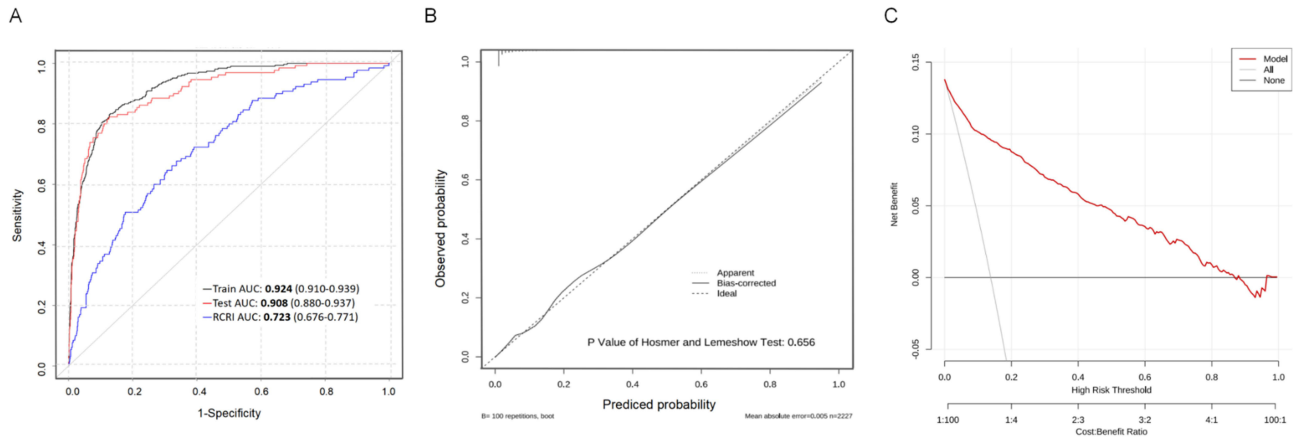

Figure 4 Discrimination, calibration and visualization of clinical utility of MACEs model. (**A**) AUCs of MACEs nomogram in the training and validation sets and comparison with the RCRI. (**B**) Calibration plot of the MACEs nomogram in the study. (**C**) DCA of the MACEs nomogram in the study.
Abbreviations: MACEs, major adverse cardiovascular events; RCRI, revised cardiac risk index.

Online Risk Calculator for MACEs and Bleeding Events

We have successfully developed an online risk calculator for calculating the risk of specific biomedical events, which is based on our prediction model. Clinicians can input relevant biomedical parameters and indicators on the calculator before surgery to obtain risk estimates related to the outcomes (Figure 6).

Table 4 Univariate and Multivariate Logistic Regression Analysis for the Risk Factors Associated with Bleeding Events

Variable	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Age (yr)	1.543 (0.778–1.953)	0.854		
BMI (kg/m^2)	2.127 (0.235–2.578)	0.731		
Diabetes mellitus	1.348 (0.337–1.958)	0.505		
Cerebrovascular disease	1.763 (0.793–1.907)	0.487		
Acute coronary syndrome	1.781 (1.252–1.927)	**0.015**	1.627 (0.947–2.692)	0.413
Chronic kidney disease	2.672 (1.419–3.572)	**0.025**	3.871 (2.734–5.478)	**< 0.001**
Previous bleed	1.738 (1.202–1.971)	**0.023**	2.189 (1.578–3.038)	**< 0.001**
Aspirin	1.715 (1.405–1.897)	**0.013**	1.645 (1.131–2.393)	**0.009**
Clopidogrel	2.362 (2.131–3.934)	**0.027**	1.799 (0.998–1.874)	0.891
Calcium channel blockers	1.427 (0.916–1.669)	0.512		
Enlarged lymph node dissection	2.176 (1.523–3.102)	**< 0.001**	2.659 (1.875–3.769)	**< 0.001**
Vascular thrombus	1.224 (0.896–1.425)	0.314		
Leukocyte(10^9)	2.816 (1.102–2.997)	0.112		
ALT(U/L)	1.812 (1.705–1.989)	**< 0.001**	1.689 (1.112–9.545)	0.291
Scr(μmol/L)	1.356 (0.815–1.773)	0.523		
NT-proBNP(pg/mL)	1.852 (1.179–2.261)	**0.021**	1.797 (1.122–4.273)	0.622
Emergency	1.712 (1.449–1.876)	**0.013**	1.157 (0.876–1.528)	0.305
Transfusion	1.514 (0.951–1.917)	0.364		
TNM stage IIa vs I	1.741 (1.142–2.009)	**< 0.001**	2.105 (1.142–3.881)	**< 0.001**
TNM stage IIb vs I	2.546 (2.273–2.871)	**< 0.001**	3.023 (2.273–3.967)	**< 0.001**
TNM stage IIIa vs I	3.799 (3.258–4.183)	**< 0.001**	4.551 (3.995–4.872)	**< 0.001**
TNM stage IIIb vs I	4.552 (4.273–5.001)	**< 0.001**	5.283 (5.012–6.201)	**< 0.001**

(*Continued*)

Table 4 (Continued).

