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Retrospective Study

Machine-learning predicts portal vein thrombosis after splenectomy in patients with portal hypertension: A comparative analysis of postoperative platelet elevation rate-based models

Jian Li *et al.* The PPER-based models for predicting PVT

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Abstract

BACKGROUND

For patients with portal hypertension (PH), portal vein thrombosis (PVT) is a fatal complication after splenectomy. Postoperative platelet elevation is considered as the foremost reason for PVT. However, the value of postoperative platelet elevation rate (PPER) in predicting PVT has never been studied.

AIM

To investigate the predictive value of PPER for PVT and establish PPER-based prediction models to early identify individuals at high risk of PVT after splenectomy.

METHODS

We retrospectively reviewed 483 patients with PH related to hepatitis B virus (HBV) who underwent splenectomy between July 2011 and September 2018, and they were randomized into the training ($n=338$) and validation ($n=145$) cohorts. The generalized linear (GL), least absolute shrinkage and selection operator (LASSO), and random forest (RF) were used to construct models. The receiver operating characteristic curves (ROC), calibration curve, decision curve analysis (DCA), and clinical impact curve (CIC) were performed to evaluate the robustness and clinical practicability of the GL model (GLM), LASSO model (LSM), and RF model (RFM), respectively.

RESULTS

Multivariate analysis exhibited that the first and third days for PPER (PPER1, PPER3) were strongly associated with PVT [odds ratio (OR): 1.78, 95% confidence interval (CI): 1.24-2.62, $P=0.002$; OR: 1.43, 95%CI: 1.16-1.77, $P<0.001$, respectively]. The areas under ROC (AUC) of the GLM, LSM, and RFM in training cohort were 0.83 (95%CI: 0.79-0.88), 0.84 (95%CI: 0.79-0.88), and 0.84 (95%CI: 0.79-0.88), respectively; and were 0.77 (95%CI: 0.69-0.85), 0.83 (95%CI: 0.76-0.90), and 0.78 (95%CI: 0.70-0.85) in validation cohort, respectively. The calibration curves showed satisfactory agreement between prediction

by models and actual observation. DCA and CIC indicated that all models conferred high clinical net benefits.

CONCLUSION

The PPER1 and PPER3 were effective indicators for postoperative prediction of PVT. We successfully developed PPER-based practical models to accurately predict PVT, which would conveniently help clinicians rapidly differentiate individuals at high risk of PVT, and thus guide the adoption of timely interventions.

Key Words: Portal hypertension; Splenectomy; Portal vein thrombosis; Postoperative platelet elevation rate; Practical model; Machine learning

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Core Tip: For patients with PH related to HBV, PPER was an important predictor for the formation of PVT after splenectomy. This study was the first to construct PPER-based practical models for predicting PVT, which would be helpful for clinicians to recognize individuals at high risk of PVT as soon as possible.

INTRODUCTION

Liver cirrhosis is recognized as an extremely important and rapidly increasing disease burden in the world^[1]. In the progressive stage of liver cirrhosis, the complications caused by portal hypertension (PH) including esophagogastric variceal bleeding and hypersplenism, pose a great threat to the patients' life and health^[2, 3]. Liver transplantation is currently recommended as a curative treatment for liver cirrhosis combined with PH, however, due to the shortage of liver sources and high

transplantation cost, its clinical practicability is limited^[4, 5]. The transjugular intrahepatic portosystemic shunt (TIPS) seems to be a gospel for PH, but unfortunately, restenosis or/and hepatic encephalopathy will occur in more than 60% of patients^[6, 7]. In Asia, splenectomy (or combined with devascularization) has been widely adopted as an effective treatment for hypersplenism or esophageal and gastric variceal bleeding caused by PH^[8, 9].

