Risk Prediction for Early Recurrence of Advanced Neoplasia After Colorectal Adenoma Resection: A Post-print Study

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Abstract

Background: Colorectal adenoma resection is an effective method to reduce the incidence of colorectal cancer. Currently, the recurrence rate of advanced colorectal neoplasia (ACRN) within 1 year after colorectal adenoma resection is high, and there is a lack of relevant research on the construction of prediction models for early recurrence of ACRN after colorectal adenoma resection.

Objective: To explore the influencing factors of early recurrence of ACRN in patients after colorectal adenoma resection using machine learning methods, and to construct a prediction model for early recurrence of ACRN in patients after colorectal adenoma resection.

Methods: A total of 222 patients who underwent colorectal adenoma resection and had undergone colonoscopy more than 3 times at the First Affiliated Hospital of Zhengzhou University from January 2017 to August 2023 were retrospectively included as study subjects. According to whether ACRN occurred within 1 year after surgery, they were divided into an early recurrence group (n=68) and a non-early recurrence group (n=154). General patient data and laboratory examination indicators were collected. The study subjects were divided into training and test sets at an 8:2 ratio. Predictive factors were jointly screened using Boruta and Lasso regression methods. Four machine learning methods—Categorical Boosting (Catboost), Random Forest (RF), Logistic Regression (LR), and Support Vector Machine (SVM)—were used to construct prediction models. Receiver Operating Characteristic (ROC) curves, calibration curves, and Decision Curve Analysis (DCA) curves were plotted to evaluate the performance of the prediction models. Feature importance and SHAP interpretability analysis were employed to discuss the risk factors associated with early recurrence of ACRN in patients after colorectal adenoma resection.

Results: There were statistically significant differences between the early recurrence group and the non-early recurrence group in adenoma number, adenoma size, adenoma location, adenoma dysplasia degree, abdominal distension, number of clinical symptoms, drinking history, platelet count, and neutrophil-to-lymphocyte ratio (NLR) ($P<0.05$). Based on the joint screening by Boruta and Lasso methods, seven predictive factors were identified: adenoma size, platelet count, adenoma dysplasia degree, number of clinical symptoms, triglyceride-glucose (TyG), drinking history, and adenoma number. Four prediction models for early recurrence of ACRN after colorectal adenoma resection—Catboost, RF, LR, and SVM—were constructed based on these seven predictive factors. ROC curve analysis showed that in the training set, the AUCs of the Catboost, RF, LR, and SVM models were 0.802, 0.836, 0.788, and 0.860, respectively; in the test set, the AUCs of the four models were 0.772, 0.749, 0.705, and 0.685, respectively. Delong test results showed that pairwise comparisons of AUCs among the four models revealed no statistically significant differences (all $P>0.05$). Calibration curve analysis showed that in the training set, the Brier scores of the Catboost, RF, LR, and SVM models were 0.178, 0.197, 0.169, and 0.153, respectively; in the test set, the Brier scores of the four models were 0.188, 0.201, 0.191, and 0.198, respectively. DCA curve analysis showed that in the training set, higher clinical net benefits were obtained based on the Catboost, LR, and SVM models; in the test set, the Catboost and SVM models could achieve better clinical net benefits. SHAP interpretability analysis based on the Catboost model showed that the number of clinical symptoms, adenoma size, and adenoma number were the top three important features for predicting early recurrence of ACRN after surgery, respectively. Among them, the number of clinical symptoms, adenoma size, adenoma number, adenoma dysplasia degree, TyG, and platelet count (SHAP values: 0.043, 0.042, 0.025, 0.020, 0.012, 0.005) were all positively correlated with early postoperative recurrence of ACRN, while drinking history (SHAP value: 0.015) was negatively correlated with early postoperative recurrence of ACRN.

Conclusion: The risk prediction model constructed based on the Catboost method demonstrates good predictive performance and clinical utility, and can be used to predict early recurrence of ACRN after colorectal adenoma resection.