Variable	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
TNM stage IIIIc vs I	6.607 (6.381–7.110)	**< 0.001**	7.241 (6.556–7.593)	**< 0.001**
Blood loss	1.584 (1.448–2.002)	**0.026**	1.824 (1.663–1.991)	**< 0.001**
RBC(10^{12})	0.178 (0.023–3.102)	0.342		
HGB(g/L)	0.272 (0.181–5.368)	0.682		
CRP(mg/L)	1.136 (1.017–1.229)	**< 0.001**	1.326 (1.017–1.562)	**< 0.001**
Anti-Xa(IU/mL)	2.042 (1.979–2.841)	**< 0.001**	2.479 (1.959–3.137)	**< 0.001**
Surgery duration	1.303 (0.889–1.572)	0.419		
Urine volume	1.033 (0.879–1.432)	0.216		

Note: Bold font represented P value < 0.05.
Abbreviations: BMI, body mass index; TNM, the American Joint Committee on Cancer tumor nodes metastasis stage; RBC, red blood cell; HGB, hemoglobin; ALT, alanine transaminase; Scr, serum creatinine; NT-proBNP, N-terminal pro-brain natriuretic peptide; CRP, C-reactive protein; Anti-Xa, Anti-factor Xa.

Discussion

Main Interpretation

The advantage of this study is that the MACEs model (AUC: 0.924; 95% CI: 0.910–0.939) and the bleeding model (AUC: 0.862; 95% CI: 0.843–0.882) were developed in the same cohort and were well validated in the external validation set. Meanwhile, this study introduced the classic MACEs risk score RCRI (AUC: 0.723; 95% CI: 0.676–0.771) and the bleeding risk score PRECISE-DAPT (AUC: 0.733; 95% CI: 0.686–0.799), both of which had good predictive ability in the external validation set. Many studies reached the same conclusion,[28] but the AUCs were still lower than the predictive instrument of this study, probably because the bleeding and ischemia risk of this study population are higher than those of patients after stent surgery or non-cardiac surgery, indicating that the generalization ability of the classic risk score in local populations also has limitations. This is also the significance of this study. We also found the cut points of the two nomogram scores according to the method of data fitting. If the nomogram score of the patient is greater than 131, the occurrence of MACEs after operation is over 23%; Similarly, if the patient's nomogram score is greater than 124, the occurrence of the bleeding events is over 21%. In addition, this study developed the online risk calculators, which can show clinicians the risk of ischemia and bleeding of patients at the same time by inputting