¹ Portal vein thrombosis (PVT) is often defined as thrombosis within the portal vein trunk or intrahepatic portal branches, with or without the splenic vein or superior mesenteric vein involvement^[10, 11]. PVT is considered as a dreaded complication after splenectomy for patients with PH^[12], and the probability of PVT has been reported to be 4.8%-51.5%^[13-15]. For those with acute PVT and resulting in superior mesenteric vein thrombosis, it has been reported that it may be closely associated with acute liver failure and could influence mortality^[16]. Hence, strategies are needed to prevent PVT in patients who underwent splenectomy. In clinical practice, anticoagulation is a critical method for the prevention and treatment of PVT in patients after splenectomy. However, when the anticoagulation therapy should be started remains controversial. Early anticoagulation may result in life-threatening bleeding events for patients with liver cirrhosis. Whether anticoagulant therapy should be prescribed to all patients after splenectomy deserves careful consideration. In addition, the majority of patients with PVT are asymptomatic and only a few experience abdominal discomfort^[12]. Therefore, there is an urgent requirement to find effective diagnostic methods to early and rapidly identify individuals with high risk of PVT after splenectomy, and then further guide clinicians to take intervention measures. The color Doppler ultrasonography or contrast-enhanced computed tomography (CT) is commonly applied for the final diagnosis of PVT^[17], however, it seems to be useless for screening out the high-risk individuals who are vulnerable to PVT. Given this, many scholars attempted to investigate the risk factors closely related to the occurrence of PVT after splenectomy^[8, 18-21]. Several investigators paid attention to the fact that preoperative low platelet count

and postoperative high platelet count may be crucial predictors for the risk of PVT postoperatively^[19, 22].

Generally speaking, patients with PH will experience rebounding rises in platelet count after splenectomy^[23], combined with hemodynamic changes in the portal venous system, and thus these patients are highly prone to developing PVT^[24]. However, the effect of the amplitude of sharp postoperative rises in platelet count on PVT has received little attention. We speculate the postoperative platelet elevation rate (PPER) should be an important predictor of PVT. To the best of our knowledge, there are no reports on the relationship between PPER and PVT.

In recent years, to meet the urgent demand of finding effective methods to predict PVT after splenectomy, several studies have attempted to construct predictive models for PVT after splenectomy in patients with cirrhosis using multivariate regression analysis^[25, 26]. However, there are few clinical variables included in the analysis and the accuracy of these prediction models is still unsatisfactory. Therefore, there is an urgent need for an efficient and accurate visualization model.

Nowadays, novel machine learning algorithms based on more clinical features have shown great potential in various aspects of medical research, especially in the construction of predictive models, and the features screened for model construction are clinically interpretable^[27-29]. Gao *et al*^[28] constructed four machine learning models based on COVID-19 patients' 53 raw clinical features to distinguish individuals with the high-risk of mortality, with the areas under the curve (AUC) of 0.976. Kawakami *et al*^[29] developed seven supervised machine learning classifiers based on 32 clinical parameters, among which the Random Forest model showed the best performance in distinguishing epithelial ovarian cancer from benign ovarian tumors with an AUC of 0.968. The wide range of applications of machine learning methods has surpassed conventional statistical analysis due to their higher accuracy, which might enable machine learning to be increasingly applied in the field of medical research^[30-32]. Although compared with traditional multivariate analysis methods, machine learning algorithms have overwhelming advantages in constructing clinical prediction models.

However, so far, only Wang *et al* [33] tried to construct a prediction model of PVT after splenectomy in cirrhotic patients with PH using machine learning algorithms. The model they constructed has greatly improved the prediction efficiency compared with the traditional models. However, the clinical parameters involved in the construction of the model are extremely complex, which limits its clinical use.

Therefore, the purpose of this study was to evaluate the predictive value of PPER in the risk of PVT after splenectomy for patients with PH. In addition, we sought to build a simple, efficient and accurate practical models for predicting PVT by machine learning algorithms to facilitate assisting clinicians in the early identification of individuals at high risk of PVT after splenectomy and taking intervention measures in time. We present the following article in accordance with the TRIPOD reporting checklist.

MATERIALS AND METHODS

Study population

We retrospectively recruited 944 consecutive patients aged no less than 18 years who underwent splenectomy in our institution between July 4, 2011, and September 7, 2018. The patients with the following conditions were excluded: (1) splenic space-occupying lesion; (2) hematological disease; (3) PH was caused by non-HBV related etiologies, such as schistosome, hepatitis C virus (HCV), or other unknown causes; (4) preoperative imaging confirmed the presence of PVT; (5) previous history of endoscopic therapy, splenic embolization, shunt surgery or anticoagulants; (6) clinical features were incomplete; (7) platelet count on the first and third day after the operation (PLT1, PLT3) were not elevated compared to the preoperative values; (8) postoperative prophylactic anticoagulation. Finally, a total of 483 patients with PH interrelated to HBV were included in this study. The flow diagram of patient selection and study design was shown in Figure 1A. The study was approved by the Medical Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology. Owing to the retrospective nature of this study, written informed consent was waived.