Full Text

Risk Prediction of Early Recurrence of Advanced Colorectal Neoplasm After Colorectal Adenoma Resection

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Abstract

Background
Colorectal adenoma resection is an effective method to reduce colorectal cancer incidence. However, the recurrence rate of advanced colorectal neoplasm (ACRN) within one year after resection remains high, and research on predictive models for early ACRN recurrence is lacking.

Objective
To identify risk factors for early ACRN recurrence after colorectal adenoma resection using machine learning methods and to develop a predictive model for this outcome.

Methods
We retrospectively enrolled 222 patients who underwent three or more colonoscopies and surgical resection of colorectal adenomas at the First Affiliated Hospital of Zhengzhou University between January 2017 and August 2023. Patients were divided into an early recurrence group (n=68) and non-early recurrence group (n=154) based on ACRN occurrence within one year post-surgery. General patient data and laboratory indicators were collected. The cohort was randomly split 8:2 into training and test sets. Predictive features were jointly selected using Boruta and Lasso regression methods. Four machine learning models—Categorical Boosting (Catboost), Random Forest (RF), Logistic Regression (LR), and Support Vector Machine (SVM)—were constructed. Model performance was evaluated using ROC curves, calibration curves, and Decision Curve Analysis (DCA). Feature importance and SHAP interpretability analysis were employed to discuss risk factors for early postoperative ACRN recurrence.

Results
Significant differences between the early and non-early recurrence groups were observed in adenoma number, adenoma size, adenoma location, adenoma dysplasia degree, abdominal bloating, number of clinical symptoms, drinking history, platelet count, and neutrophil-to-lymphocyte ratio (NLR) ($P<0.05$). Boruta and Lasso methods jointly identified seven predictors: adenoma size, platelet count, adenoma dysplasia degree, number of clinical symptoms, triglyceride-glucose (TyG) index, drinking history, and adenoma number. Four prediction models were developed using these variables. ROC analysis showed AUCs in the training set of 0.802, 0.836, 0.788, and 0.860 for Catboost, RF, LR, and SVM, respectively; corresponding AUCs in the test set were 0.772, 0.749, 0.705, and 0.685. Delong tests revealed no statistically significant differences in pairwise AUC comparisons (all $P>0.05$). Calibration analysis yielded Brier scores of 0.178, 0.197, 0.169, and 0.153 in the training set, and 0.188, 0.201, 0.191, and 0.198 in the test set for Catboost, RF, LR, and SVM, respectively. DCA demonstrated that Catboost, LR, and SVM models achieved higher clinical net benefit

in the training set, while Catboost and SVM showed better performance in the test set. SHAP interpretability analysis of the Catboost model identified number of clinical symptoms, adenoma size, and adenoma number as the top three predictive features. Number of clinical symptoms, adenoma size, adenoma number, adenoma dysplasia degree, TyG index, and platelet count (SHAP values: 0.043, 0.042, 0.025, 0.020, 0.012, 0.005) were positively associated with early postoperative ACRN recurrence, while drinking history (SHAP value: 0.015) showed a negative association.

Conclusion
The risk prediction model developed using Catboost demonstrates excellent predictive performance and clinical applicability, making it suitable for predicting early postoperative ACRN recurrence following colorectal adenoma resection.

Keywords: Advanced colorectal neoplasia; Early recurrence; Influence factor; Prediction model; Interpretability analysis

Introduction

Colorectal cancer (CRC) represents a high-incidence malignancy of the digestive system and poses a significant threat to human health. According to the 2022 Global Cancer Statistics (GLOBOCAN 2022) [1], CRC ranks third in global incidence and second in mortality worldwide, surpassed only by lung cancer. Without timely intervention, CRC incidence and mortality are projected to increase to 3.2 million new cases and 1.6 million deaths by 2040 [2]. In China, CRC demonstrates a marked epidemiological upward trend, ranking second among all malignant tumors nationally [3], creating a substantial societal burden.

