

Predicting bowel function after diverting stoma closure in patients with rectal cancer

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Background: Patients with rectal cancer undergoing laparoscopic anterior resection and diverting stomas often suffer from bowel dysfunction after stoma closure, impairing their quality of life. This study aims to develop a machine learning tool to predict bowel function after diverting stoma closure.

Methods: Clinicopathological data and post-operative follow-up information from patients with mid-low rectal cancer after diverting stoma closure were collected and analyzed. Patients were randomly divided into training and test sets in a 7:3 ratio. A machine learning model was developed in the training set to predict major low anterior resection syndrome (LARS) and evaluated in the test set. Decision curve analysis (DCA) was used to assess clinical utility.

Results: The study included 396 eligible patients who underwent laparoscopic anterior resection and diverting stoma in Tongji Hospital affiliated with Huazhong University of Science and Technology from 1 January 2012 to 31 December 2020. The interval between stoma creation and closure, neoadjuvant therapy, and body mass index were identified as the three most crucial characteristics associated with patients experiencing major LARS in our cohort. The machine learning model achieved an area under the receiver operating characteristic curve (AUC) of 0.78 [95% confidence interval (CI): 0.74–0.83] in the training set (n=277) and 0.74 (95% CI: 0.70–0.79) in the test set (n=119), and area under the precision-recall curve (AUPRC) of 0.73 and 0.69, respectively, with sensitivity of 0.67 and specificity of 0.66 for the test set. DCA confirmed clinical applicability.

Conclusions: This study developed a machine learning model to predict major LARS in rectal cancer patients after diverting stoma closure, aiding their decision-making and counseling.

Keywords: Rectal cancer; diverting stoma; low anterior resection syndrome (LARS); machine learning; predicting

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Introduction

A diverting stoma can effectively prevent potential or even life-threatening clinical consequences, such as anastomotic leakage, especially in patients with mid-to-low rectal cancer after radical resection (1,2). However, it carries risks such as infection, ulceration, parastomal hernias, stomal obstruction and even psychological disorders (3-8). Patients frequently require regular follow-up at a wound ostomy clinic to monitor the stoma and ensure their overall well-being. Moreover, some patients report a negative impact on their quality of life, such as toilet dependence and are eager to close the stoma as soon as possible (7,9,10). Previous randomized clinical trials showed that closing diverting stoma 8–13 days after primary surgery is feasible and safe in selected patients (11,12). However, bowel dysfunction, also known as low anterior resection syndrome (LARS), frequently occurs after diverting stoma closure and consists of a variable symptom spectrum that typically includes incontinence of flatus, incontinence of liquid stool, frequency, clustering, urgency and impairs quality of life (13,14). Furthermore, these bowel functional changes reduce the expectations of the patients after diverting stoma closure owing to a significant decline in quality of life (15). A qualitative study of bowel function in patients with rectal cancer after stoma closure found that patients often need to deal with acute and troublesome intestinal symptoms and it is difficult for them to control their defecation function, resulting in toilet dependence (15). Therefore, patients with

severe bowel dysfunction often need to weigh the pros and cons and re-examine the decision to undergo stoma closure prior to the actual procedure.

Currently, the machine learning algorithm based on artificial intelligence is widely used to predict disease prognosis by combining clinical multidimensional nonlinear features and assist doctors or patients in making their decisions, achieving accuracy beyond the traditional linear model (16-20). The present study aimed to create and validate a machine learning model that could predict the risk probabilities of developing major LARS before stoma closure by combining clinicopathological features. We present this article in accordance with the TRIPOD reporting checklist (available at <https://jgo.amegroups.com/article/view/10.21037/jgo-23-1019/rc>).

Methods

Study design and participants

A total of 636 patients diagnosed as mid-low rectal cancer (cases located less than 10 cm from the anal verge), who underwent laparoscopic anterior resection at Tongji Hospital affiliated with Huazhong University of Science and Technology between January 1, 2012, and December 31, 2020, were included in the present retrospective study. All patients' surgeries were performed by senior surgeons, and during the procedures, comprehensive measures were taken to ensure total nerve preservation. Patients with incomplete medical records, ≤ 18 years old, lost to follow-up or death were excluded. Patients whose diverting stoma was not closed or had been closed for < 1 year were also excluded. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the ethics committees of Tongji Hospital, Huazhong University of Science and Technology (No. TJ-IRB20230364). The requirement for informed consent was waived due to the retrospective nature of the study.

Predictors

Only clinicopathological data before diverting stoma closure were selected as predictors, including age, sex, body mass index (BMI), hypertension, diabetes, neoadjuvant therapy, the length (cm) of the removed bowel, pathological stage of tumor, anastomotic height (cm), the interval (days) between stoma creation and closure, American Society of Anesthesiologists (ASA) classification, operation time,

Highlight box

Key findings

- The interval between stoma creation and closure, neoadjuvant therapy, and body mass index were identified as the three most crucial characteristics associated with patients experiencing major low anterior resection syndrome (LARS) in this analysis.

