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Analysis of risk factors for gastrointestinal bleeding in percutaneous coronary intervention patients treated with dual antiplatelet therapy after surgery

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Abstract

Following percutaneous coronary intervention (PCI), dual antiplatelet therapy (DAPT) is key to preventing thrombosis. However, the use of DAPT is strongly associated with an increased risk of Gastrointestinal Bleeding, which not only affects patient recovery but also increases the healthcare burden. This study aims to determine the influence of past medical history and factors during hospitalization on the development of postoperative GIB in patients undergoing PCI with DAPT. A total of 380 patients were collected in this study. A total of 42 patients developed GIB during the 1-year follow-up period. Preoperative and postoperative clinical data and past medical history of patients were collected to study the correlates affecting the occurrence of GIB in the postoperative period in patients undergoing PCI with DAPT and to establish a prediction model. Single-factor logistic regression analysis showed: gender, age, past history of bleeding, past history of cancer or tumor, smoking history, history of heart failure, history of PPI use, renal insufficiency, and hypoproteinemia are potential risk factors that may influence the occurrence of GIB postoperatively in patients undergoing DAPT for PCI, $P < .2$. The data obtained were further included in multi-factor logistic regression analysis: gender (female), past history of bleeding, past history of cancer or tumor, smoking history, heart failure, renal insufficiency were independent risk factors influencing the occurrence of GIB postoperatively in PCI patients undergoing DAPT, $P < .05$. The findings of this study confirm that gender (female), past history of bleeding, past history of cancer or tumor, smoking history, heart failure and renal insufficiency are independent risk factors for the development of GIB postoperatively in PCI patients undergoing DAPT.

Abbreviations: 95% CI = 95% confidence interval, AUC = area under the curve, BMI = body mass index, DAPT = dual antiplatelet therapy, DCA = the decision curve, GIB = gastrointestinal bleeding, OR = odds ratio, *P* = *P*-value, PCI = percutaneous coronary intervention, PPI = protonpump inhibitors, ROC = receiver operating characteristic, SE = standard error, β = beta.

Keywords: dual antiplatelet therapy, gastrointestinal bleeding, percutaneous coronary intervention, predictive model, risk factors

1. Introduction

Percutaneous coronary intervention (PCI) is 1 of the most important treatments for coronary heart disease. The role of PCI in improving the prognosis of patients has become increasingly evident with the continuous advancement of technology.[1–4] After surgery, patients are usually required to receive dual antiplatelet therapy (DAPT) to reduce the risk of thrombosis and prevent cardiovascular events.[5–7] However, studies have shown that the use of DAPT may also significantly increase the risk of gastrointestinal bleeding (GIB), an issue that has attracted widespread attention in clinical practice.[8,9] The mechanisms of GIB are complex and are mainly related to the inhibitory effect of antiplatelet drugs on platelet function and the potential damage to the mucosa of the gastrointestinal tract. DAPT usually includes aspirin and another antiplatelet drug (such as clopidogrel or ticagrelor), which prevent thrombosis by inhibiting platelet aggregation. However, they may also interfere with the repair process of the mucosa of the gastrointestinal tract, making it more susceptible to damage, which can lead to bleeding. In addition, long-term use of DAPT may lead to an increase in gastric acid secretion or a weakening of the gastric mucosal barrier function, which in turn triggers a rise in the risk of ulceration

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Written informed consent was obtained from the individual for the publication of any potentially identifiable images or data included in this article. The Ethics Committee of Hangzhou cancer Hospital approved the study (Ethics approval number: W-2024-029-101). This study has obtained the informed consent of the participating patients.