Data collection

All the patients' clinical features were acquired from the electronic medical record system in our institution, which mainly included sex, age, smoking and drinking history, previous treatment history, etiologies, blood biochemical parameters, and imaging information. The blood biochemical parameters included blood routine (red blood cells, RBC, reference interval: $4.30\text{--}5.80 \times 10^{12}/\text{L}$; hemoglobin, HLB, reference interval: $130.0\text{--}175.0 \text{ g/L}$; white blood cells, WBC, reference interval: $3.50\text{--}9.50 \times 10^9/\text{L}$; neutrophil count, N, reference interval: $1.80\text{--}6.30 \times 10^9/\text{L}$; lymphocyte count, L, reference interval: $1.10\text{--}3.20 \times 10^9/\text{L}$; neutrophil to lymphocyte ratio, NLR; platelet count, PLT, reference interval: $125.0\text{--}350.0 \times 10^9/\text{L}$; platelet to lymphocyte ratio, PLR), coagulation function (prothrombin time, PT, reference interval: $11.5\text{--}14.5 \text{ s}$; prothrombin activity, PTA, reference interval: $75.0\text{--}125.0 \%$; international normalized ratio, INR, reference interval: $0.80\text{--}1.20$; fibrinogen, FIB, reference interval: $2.00\text{--}4.00 \text{ g/L}$; activated partial thromboplastin time, APTT, reference interval: $29.0\text{--}42.0 \text{ s}$), and liver function (alanine aminotransaminase, ALT, reference interval: $\leq 41 \text{ U/L}$; aspartate aminotransaminase, AST, reference interval: $\leq 40 \text{ U/L}$; serum albumin, ALB, reference interval: $35.0\text{--}52.0 \text{ g/L}$; total serum bilirubin, TBIL, reference interval: $\leq 26 \mu\text{mol/L}$) within 7 days before surgery; platelet counts on the first and third postoperative days (PLT1, PLT3). The preoperative Child-Pugh grade was divided into three levels of A, B, and C^[34], with grade C excluded. Information on the esophageal and gastric varices (EGV), spleen thickness (SPT), diameter of the portal vein (DPV), and blood transfusion (PBT) within 7 days before the operation.

Definition of variables

We diagnosed PVT by color Doppler ultrasound examination^[35] and contrast-enhanced CT would be applied as an auxiliary examination when its diagnosis was questioned^[36]. In this study, abdominal ultrasound and contrast-enhanced CT examinations were routinely performed within 7 days before the operation. Routine ultrasonography was

performed on the 7th day after the operation^[19, 20], or at any time when there were suspected clinical symptoms of PVT such as fever, severe abdominal pain, vomiting, abnormal liver function, and leukocytosis^[12].

According to the definition of varices^[8], EGV was divided into without varices and varices in this study. SPT was defined as the vertical distance between the splenic hilum and the cut point of the lateral margin, and DPV was measured as the largest anteroposterior diameter at the point of intersection with the hepatic artery, during the patient's breath holding^[37].

The postoperative platelet elevation rate (PPER) was calculated from the preoperative platelet count and postoperative platelet count. For example, the first day for postoperative platelet elevation rate $(PPER1) = (PLT1 - PLT) / PLT \times 100\%$; the third day for postoperative platelet elevation rate $(PPER3) = (PLT3 - PLT) / PLT \times 100\%$.

Development of models

All candidates were randomly divided into two parts by using the "caret" package, of which 70% were assigned to the training cohort and 30% were assigned to the validation cohort. All model building was performed in the training cohort. Multivariate logistic regression analysis with forward stepwise was used to select valuable variables to construct the generalized linear model (GLM). The least absolute shrinkage and selection operator (LASSO) was a well-established shrinkage method that can effectively screen meaningful variables from a large set of variables with potential multicollinearity to develop the LASSO model (LSM)^[38], which was implemented by the "glmnet" package. Random forest (RF) was composed of a great number of individual decision trees running as a whole^[39]. These multifarious decision tree models were applied for the construction of the RF model (RFM)^[40]. The importance of candidate variables was reflected by the mean decreased Gini (MDG) score.

Evaluation of models

The robustness and clinical practicability of models were assessed by the receiver operating characteristic curves (ROC), calibration curve, decision curve analysis (DCA), and clinical impact curve (CIC), respectively. The areas under ROC (AUC) were used to estimate the discernment of each model by using “rms” packages. The calibration curves were applied to examine the calibration ability of each model and calibrated with 1000 bootstrap samples to reduce overfitting bias. The clinical applicability of each model was informed by DCA and CIC using “rms” and “rmda” packages.