Most CRCs develop from colorectal adenomas, which represent the primary precancerous lesions [4]. With widespread application of colonoscopy technology, endoscopic resection of colorectal adenomatous polyps can effectively reduce the risk of malignant transformation and thereby decrease CRC incidence [5]. Studies indicate that 36% to 61% of patients are found to have new or recurrent adenomas at their first surveillance colonoscopy following adenoma resection [6-7]. Furthermore, earlier postoperative recurrence correlates with shorter median survival: from 9.9 months for recurrence within one year to 19.1 months for recurrence after more than four years [8]. To date, the risk of metachronous advanced colorectal neoplasia (ACRN) has been considered a surrogate marker for CRC risk [9], with previous studies defining recurrence within one year as early recurrence [10].

This study examined a broader range of adenoma patient characteristics, including baseline demographic data, adenoma features, and common laboratory indicators, with longitudinal follow-up to determine the timing of postoperative ACRN recurrence (advanced adenoma and/or CRC), identify risk factors for early recurrence, and establish a risk prediction model to precisely assess

individual risk.

1.1 Research Subjects

This retrospective cohort study included patients who underwent three or more colonoscopies and surgical resection of colorectal adenomas at the First Affiliated Hospital of Zhengzhou University between January 2016 and August 2023. According to inclusion and exclusion criteria, 222 patients were ultimately enrolled. ACRN was defined as advanced adenoma (meeting any of the following criteria: diameter >10 mm, containing villous components, or high-grade intraepithelial neoplasia) [11] or CRC.

Inclusion criteria: (1) Age $ $18 years; (2) Complete colonoscopy with adequate bowel preparation and cecal intubation; (3) Follow-up duration $ $6 months; (4) Recurrent ACRN. All subjects had Boston Bowel Preparation Scale scores >6 and withdrawal time $ $6 minutes.

Exclusion criteria: (1) Prior history of CRC or adenoma; (2) Concomitant inflammatory bowel disease, familial adenomatous polyposis, or other colorectal diseases; (3) Missing baseline pathology reports or laboratory data for key variables.

This study was approved by the Ethics Review Committee of the First Affiliated Hospital of Zhengzhou University (2022-KY-0018-002), and all subjects provided informed consent.

1.2 General Data Collection

We collected data on patient sex, age, adenoma number, adenoma size, adenoma histology, adenoma location, adenoma dysplasia degree, abdominal pain, abdominal bloating, bowel habit changes, stool characteristics, number of clinical symptoms (including abdominal pain, bloating, bowel habit changes, and stool characteristics), diabetes, hypertension, hyperlipidemia, cancer history, smoking history (self-reported continuous or cumulative smoking >6 months within the past year or average >1 cigarette/day), drinking history (self-reported ethanol intake $ $25 g/day for men and $ $15 g/day for women within the past year), family history (self-reported first-degree relatives with CRC or colorectal adenoma), and body mass index (BMI) (normal range: 18.5–23.9 kg/m^{2}$).

1.3 Laboratory Examination Indicators

Laboratory indicators included red blood cells (normal: male 4.3–5.8$×10^{{12}/L, female 3.8–5.1×10{12}/L), white blood cells (normal: 3.5–9.5×10^{{9}/L), platelets (normal: 125–350×10{9}$/L), total cholesterol (normal: <5.2 mmol/L), triglycerides (normal: <1.7 mmol/L), high-density lipoprotein (normal: >0.91 mmol/L), low-density lipoprotein (normal: <3.61 mmol/L), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and triglyceride-glucose (TyG)

index. Patients were categorized into four groups (Q1–Q4) based on quartiles of NLR, PLR, SII, and TyG index.

1.4 Follow-up and Grouping

Patients diagnosed with colorectal adenoma at initial colonoscopy underwent resection, with a second colonoscopy performed within one year to identify potentially missed adenomas. Follow-up continued until ACRN detection or the final colonoscopy, with follow-up duration ranging from 6 to 77.5 months. Patients were divided into early recurrence group (n=68) and non-early recurrence group (n=154) based on whether ACRN occurred $ $1 year after adenoma resection.