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and hemorrhage.[10–12] According to data from international epidemiological studies, the incidence of GIB after DAPT treatment ranges from 5% to 20%, depending on a variety of factors.[13–15] For example, Asdis Sveinsdottir et al[16] found in their study that the incidence of GIB was as high as 20% in PCI patients who underwent DAPT. Such results significantly suggest the potential impact of DAPT in increasing the risk of GIB, and the risk of bleeding is further increased in patients with concomitant underlying conditions such as hypertension and diabetes. These data highlight the importance of personalized management of patients at high risk of GIB. Although it has been suggested that certain factors (e.g., age, gender, comorbidities, and underlying diseases) are strongly associated with the risk of GIB, a systematic assessment and comprehensive analysis are lacking. In addition, most of the available studies have focused on the assessment of individual risk factors, and there is a lack of exploration of the development of comprehensive risk assessment models. This research gap makes it challenging for clinicians to provide accurate prevention strategies for different patients. Therefore, the aim of this study was to construct and validate a set of risk factor assessment models for GIB in patients with PCI and to explore the value of its clinical application. By comprehensively analyzing several clinical variables, this study hope to provide clinicians with a scientific basis to help them effectively reduce the incidence of GIB and improve the overall prognosis of patients while implementing DAPT. This study not only fills the knowledge gap in the relevant field, but also provides practical recommendations for clinical practice and promotes the further development of risk management for GIB.

2. Materials and methods

2.1. Research object

The research objects comprised patients admitted to the cardiology department of the hospital from January 2019 to June 2023, who underwent PCI surgery and thereafter received consistent DAPT as part of their postoperative care. A total of 380 patients were included in the study. Of these, 201 were males and 179 were females. Forty-two patients developed GIB during the 1-year postoperative follow-up period. The study was approved by the Ethics Committee of Hangzhou Cancer Hospital (Ethics approval number: W-2024-029-101).

2.2. Research methods

Forty-two patients developed GIB during the 1-year postoperative follow-up period. Data related to the patient's medical history and during hospitalization were collected separately to study the risk factors affecting the development of GIB in PCI patients treated with DAPT postoperatively.

2.3. Collecting indicators

Gender, age, body mass index (BMI), hypertension, diabetes mellitus, hyperlipidemia, past history of bleeding, past history of cancer or tumor, smoking history, history of alcohol consumption, history of heart failure, anemia, history of PPI use, hyponatraemia, hypokalemia, renal insufficiency, and hypoproteinaemia were collected in this study.

2.4. PCI and DAPT

PCI is a treatment that involves a cardiac catheterization technique to unblock the lumen of a narrowed or even occluded coronary artery, thereby improving blood perfusion to the heart muscle. Currently the femoral or radial route is usually used: Delivery of a guide catheter to the opening of the coronary artery to be dilated; A balloon or stent of the appropriate size is delivered along the guidewire to the stenotic segment; Dilatation with appropriate pressure and time according to the characteristics of the lesion to achieve the purpose of lifting the stenosis. A period of DAPT is usually given after PCI, depending on the patient's condition. However, the use of DAPT may also significantly increase the risk of GIB. DAPT usually includes aspirin and another antiplatelet drug (such as clopidogrel or ticagrelor), which prevent thrombosis by inhibiting platelet aggregation in order to avoid thrombosis-related complications after surgery. The subjects in this study were treated in accordance with the AHA/ACC/ACCP/ASPC/NLA/PCNA guidelines for the management of chronic coronary heart disease 2023,[17] and received standardized treatment throughout the entire course of the study, and were followed up regularly in the hospital after the operation.

2.5. Inclusion and exclusion criteria

2.5.1. Inclusion criteria. Those with a clear clinical diagnosis of coronary artery disease and have successfully undergone PCI, those with complete relevant surgical data and case files, those with a clinically confirmed diagnosis of GIB or patients who died from GIB, those aged 30 to 80 years old, and those who have signed an informed consent form.

2.5.2. Exclusion criteria. Patients with incomplete surgical data or related case information, those with severe combined hepatic, renal, and coagulation dysfunction, patients who were lost to follow-up or patients who died from causes other than GIB causes, and patients who were previously enrolled in other clinical trials, in addition to the oral anticoagulants used for DAPT, other oral anticoagulants were also used.