Statistical analysis

Statistical analyses were performed by R Statistical Software (version 4.1.2, <https://www.r-project.org/>). Continuous variables were tested for normality. Those with normality were described by mean \pm standard deviation (SD), while those without normality were described by median [interquartile range (IQR)], and compared with the student's *t*-test or non-parametric rank-sum test (Kruskal-Wallis Test) as appropriate. Categorical variables were described in numbers (percentage) using the Chi-square test or Fisher exact test for comparison as appropriate. Correlations between candidate variables were determined by Spearman's correlation coefficient. All statistical tests were two-tailed, and $P < 0.05$ was considered significant.

RESULTS

Patient demographics and characteristics

The detailed clinical characteristics of 483 patients with PH were summarized in Table 1. All participants were randomly and automatically divided into the training cohort ($n = 338$, 70%) and validation cohort ($n = 145$, 30%). The presence of PVT was diagnosed in 200 (41.4%) cases, 135 (39.9%) cases, and 65 (44.8%) cases in the overall cohort, training cohort, and verification cohort, respectively. Consistent with the results of the intergroup comparison, among the 31 candidate variables included, 14 were associated with PVT, including RBC, WBC, L, NLR, PLT, PTA, ALT, AST, EGV, SPT, DPV, PBT,

PPER1, and PPER3 (Figure 1B and S1), which indicated that the PPER1 and PPER3 were highly likely to be potential predictors of PVT.

Logistic regression analysis

Univariate and multivariate logistic regression analysis for risk factors associated with PVT in the overall cohort were presented in Table 2. In the univariate analysis, a total of 11 variables with $P < 0.05$ were included in the further multivariate analysis. Finally, the following 6 variables were revealed to be closely associated with the occurrence of PVT: L (OR: 0.28, 95%CI: 0.14-0.54, $P < 0.001$), EGV (OR: 0.51, 95%CI: 0.32-0.79, $P = 0.003$), SPT (OR: 1.22, 95%CI: 1.06-1.40, $P = 0.005$), DPV (OR: 3.57, 95%CI: 1.86-7.03, $P < 0.001$), PPER1 (OR: 1.78, 95%CI: 1.24-2.62, $P = 0.002$), and PPER3 (OR: 1.43, 95%CI: 1.16-1.77, $P < 0.001$). With great certainty, it illustrated that the PPER1 and PPER3 were independent risk factors for the occurrence of PVT.

Establishment of the PPER-based models

As shown in S2, the following 5 variables strongly associated with PVT were picked out to construct the GLM, including the L (OR: 0.34, 95%CI: 0.14-0.77, $P = 0.01$), SPT (OR: 1.21, 95%CI: 1.02-1.44, $P = 0.02$), DPV (OR: 5.85, 95%CI: 2.57-14.05, $P < 0.001$), PPER1 (OR: 1.77, 95%CI: 1.13-2.82, $P = 0.01$), and PPER3 (OR: 1.42, 95%CI: 1.12-1.84, $P = 0.005$). The optimal LSM was obtained when all 31 candidate variables were shrunk to 10 through the LASSO (Figure 2A, B), which included the L, NLR, PLT, PTA, AST, EGV, SPT, DPV, PPER1, and PPER3. In the RF, the total sample group had the smallest error of 24.56%, when the number of random trees was 133 (Figure 2C). When a total of 133 random trees were set and passed through 5 iterations, the importance scores of the candidate variables were presented in Figure 2D. Ultimately, 9 variables with higher MDG scores were selected to participate in the construction of the RFM.

Assessment and verification of the PPER-based models

The ROC of the GLM, LSM, and RFM in the training cohort were shown in Figure 3A, and their AUC were as follows: 0.83 (95%CI: 0.79-0.88), 0.84 (95%CI: 0.79-0.88), and 0.84 (95%CI: 0.79-0.88), respectively. All models had excellent calibration ability in the training cohort (Figure 3B). Meanwhile, DCA and CIC revealed that they both conferred high clinical net benefits (Figure 3C, and Figure 4A, B, C).