1.5 Statistical Analysis

Data were analyzed using SPSS 27.0 and R 4.3.3 software. Missing values were imputed using random forest algorithms. Categorical data are presented as frequencies, with inter-group comparisons performed using ^{2} tests or Fisher's exact tests. The dataset was randomly split 8:2 into training (n=179) and test sets (n=43). Boruta and Lasso regression jointly selected predictive features from the training set, with collinearity tested and variables with variance inflation factor (VIF) >5 excluded. Four machine learning methods—Catboost, Random Forest (RF), Logistic Regression (LR), and Support Vector Machine (SVM)—were used to construct prediction models for early postoperative ACRN recurrence. Model performance was evaluated using ROC curves, calibration curves, and DCA. Delong tests compared AUC differences among the four models, and SHAP values were used for feature importance and interpretability analysis.

Results

2.1 Comparison of Clinical Characteristics and Laboratory Findings

Among 222 patients (153 men [68.9%] and 69 women [31.1%]), the mean age was 57.2$±$11.4 years. The early recurrence group included 68 patients (30.6%), while the non-early recurrence group included 154 patients (69.4%). Significant differences between groups were observed in adenoma number, adenoma size, adenoma location, adenoma dysplasia degree, abdominal bloating, number of clinical symptoms, drinking history, and platelet count (P<0.05). No significant differences were found in sex, age, adenoma histology, abdominal pain, bowel habit changes, stool characteristics, diabetes, hypertension, hyperlipidemia, cancer history, smoking history, family history, BMI, white blood cell count, red blood cell count, total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, NLR, PLR, SII, or TyG index (P>0.05) .

2.2 Feature Variables for Early Postoperative ACRN Recurrence

The dataset was randomly divided 8:2 into training (n=179) and test sets (n=43). Feature selection was performed using Boruta and Lasso regression on the training set. Based on feature importance, the Boruta method identified seven significant features: adenoma size, platelet count, adenoma dysplasia degree, number of clinical symptoms, TyG index, drinking history, and adenoma number [Figure 1: see original paper]. In Lasso regression analysis, the optimal penalty coefficient was selected within one standard error of the minimum cross-validation error ($ $1SE=0.0356), retaining 13 important features: adenoma location, adenoma number, adenoma size, dysplasia degree, number of clinical symptoms, hypertension, hyperlipidemia, drinking history, red blood cell count, platelet count, low-density lipoprotein, NLR, and TyG index [Figure 2: see original paper].

Integrating both selection results, seven variables were finalized for model construction: adenoma size, platelet count, adenoma dysplasia degree, number of clinical symptoms, TyG index, drinking history, and adenoma number. Multicollinearity testing confirmed no collinearity among these seven variables (VIF<5).

2.3 Model Construction

Using the seven selected features, we constructed Catboost, RF, LR, and SVM models. Grid search was employed with AUC as the evaluation metric to determine optimal parameters in the training set: Catboost (number=5, repeats=5, depth=4, learning_{rate}=0.01, iterations=200, l2_{{{leaf}}*{{reg}}}=5, rsm=0.95, border{count}=32); RF (number=5, repeats=5, mtry=1, ntree=200, maxnodes=10, nodesize=5); LR (using glm with default parameters); and SVM (number=5, repeats=5, method= “svmRadial” , preProcess=c(“center” , “scale”), sigma=0.059, C=1).

2.4 Model Performance Comparison

ROC curves were plotted for each model to predict early postoperative ACRN recurrence, with AUC, sensitivity, and specificity calculated. In the training set, AUCs were 0.802, 0.836, 0.788, and 0.860 for Catboost, RF, LR, and SVM, respectively. In the test set, corresponding AUCs were 0.772, 0.749, 0.705, and 0.685 [FIGURE:3, TABLE:2]. Delong tests showed no statistically significant differences in pairwise AUC comparisons (all P>0.05) .

Calibration curve analysis revealed Brier scores of 0.178, 0.197, 0.169, and 0.153 in the training set, and 0.188, 0.201, 0.191, and 0.198 in the test set for Catboost, RF, LR, and SVM, respectively [Figure 4: see original paper]. DCA showed that Catboost, LR, and SVM models achieved higher clinical net benefit in the training set when risk probability threshold was <75%, while Catboost and SVM demonstrated better performance in the test set when threshold was <50% [Figure 5: see original paper].