2.6. Statistical methods

SPSS 25.0 (Chicago) was used for data processing and statistical analysis in this study. Quantitative data conforming to normal distribution were expressed as mean ± standard deviation, and the differences between groups were analyzed by independent sample T test. Comparisons between groups that did not follow a normal distribution were performed using nonparametric tests. Data for qualitative data were expressed as number of cases and percentage, and chi-square tests were used to determine whether there were differences between groups. GIB was first analyzed on the basis of the occurrence of GIB and various clinical indicators. Subsequently based on a univariate logistic regression analysis of the collected data. To identify potential risk factors for GIB in PCI patients treated with DAPT after surgery. For univariate logistic regression analysis, exposure factors with $P \leq .2$ were selected and included in the multivariate analysis. Independent risk factors for GIB in PCI patients treated with DAPT after surgery were derived. $P < .05$ was considered a statistically significant difference.

3. Results

3.1. Table of assignment for relevant indicators

See Table 1 for details.

3.2. Single-factor logistic regression analysis

A total of 380 patients were included in this study and 42 patients developed GIB during the 1-year postoperative follow-up time. Potentially relevant factors were included in a single-factor logistic regression analysis: gender, age, BMI, hypertension, diabetes mellitus, hyperlipidemia, past history of bleeding, past

history of cancer or tumor, smoking history, history of alcohol consumption, history of heart failure, anemia, history of PPI use, hyponatraemia, hypokalemia, renal insufficiency, and hypoproteinaemia. After analyzing the results: gender, age, past history of bleeding, past history of cancer or tumor, smoking history, history of heart failure, history of PPI use, renal insufficiency, and hypoproteinemia are potential risk factors that may influence the occurrence of GIB postoperatively in patients undergoing DAPT for PCI, $P < .2$ (see Table 2 for details).

3.3. Multi-factor logistic regression analysis

The data obtained were further included in multi-factor logistic regression analysis: gender (female), past history of bleeding, past history of cancer or tumor, smoking history, heart failure, renal insufficiency were independent risk factors influencing the occurrence of GIB postoperatively in PCI patients undergoing DAPT, $P < .05$ (see Table 3 for details).

3.4. Drawing of the nomogram

A nomogram of the risk of GIB in PCI patients treated with DAPT was constructed based on 6 independent predictors tested by multi-factor logistic regression analysis (Fig. 1). The nomo score of each independent Risk factor was assigned, and the Total score was obtained based on the sum of the clinical characteristics of the patient. Located on the Total points axis, the value on the risk axis corresponding to the vertical downward is the the probability of GIB in PCI patients treated with DAPT and the score of each independent predictor corresponds to the upper limit of the score of each independent predictor. The total score for each subject is the sum of the scores of the independent predictors. The risk of developing GIB in DAPT-treated PCI patients was determined by the total score on the axis of risk of developing GIB in PCI patients treated with DAPT. The model was subsequently validated internally, and the internal validation was carried out using the Bootstrap method in the R software to repeat the sampling of the column-line plots 1000 times. The calibration curve is close to the ideal curve, indicating that the column-line graph predicting the incidence of GIB in PCI patients treated with DAPT has a high degree of agreement with the actual incidence, reflecting a good predictive performance (Fig. 2). The ROC curve for this column-line graph training set has an AUC of 0.890 (95% CI = 0.841–0.939), see Figure 3 for details. It shows that this column-line diagram provides good discrimination between PCI patients treated with DAPT who are at high risk of developing GIB. The decision curve (DCA) for this column-line graph is shown: in this nomogram, when the threshold probability of individuals is >.05, the model provides more net benefits than the strategy of "everyone intervenes" or "no 1 intervenes." This finding suggests that this column-line graphical model has a good clinical application in predicting GIB in PCI patients treated with DAPT (Fig. 4).