In the validation cohort, the ROC of all models were presented in Figure 3D, and their AUC were 0.77 (95%CI: 0.69-0.85), 0.83 (95%CI: 0.76-0.90), and 0.78 (95%CI: 0.70-0.85), respectively. All models demonstrated highly satisfactory calibration capability and clinical functionality (Figure 3E, F and Figure 4D, E, F).

Demonstration of models and the importance of PPER for models

As shown in Figure 5A, the nomogram for GLM recruited a total of 5 variables, including the L, SPT, DPV, PPER1, and PPER3, which happened to be the intersection variables of the GLM, LSM, and RFM (Figure 5B). From this, it appeared that the aforementioned variables were significant predictors for the occurrence of PVT and they produced remarkable effects on the construction of the models. Moreover, the present study revealed that among these variables shared by the GLM, LSM, and RFM, the order of weight from high to low was DPV, PPER1, PPER3, SPT, and L (Figure 5C), which fully promulgated the predictive value of the PPER (PPER1 and PPER3) for PVT in all models.

Comparative analysis of the PPER-based models

The performance of three PPER-based models in predicting PVT in different cohorts was shown in Table 3. In the overall cohort, the accuracy of the GLM, LSM, and RFM were 76.2%, 77.4%, and 77.4% respectively. In the training cohort, the accuracy of the GLM, LSM, and RFM were 79.6%, 79.0%, and 78.7% respectively. In the validation cohort, the accuracy of the GLM, LSM, and RFM were 74.5%, 79.3%, and 76.6% respectively. When other metrics of the evaluation models, such as AUC, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), kappa

values, and Brier scores were comprehensively considered, the LSM and RFM appeared to be slightly superior to the GLM.

DISCUSSION

Undoubtedly, PVT contributes to being a lethal complication after splenectomy in cirrhotic patients with PH^[12]. Because once PVT exists, there will be elevated portal venous pressure, ischemic bowel necrosis, progressive impairment of liver function, and even liver failure, which can eventually be life-threatening^[41, 42]. Therefore, research on the optimization of early detection of individuals at high risk of PVT after splenectomy is urgently needed. In this study, we successfully constructed the PPER-based models for predicting PVT by machine deep learning, which would be conducive to early identifying the population with high risk of PVT.

In the present study, conventional generalized linear (CGL) and machine deep learning (including the LASSO and RF) were applied separately to screen out the variables that greatly affected the PVT prediction. The CGL is characterized by strong interpretability, especially when the multifactorial forward stepwise regression method is used, and therefore, it has been widely applied as the traditional method to construct a predictive model^[43]. However, with the rapid progress of artificial intelligence technology, a novel prediction model based on machine deep learning has emerged with a higher probability of accuracy, which has led some clinicians to question the value of the CGL model in the clinical application of individualized patients^[44]. Coincidentally, our research results proclaimed that the performance of the LSM and RFM seemed to be slightly better than the GLM.

Interestingly, the PPER-based models contained the following 5 intersecting factors, namely the SPT, DPV, L, PPER1, and PPER3, which sufficiently illustrated that these were the main contributors to the higher incidence of PVT. Previous studies considered that preoperative SPT and DPV were important predictors for the formation of PVT after splenectomy in patients with PH^[8, 45], which was highly consistent with our findings. A very reasonable explanation was that a wide preoperative DPV and SPT

would lead to slow portal vein blood flow, which was closely related to postoperative thrombosis^[45, 46].

In most cases, platelet, erythrocyte, and leukocyte counts rose dramatically over a short time after splenectomy in patients with PH, and the blood was hypercoagulable^[8]. Therefore, previous studies suggested that preoperative low platelet and leukocyte count were founders of the formation of PVT postoperatively^[47]. This study revealed that the preoperative lymphocyte count was an influential factor in PVT postoperatively, which coincided with the above view. Of note, the present study employed the PPER to reflect the magnitude of dynamic changes in preoperative and postoperative platelet count. Subsequently, it was found that the PPER had high predictive values for the risk of PVT postoperatively, which was not addressed previously.

Stamou *et al*^[48] reported that the median time to the formation of PVT after splenectomy in patients with PH was the 6th day (range, 3-11 days). Lu S *et al*^[8] concluded that 49.19% of patients developed PVT within 7 days after splenectomy. Therefore, scholars routinely applied ultrasonography examination to diagnose the PVT on the 7th day after splenectomy^[8, 19, 20]. In this study, combined with the preoperative predictors and PPER, the PPER-based models we constructed can effectively discriminate individuals with high risk of PVT as early as the first 3 days after the operation, which was extremely critical for guiding clinicians' treatment strategies.