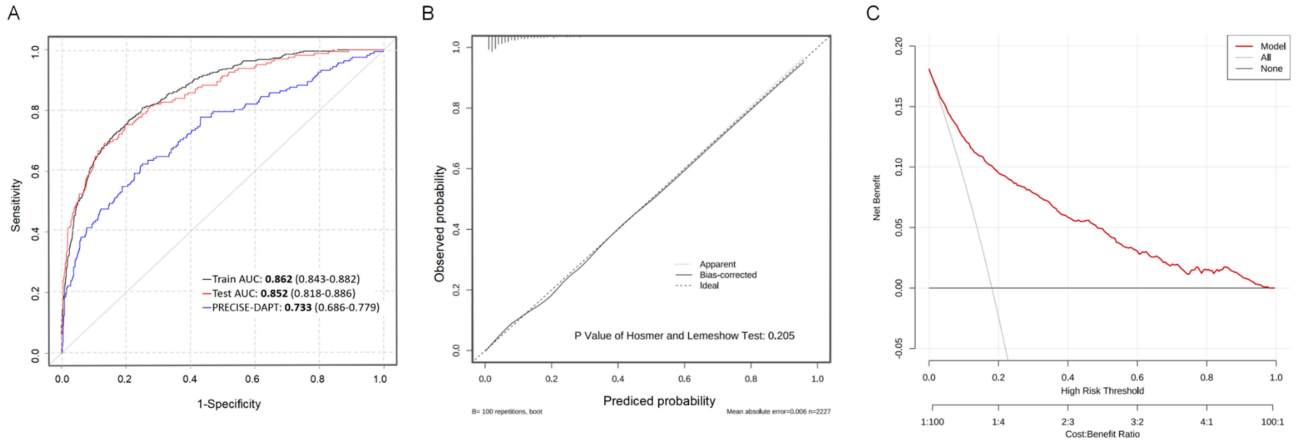

Figure 5 Discrimination, calibration and visualization of clinical utility of MBs model. (**A**) AUCs of MBs nomogram in the training and validation sets and comparison with the PRECISE-DAPT. (**B**) Calibration plot of the MBs nomogram in the study. (**C**) DCA of the MBs nomogram in the study.
Abbreviations: MBs, major bleeding events; PRECISE-DAPT, predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy.

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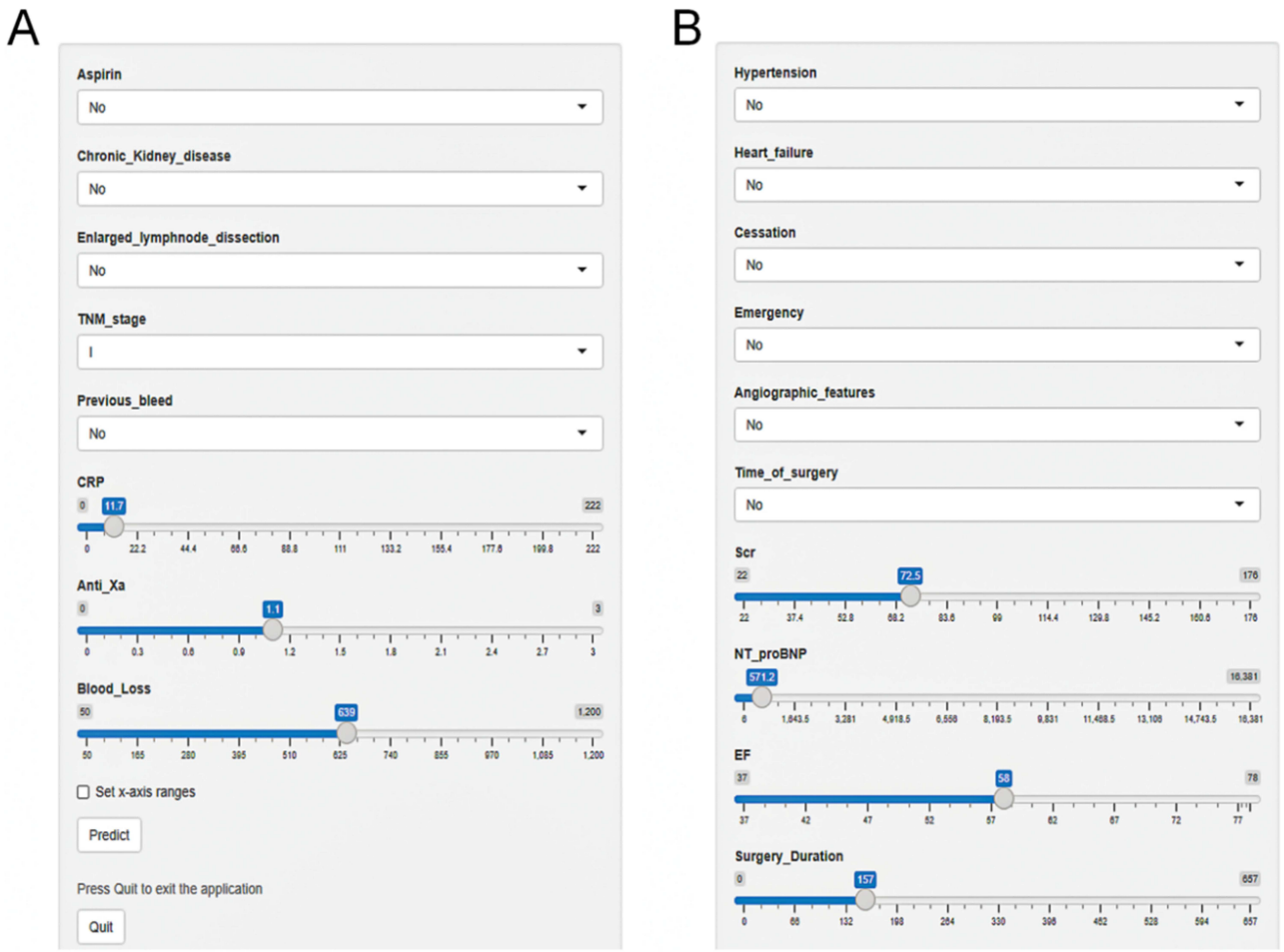