Table 1

Assignment table.

Name	Variable assignment and description
GIB	Yes – 1; No – 0
Age	≤60-0, >60-1
Hypertension	Yes – 1; No – 0
Diabetes mellitus	Yes – 1; No – 0
Past history of bleeding	Yes – 1; No – 0
Past history of cancer or tumor	Yes – 1; No – 0
History of heart failure	Yes – 1; No – 0
Renal insufficiency	Yes – 1; No – 0
Hypoproteinemia	Yes – 1; No – 0
Anaemia	Yes – 1; No – 0

4. Discussion

4.1. Discussion of the main findings of the study

Although DAPT is effective in reducing the risk of cardiovascular events, its concomitant risk of bleeding should not be ignored. A study by Khan et al noted that the incidence of GIB after DAPT treatment was significantly higher than in patients treated with single antiplatelet therapy.[18] With the risk predictive model, doctors are able to adjust their treatment strategies accordingly. For example, shorter courses of DAPT or lower drug doses are chosen to balance cardiovascular protection with bleeding risk. Secondly, the establishment of risk prediction models helps to optimize the allocation of healthcare resources. According to Campbell HE et al, GIB leads to prolonged hospital stays and significantly higher healthcare costs.[19] Early identification of patients at high risk of bleeding can provide valuable information to healthcare providers, facilitate rational

Table 2

Single-factor logistic regression analysis.

Variables	β	SE	Z	P	OR (95% CI)
Gender					
Female					1.00 (reference)
Male	-0.68	0.34	–2.01	.044	0.51 (0.26–0.98)
Age					
0					1.00 (reference)
1	0.43	0.33	1.30	.193	1.54 (0.80–2.96)
Hypertension					
0					1.00 (reference)
1	–0.18	0.33	–0.55	.584	0.84 (0.44–1.59)
Diabetes mellitus					
0					1.00 (reference)
1	0.25	0.40	0.63	.527	1.29 (0.59–2.84)
Hyperlipidaemia					
0					1.00 (reference)
1	–0.14	0.44	–0.31	.756	0.87 (0.37–2.06)
Past history of bleeding					
0					1.00 (reference)
1	2.55	0.40	6.41	<.001	12.86 (5.89–28.06)
Past history of cancer or tumor					
0					1.00 (reference)
1	1.72	0.35	4.86	<.001	5.59 (2.79–11.19)
Smoking history					
0					1.00 (reference)
1	1.02	0.33	3.06	.002	2.76 (1.44–5.31)
History of alcohol consumption					
0					1.00 (reference)
1	0.13	0.35	0.38	.705	1.14 (0.58–2.26)
History of heart failure					
0					1.00 (reference)
1	0.66	0.39	1.67	.095	1.93 (0.89–4.20)
Anaemia					
0					1.00 (reference)
1	–0.04	0.40	–0.11	.911	0.96 (0.44–2.09)
Hyponatraemia					
0					1.00 (reference)
1	0.19	0.56	0.34	.732	1.21 (0.40–3.65)
Proton pump inhibitors					
0					1.00 (reference)
1	0.75	0.58	1.28	.199	2.12 (0.67–6.66)
Hypokalaemia					
0					1.00 (reference)
1	–0.12	0.63	–0.19	.848	0.89 (0.26–3.06)
Renal insufficiency					
0					1.00 (reference)
1	1.55	0.43	3.64	<.001	4.72 (2.04–10.89)
Hypoproteinaemia					
0					1.00 (reference)
1	0.65	0.48	1.35	.178	1.92 (0.74–4.96)

SE = standard error.