2.5 Interpretability Analysis of Catboost Model

SHAP value analysis of the Catboost model ranked feature importance, revealing that number of clinical symptoms, adenoma size, and adenoma number were the top three predictive features. Feature swarm plots demonstrated that number of clinical symptoms, adenoma size, adenoma number, adenoma dysplasia degree, TyG index, and platelet count (SHAP values: 0.043, 0.042, 0.025, 0.020, 0.012, and 0.005) were positively associated with early postoperative ACRN recurrence, while drinking history (SHAP value: 0.015) showed a negative association [Figure 6: see original paper].

Discussion

Colorectal adenoma resection is a crucial surgical intervention that delays adenoma-to-carcinoma progression and significantly reduces CRC incidence. To ensure data accuracy, we performed a second colonoscopy within one year to identify potentially missed adenomas. Among 222 enrolled patients, 30.63% experienced early ACRN recurrence, consistent with existing literature. Studies have reported early recurrence rates of 59.46% after colorectal adenoma resection, with recurrence peaks concentrated almost entirely in the first year [7]. Our finding of 30.6% early recurrence aligns with CHEN et al. [12]. Currently, research on predictive models for early postoperative ACRN recurrence is limited, making our model valuable for providing reference for endoscopists to reduce CRC incidence.

We constructed four machine learning models (Catboost, RF, LR, SVM), with Catboost demonstrating superior predictive capability. In the test set, Catboost achieved an AUC of 0.772 and Brier score of 0.188, while in the training set, AUC was 0.802 and Brier score was 0.178. DCA curves indicated that Catboost yielded high clinical net benefit in both training and test sets. SHAP interpretability analysis identified number of clinical symptoms, adenoma size, adenoma number, adenoma dysplasia degree, TyG index, and platelet count as important risk factors positively associated with early recurrence, while drinking history showed a negative association.

Our findings indicate that increased number of clinical symptoms positively impacts model prediction, elevating predicted risk for early adenoma recurrence. Clinical symptoms in this study included abdominal pain, bloating, bowel habit changes, and stool characteristics. Bowel habit changes primarily comprised constipation (<3 bowel movements per week, hard stools, difficult defecation) or diarrhea (>3 bowel movements daily, stool weight >200 g/day, loose consistency, water content >85%). Stool characteristic changes included blood in stool, melena, and loose stools. Increased symptom count reflects disease severity. ZHANG et al. [13] used a "symptom score" system and found that each 1-point increase elevated recurrence risk by 18%, consistent with our results.

Adenoma size was positively associated with early recurrence. Current guidelines classify adenomas >10 mm as high-risk, considering 1–9 mm adenomas as

having equivalent recurrence risk. However, multiple studies have challenged this, showing that patients with 6–9 mm adenomas have higher ACRN recurrence risk than those with 1–5 mm adenomas and should not be considered equivalent risk [14-16]. HARTSTEIN et al. [14] found that patients with at least one 6–9 mm adenoma had significantly higher absolute risk of ACRN than those with only 1–5 mm adenomas. Research also confirms an inverse relationship between adenoma size and time-to-recurrence, with median recurrence time decreasing from 20.1 months for adenomas $ $10 mm to 7.7 months for adenomas >10 mm [17-18], demonstrating that larger adenomas increase both recurrence rate and shorten recurrence time.

Adenoma number was positively associated with early ACRN recurrence, with greater numbers indicating higher risk. Studies show recurrence rates of 19.6%, 23.2%, and 30.8% for patients with 1, 2, and $ $3 adenomas, respectively [19]. GENG [20] and GE et al. [21] similarly identified $ $3 polyps as an independent risk factor for recurrence, possibly because multiple adenomas indicate genetic phenotypes and gut microbiota conditions favorable for polyp growth [22-23].