Currently, there is no standard prevention regimen for PVT after splenectomy in cirrhotic patients with PH^[49]. Most scholars have recently advocated that the earlier the prophylactic anticoagulant therapy is administered postoperatively, which will be more helpful in reducing the incidence of PVT^[50, 51]. However, it should be cautiously chosen because in patients with liver cirrhosis it cannot avoid the risk of inducing bleeding^[51]. In addition, if the preventive regimens are routinely adopted for all individuals with PH after splenectomy, it is bound to raise the suspicion of overtreatment. Excitingly, in the present study, the accuracy of the PPER-based models in predicting PVT is up to

80%, which can distinguish individuals at high risk of PVT with high efficiency, and thus guide clinicians to take targeted individualized preventive measures in time.

The present study has some limitations. First, due to the retrospective nature of the study, selection bias cannot be eliminated; Second, the uncommon preoperative factors that may influence the formation of PVT, such as splenic vein diameter, spleen volume, and portal vein flow velocity^[8, 19], were not routinely measured in our institution and thus failed to be included in the present study. However, the SPT and DPV in this study can indirectly reflect these indicators to a certain extent^[45, 46]; Third, this was a monocentric study design. Although the PPER-based models demonstrated excellent performance for predicting PVT, they still lacked the verification of external cohorts. Therefore, large-scale prospective multicenter studies are warranted, which are beneficial to the popularity and application of the PPER-based models.

CONCLUSION

The PPER1 and PPER3 were effective indicators for postoperative prediction of PVT. We successfully developed the PPER-based practical models for predicting PVT, which could help clinicians identify individuals at high risk for PVT early and efficiently, and thus guide the timely intervention measures.

ARTICLE HIGHLIGHTS

Research background

Patients with portal hypertension (PH) often rapidly rebound ascending in platelets following splenectomy. However, the value of postoperative platelet elevation rate (PPER) in predicting portal vein thrombosis (PVT) is unknown.

Research motivation

PVT is a potentially fatal complication after splenectomy for patients with PH, and the probability of PVT has been reported to be nearly 50%. Therefore, there is an imperious demand for effective diagnostic methods to early and rapidly identify individuals at

high risk of PVT after splenectomy, to further help clinicians take intervention measures as soon as possible.

Research objectives

We aimed to investigate the predictive value of PPER for PVT and establish PPER-based practical prediction models to early identify individuals at high risk of PVT after splenectomy.

Research methods

We retrospectively reviewed 483 patients with PH related to hepatitis B virus (HBV) who underwent splenectomy between July 2011 and September 2018, and they were randomized into the training ($n = 338$) and validation ($n = 145$) cohorts. The generalized linear (GL), least absolute shrinkage and selection operator (LASSO), and random forest (RF) were used to construct models. The receiver operating characteristic curves (ROC), calibration curve, decision curve analysis (DCA), and clinical impact curve (CIC) were performed to evaluate the robustness and clinical practicability of the GL model (GLM), LASSO model (LSM), and RF model (RFM), respectively.

Research results

The first and third days for PPER (PPER1, PPER3) were strongly associated with PVT (OR: 1.78, 95%CI: 1.24-2.62, $P = 0.002$; OR: 1.43, 95%CI: 1.16-1.77, $P < 0.001$, respectively) in the multivariate logistic regression analysis. The areas under ROC (AUC) of the GLM, LSM, and RFM in training cohort were 0.83 (95%CI: 0.79-0.88), 0.84 (95%CI: 0.79-0.88), and 0.84 (95%CI: 0.79-0.88), respectively; and were 0.77 (95%CI: 0.69-0.85), 0.83 (95%CI: 0.76-0.90), and 0.78 (95%CI: 0.70-0.85) in validation cohort, respectively. The calibration curves showed satisfactory agreement between prediction by models and actual observation. DCA and CIC indicated that all models conferred high clinical net benefit.

Research conclusions

The PPER1 and PPER3 were effective indicators for predicting PVT. We successfully developed the PPER-based practical models to accurately predict PVT, which could conveniently help clinicians rapidly differentiate individuals at high risk of PVT, and further guide the adoption of timely interventions.

Research perspectives

According to our experience, patients with a more remarkable increase in platelet count in the first 3 days after operation have a higher probability of PVT, which should be prioritized for prophylactic anticoagulation.

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