allocation of healthcare resources, and improve overall treatment efficiency. In this study, 6 independent predictors were selected from a large number of potential factors through multi-factor logistic regression analysis. The results showed that 6 factors such as gender (female), past history of bleeding, past history of cancer or tumor, smoking history, history of heart failure and renal insufficiency were independent risk factors for postoperative GIB in PCI patients treated with DAPT. And a predictive model for the risk of GIB in PCI patients treated with DAPT after surgery was constructed. The results of the internal validation of this model show that the calibration curve of the model is highly close to the ideal curve, which indicates a good agreement between the predicted values and the actual observations. This is an important metric for assessing the accuracy of predictive models. The predictive model AUC was 0.890 (95% CI = 0.841–0.939), which suggests that the nomogram discriminates well between PCI patients treated with DAPT who are at high risk of developing GIB. Similar predictive models for the risk of GIB in PCI patients treated with DAPT have been barely addressed in previous studies. However, there are studies involving predictive models of the risk of developing GIB in the remaining conditions. For example, Ruijun Ji et al developed a clinical feature-based scoring system for predicting GIB after acute ischemic stroke with an AUC value of 0.790, which demonstrated good discriminatory ability.[20] Compared to the AUC value of 0.890 in this study, the model performed slightly less well in predicting high-risk patients. This study suggests that the superiority of the model may derive from combining more clinical factors that influence the risk of GIB, including patient age, comorbidities, and medication use, which underscores the importance of multifactorial analysis in risk assessment.

4.2. Interpretation of independent predictors

Women may be more susceptible to bleeding events during antiplatelet therapy due to changes in physiology and hormone levels.[21,22] The fluctuation of estrogen in the female body directly affects the function of platelets and coagulation mechanism. Estrogen has some degree of antiplatelet effect. Long-term

Table 3

Multi-factor logistic regression analysis.

Variables	β	S.E	*Z*	*P*	OR (95% CI)
Gender					
Male					1.00 (reference)
Female	–0.90	0.43	–2.08	**.037**	2.44 (1.05–5.56)
Past history of bleeding					
0					1.00 (reference)
1	2.52	0.44	5.73	**<.001**	12.38 (5.24–29.24)
Past history of cancer or tumor					
0					1.00 (reference)
1	1.63	0.45	3.63	**<.001**	5.10 (2.12–12.27)
Smoking history					
0					1.00 (reference)
1	1.17	0.42	2.78	**.005**	3.22 (1.41–7.33)
History of heart failure					
0					1.00 (reference)
1	1.28	0.52	2.44	**.014**	3.60 (1.29 ~ 10.05)
Renal insufficiency					
0					1.00 (reference)
1	1.41	0.59	2.40	**.016**	4.11 (1.30–13.05)

Bold values indicate statistically significant.