Guidelines recommend shortened surveillance intervals for patients with high-grade dysplasia, consistent with their higher recurrence rates, shorter recurrence times, and propensity for advanced adenoma recurrence. We classified adenoma dysplasia as high-grade or low-grade intraepithelial neoplasia, finding dysplasia degree positively associated with early ACRN recurrence, aligning with all guideline recommendations [24-26]. Dysplasia represents morphological, size, and arrangement differences from normal cells and constitutes an important step in tumorigenesis. Higher dysplasia grades indicate greater malignant potential and increased recurrence risk. Studies show patients with high-grade dysplasia have higher ACRN recurrence risk than those with low-grade dysplasia [27]. BAILE-MAXÍA et al. [28] identified high-grade dysplastic adenomas as an independent risk factor for metachronous CRC or advanced adenoma after endoscopic resection of high-risk adenomas. Some discrepant results [29-30] may stem from different pathological classification methods or insufficient sample sizes.

The TyG index, a combined indicator of triglyceride and glucose levels, serves as a simple and reliable surrogate for insulin resistance. Elevated TyG index increases digestive tract tumor risk [31]. LI et al. [32] found that the highest TyG index quartile had significantly higher risk of advanced adenoma recurrence, with each unit increase raising colorectal adenoma risk by 22.5% (95%CI=1.027-1.460), possibly through insulin resistance mechanisms. The insulin and insulin-like growth factor axis promotes tumor progression directly through cell proliferation and indirectly through altered glucose metabolism [33]. Insulin may also promote tumorigenesis by upregulating acyl-CoA:cholesterol acyltransferase-1, which mediates proliferation and metastasis in CRC cells [34], and by increasing vascular cell adhesion molecule-1 expression in tumor endothelial cells, altering immune cell homing to the tumor microenvironment [35].

Platelet count (PLT) represents an important factor for early ACRN recurrence,

with abnormal platelet counts positively associated with recurrence. KOPERLENKIEWICZ et al. [36] showed that each 10$\times$10^{3}$/μL increase in PLT was associated with a 4% increase in serum interleukin-6 concentration, suggesting platelets directly participate in inflammation and tumorigenesis beyond their role in thrombosis.

Interestingly, drinking history emerged as a protective factor for early ACRN recurrence in our study, though our previous work on risk prediction models for advanced tumors after colorectal adenoma resection did not include drinking history [37]. This discrepancy may reflect our definition of early recurrence as within one year, where the temporal effect of drinking history is not significant. The relationship between alcohol consumption and early ACRN recurrence is complex and likely dose-dependent. The observed protective effect may be limited to low-to-moderate consumption ranges. Moderate alcohol intake, particularly red wine (rich in antioxidants like resveratrol), may have anti-inflammatory or antioxidant properties that could theoretically provide weak protective effects. However, this remains scientifically controversial, and excessive alcohol consumption is an established CRC risk factor. Future studies should analyze alcohol type, dose, and frequency patterns to clarify this association.

Our prediction model is specifically designed for patients who have undergone colorectal adenoma resection to predict early ACRN risk within one year postoperatively. Effective application requires complete clinical data and is intended as a clinical decision-support tool for endoscopists managing postoperative surveillance, not for general population screening. The model helps identify high-risk individuals requiring intensive monitoring during the critical first postoperative year.

This study has several limitations. First, its retrospective design may introduce selection and information bias, potentially affecting statistical inference given the long follow-up period and relatively small sample size. Second, although we performed internal validation with a test set, the lack of external cohort validation limits generalizability. We plan multi-center collaboration to expand sample size and strengthen evidence. Third, we used only baseline SII values without dynamic postoperative monitoring, limiting assessment of temporal inflammatory changes and recurrence risk. Future studies will employ multi-timepoint data collection strategies.

In summary, we identified seven influencing factors (number of clinical symptoms, adenoma size, adenoma number, adenoma dysplasia degree, drinking history, platelet count, and TyG index) using Boruta selection and constructed machine learning prediction models for early ACRN recurrence risk after colorectal adenoma resection. ROC curves, calibration curves, and DCA validated the model' s strong predictive performance, enabling endoscopists to predict high-risk populations and implement targeted interventions.

Author Contributions: SUN Yujie, LI Jiaoyan, CHEN Jingfeng, and DING Suying designed the study, implemented research, and collected data. SUN Yujie

performed statistical analysis, result interpretation, and manuscript writing. LI Jiaoyan, CHEN Jingfeng, and DING Suying critically reviewed the intellectual content and provided research guidance.

Conflicts of Interest: None declared.

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