Figure 6 The online risk calculator based on the nomograms. (**A**) Online calculator for MACEs risk. (**B**) Online calculator for MBs risk.The MACEs and MBs probabilities of patients can be obtained by inputting the relevant indicators of patients during the perioperative period.

some easily obtained preoperative indicators, which is conducive to formulating individualized perioperative treatment plan for patients through multidisciplinary discussion.[29]

In the predictive instrument developed in this study, 10 objective and easily accessible variables were included in the MACEs model. Compared with RCRI and the National Surgical Quality Improvement Program – Morbidity and Mortality Calculator (NSQIP-MICA),[30] we add variables such as NT-Pro BNP, EF, time of surgery, and angiographic features, instead of just including demographics, past medical history, and some conventional blood test indicators, which enables us to comprehensively assess the patients' condition from multidimensional data. Current guidelines also recommend the utilization of biomarkers in assessment of the perioperative complications, encompassing NT-Pro BNP, cardiac troponin, and CRP.[31] However, some studies believed that incorporating these indicators into preoperative laboratory examination will result in overuse of the medical resources.[32] We believe that it is reasonable to invest more resources in the high-risk population for comprehensive monitoring. Rodseth et al found that setting NT-pro BNP = 201 pg/mL as the critical value was determined to be the best predictor of perioperative complications, and postoperative NT-proBNP measurement could enhance the comprehensive predictive ability of death or nonfatal myocardial infarction 30 days and ≥180 days after NCS.[33] In this study, NT-proBNP was not converted from a continuous variable to a categorical variable, but the average level of its value was still higher than any of other studies. It may be that surgery and malignant tumors mediate inflammatory changes in vivo and stimulate cardiomyocytes to produce NT-proBNP.[34] Banning et al found that The risk factors of MACEs are also related to some specific clinical manifestations, including previous history of heart failure, diabetes, chronic kidney disease and ejection fraction <35%.[35] The characteristics of coronary angiography of patients, including double stents and multi vessel lesions, may have a long-term impact on the outcome of

cardiac events.[36] In this study, EF and angiographic features were directly related to cardiac function, and were also confirmed to be independent risk factors for MACEs. The reason behind these discoveries can be attributed to the level of atherosclerosis and the requirement for intricate revascularization, which increases the risk of patients being exposed to early and late ischemic events. The occurrence of significant negative heart-related incidents varied between 3% and 11% among individuals with coronary stents who have received NCS. The specific range was influenced by factors such as the definition of MACEs, the type of surgery performed, and the duration after the stent was implanted.[37] The incidence of MACEs in this study was 13.9%. Studies have shown that the risk of MACEs may be related to some specific factors.[38] Significantly, there may be special mechanisms between the timing of surgery, the management of dapt, and the severity of tumor and cardiac disease that affect postoperative adverse events. It is important to note that the main modifiable determinant of ischemic risk is the time from PCI to surgery. As recommended by the guidelines, the incidence of MACEs is significantly higher when NCS is performed within six months after PCI, but according to this, it cannot be determined that six months is the key node to change the outcomes.[39] Further subgroup analysis of time is needed, and our team will conduct a multicenter prospective study to explore it.

Limitations

There also existed some limitations in this study. Firstly, this is a retrospective study, which may be affected by selection bias. Secondly, this study selected patients with gastrointestinal cancer after stent implantation, which is a part of NCS population, and the sample size was affected to some extent. Thirdly, the Anti-Xa may not be routinely monitored in other centers, increasing the difficulty of promoting the prediction instrument in this study. Finally, the population included in this study consists of Chinese patients, belonging to the East Asian ethnic group. Compared to the Western population, East-Asians are known to have higher bleeding risk and lower thrombotic risk, especially for major bleeding events such as intracranial hemorrhage associated with antithrombotic therapy.[40]

Conclusion

The novel predictive instrument provides two online risk calculators, which could accurately quantify the risk of ischemia and hemorrhage in patients with a history of coronary stent implantation undergoing gastrointestinal cancer surgery for clinicians simultaneously.

Data Sharing Statement

Data are available from the corresponding author upon reasonable request.

Ethics Statement

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all subjects and/or their legal guardian(s). This study received approval from the Research Ethics Committee of the People's Liberation Army General Hospital, denoted by approval No. S2023-630.

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Disclosure

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