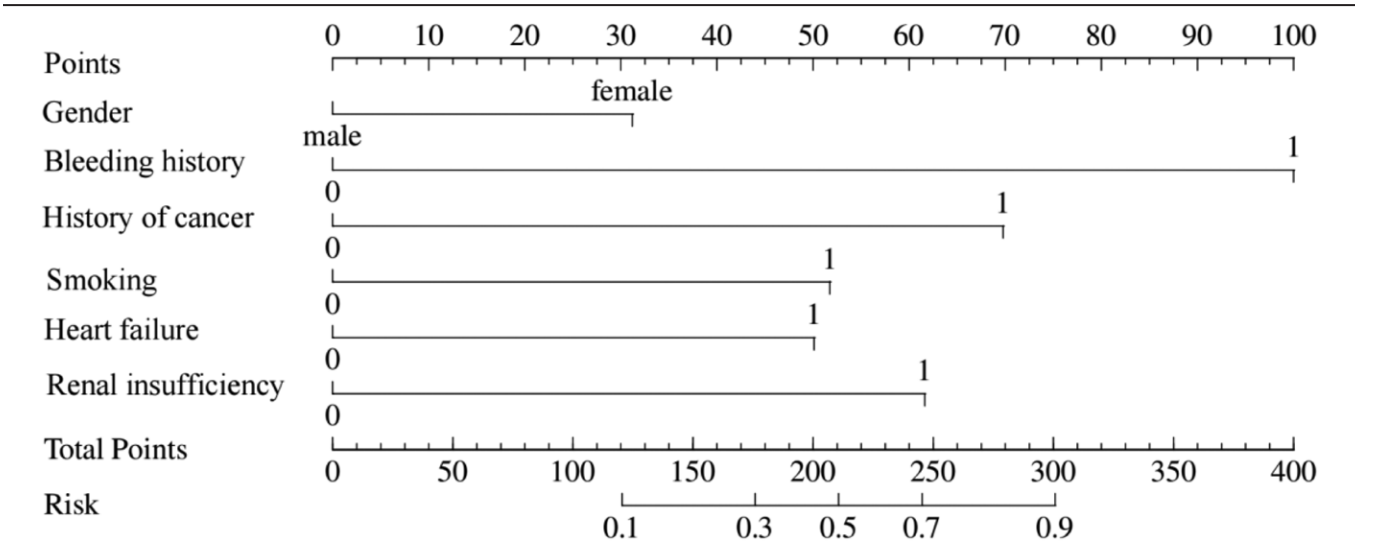

Figure 1. Risk of gastrointestinal bleeding in PCI patients treated with DAPT nomogram prediction. DAPT = dual antiplatelet therapy, PCI = percutaneous coronary intervention.

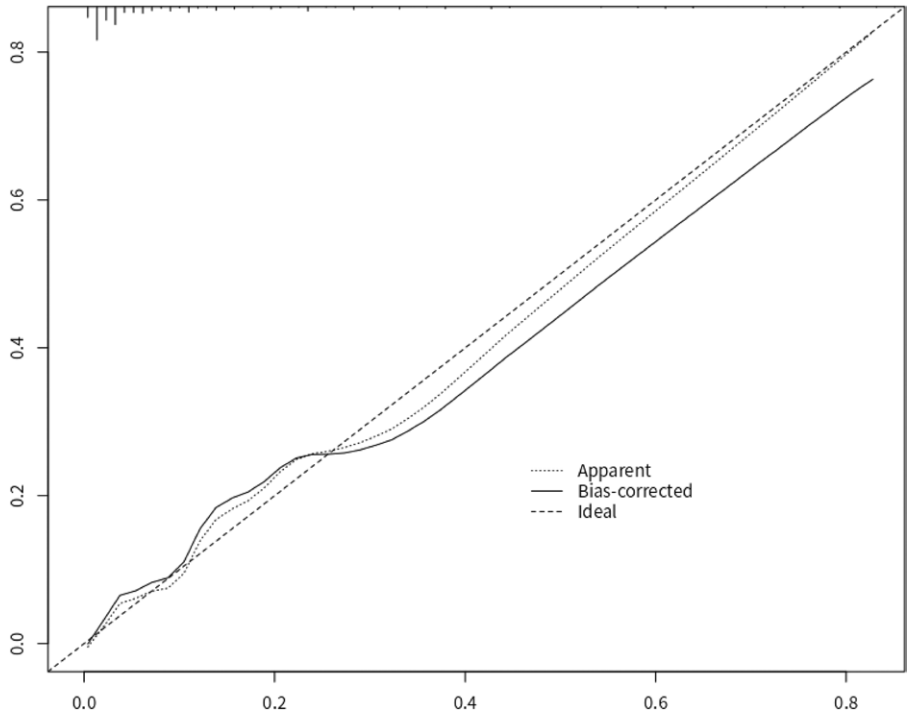

Figure 2. Internal validation of line graphs: calibration curves.

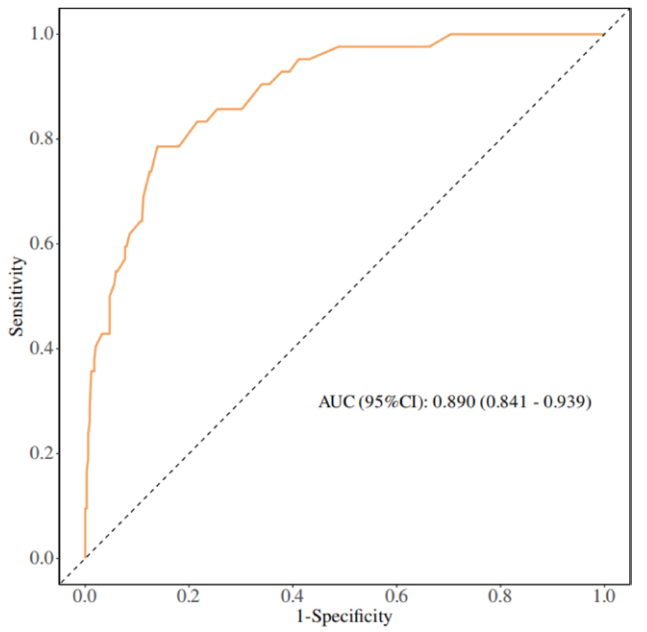

Figure 3. Receiver operating characteristic curve. AUC = area under the curve.

antiplatelet drug use in the context of DAPT therapy may exacerbate the risk of bleeding. Secondly, certain antiplatelet drugs are metabolized more slowly in the female body, which leads to an increase in their effective concentration, further enhancing the bleeding tendency. Freibert et al noted that previous bleeding events not only suggest an underlying abnormality in the patient's coagulation function, but may also be an important indicator of recurrent bleeding.[23] A study by Mahady et al found that smoking has a diminished protective effect on the gastrointestinal mucosa and may also affect the metabolism of antiplatelet drugs, increasing the risk of bleeding.[24] Studies have shown that patients with heart failure are at a significantly increased risk of bleeding due to changes in the circulatory system and reduced ability to metabolize drugs.[25] There are no studies addressing the intrinsic relationship between renal function and the development of GIB in PCI patients treated with DAPT after surgery. Considering the possibility that renal insufficiency increases the concentration of antiplatelet drugs in the body by affecting drug clearance, leads to a higher risk of bleeding. Therefore, patients with 1 of the following characteristics: past history of bleeding, past history of cancer or tumor, smoking history, history of heart failure or renal insufficiency, or female patients, should be carefully assessed for bleeding risk and consideration given to adjusting the treatment regimen during DAPT therapy.

4.3. Universality and adaptability of models in clinical practice

In today's medical field, individualized medicine has become a key concept in improving patient outcomes. Individualised predictive models for the risk of GIB after PCI in patients undergoing post-procedural DAPT have important clinical and research implications. The risk predictive model developed in this study performed well in terms of accuracy and performance assessment. And the superiority of the AUC values and the good match of the calibration curves show that the model can provide effective early warning for high-risk DAPT patients in clinical practice. Clinicians can have an initial grasp of the patient based on the model developed in this study, perform initial risk identification for the patient, and can take individualized treatment decisions to optimize anticoagulation regimens to avoid irreversible outcomes.

4.4. Limitations of the study and future directions

Although this study provides a preliminary discussion of the risk factors for GIB in PCI patients treated with DAPT after surgery, there are some limitations that need to be addressed and improved

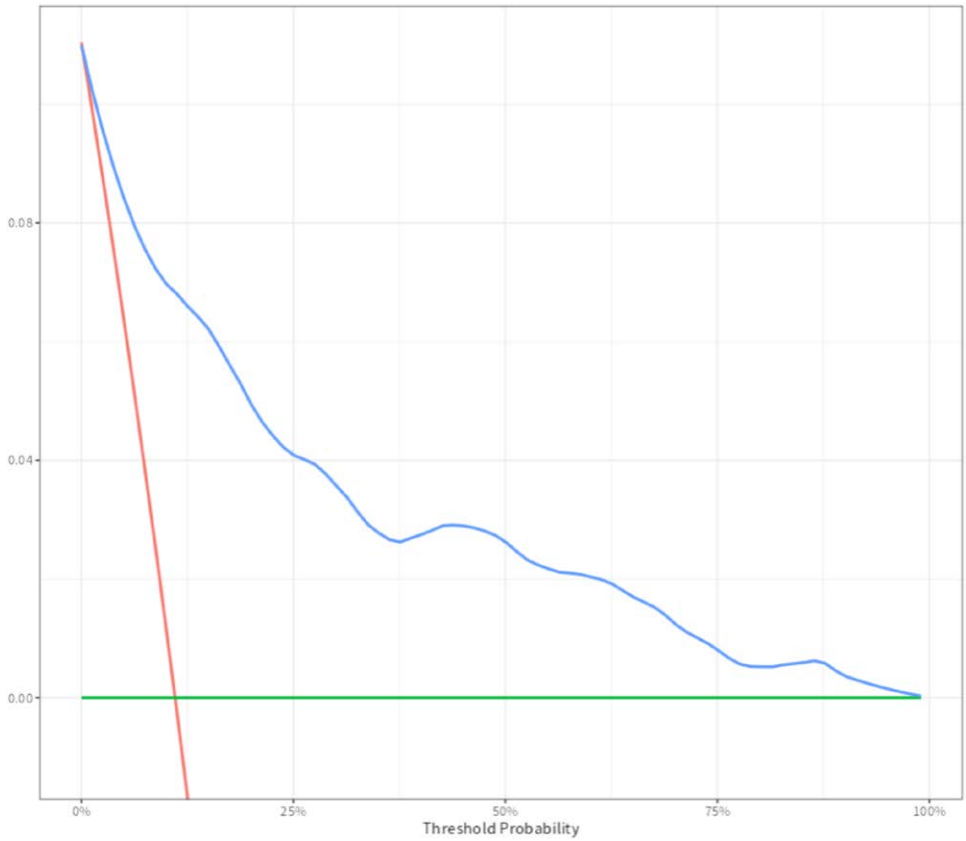

Figure 4. Decision curves in nomogram models.

in future studies. Firstly, limitations in sample selection may affect the generalisability of the results. For example, if the study sample is drawn mainly from specific regions or hospitals, the results may not be generalizable to a wider population. In addition, retrospective study designs can lead to data bias. In particular, minor or atypical hemorrhagic events may be missed in the reporting and recording of hemorrhagic events, affecting the assessment of the true incidence. Second, individual patient differences, such as comorbidities, drug interactions, and lifestyle factors, may not be adequately controlled, which may mask the true impact of certain risk factors. At the same time, the failure to analyze in depth the interaction between patients' baseline characteristics (e.g. age, gender, weight, etc) and the risk of bleeding may have led to an incomplete understanding of risk factors. Finally, long-term follow-up data may be lacking in the study due to time constraints and resource constraints, thus affecting the overall assessment of the long-term effects of DAPT treatment and its relationship with bleeding events. Future studies should continue to explore the mechanism of action of these risk factors and validate the applicability of the model in different patient groups in order to provide a more precise reference for the development of individualized treatment plans. In addition, it has been pointed out that dynamically updated predictive models are better able to adapt to changes in patients' conditions, which in turn improves the accuracy of predictions.[26,27] To enhance the reliability and clinical applicability of this model, the applicability and validity of the model can be further enhanced by real-time data monitoring and updating in the future.

5. Conclusions

The findings of this study confirm that gender (female), past history of bleeding, past history of cancer or tumor, smoking history, heart failure and renal insufficiency are independent risk factors for the development of GIB postoperatively in PCI patients undergoing DAPT. The predictive model developed in this study can help cardiovascular physicians to some extent in accurately identifying patients at high risk of bleeding. This results in more caution during treatment as well as medication.

Author contributions

Data curation: Caiping Chen.
Writing – original draft: Huimin Fan.
Writing – review & editing: Renya Shuai.

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