What is known and what is new?

- LARS frequently occurs after rectal cancer surgery, impairing the quality of life for patients.
- This model can effectively identify patients with high-risk major LARS in rectal cancer patients after diverting stoma closure, aiding their decision-making and counseling.

What is the implication, and what should change now?

- The model aids patients in informed decisions on stoma closure. Personalized estimates guide surgical management, enhancing patient understanding. Additionally, it identifies high-risk patients, enabling targeted post-operative care for improved outcomes.

tumor obstruction and tumor size. All the predictors were discussed and determined by senior physicians. Tumor obstruction indicated that the endoscope with a maximum insertion portion width of 12.8 mm could not pass through the space between the tumor and the bowel lumen before the primary surgery. Anastomotic height, which indirectly reflects the distance from the lower edge of the tumor to the anal verge, was assessed during follow-up by digital inspection, rigid sigmoidoscopy, or magnetic resonance imaging. The pathological stage of the tumor was reassessed and reviewed based on the 8th edition of the American Joint Committee on Cancer (AJCC) guidelines. Neoadjuvant therapy in the present study conformed to “The Standard for Diagnosis and Treatment of Chinese Colorectal Cancer” and its revised version. Whether employing a short-course neoadjuvant therapy approach (administering 5 Gy × 5 fractions to the primary tumor and high-risk areas) or a long-course neoadjuvant therapy approach (administering a total radiation dose of 45.0–50.4 Gy to the primary tumor and high-risk areas, with each fraction ranging from 1.8 to 2.0 Gy, totaling 25–28 fractions, and concurrently administering 5-fluorouracil (5-FU) or capecitabine monotherapy during radiotherapy), both were categorized as preoperative neoadjuvant therapy. Neoadjuvant treatment, length of the removed bowel, pathological stage of the tumor, ASA, operation time, tumor obstruction and tumor size were associated with the primary surgery, whereas age, BMI and the interval between stoma creation and closure were associated with the stoma closure surgery.

Evaluation of bowel function

The Chinese version of the LARS questionnaire was used to evaluate the intestinal function of patients. It is a proven short and effective tool for assessing intestinal function after rectal cancer surgery (13,21), including the five most prominent aspects of intestinal dysfunction, such as gas incontinence, liquid fecal incontinence, frequency, clustering and urgency. According to the scoring criteria, the following score was assigned based on LARS severity: 0–20 points without LARS; 21–29 points for minor LARS; and 30–42 points for major LARS. To accurately evaluate bowel function (22,23), the eligible patients were followed up using the LARS score questionnaire by phone, text message, outpatient or hospitalization 1 year after diverting stoma closure. To highlight major LARS, patients with major LARS were classified into one group, while patients without and with minor LARS were into another group.

Model development

The collected patient data were randomly divided into a training (70%, n=277) and a test set (30%, n=119). An ensemble learning random forest (RF) classifier was trained with 14 input features in the training set to calculate the probability of developing major LARS in patients with rectal cancer after diverting stoma closure. During the training of the model, the probability (Youden index) to balance the sensitivity and specificity of the receiver operating characteristic (ROC) curves was found to divide the continuous probability generated by RF into the predicted major LARS and non-major LARS groups. If the probability value exceeded the Youden index, the patient would be considered as “major LARS”, thus avoiding the low actual positive rate or high false positive rate caused by the default cutoff value of 0.5 and resolving the low sensitivity or specificity of the prediction results of the model. In addition, to further evaluate the performance of the model, positive predictive values (PPV), negative predictive values (NPV), accuracy, the area under the ROC curves (AUC) and area under the precision-recall curves (AUPRC), Brier score and concordance index (C-index) of the model were calculated. To compare machine learning models with traditional linear models, we additionally constructed a logistic regression (LR) model. We calculated the AUC, sensitivity, specificity, positive predictive PPV, and NPV of the LR model in the training set to evaluate its predictive ability.

Model validation

To test the discrimination power of the Youden index, the latter was used to validate the model in the test set and obtain the accuracy, specificity, sensitivity, PPV, NPV, AUC, AUPRC, Brier score and C-index of the model. The AUC and C-index were used to evaluate the ability of the model to discriminate major LARS after diverting stoma closure. The calibration degree of the model was assessed using the calibration curve and the Brier score (24). The Brier score is always between 0 and 1, and the closer to 0 the better the calibration of the model and vice versa. Accuracy, specificity, sensitivity, PPV, NPV and AUPRC were used to evaluate the accuracy of the model.

Feature importance analysis

The influence of each feature on the prediction of

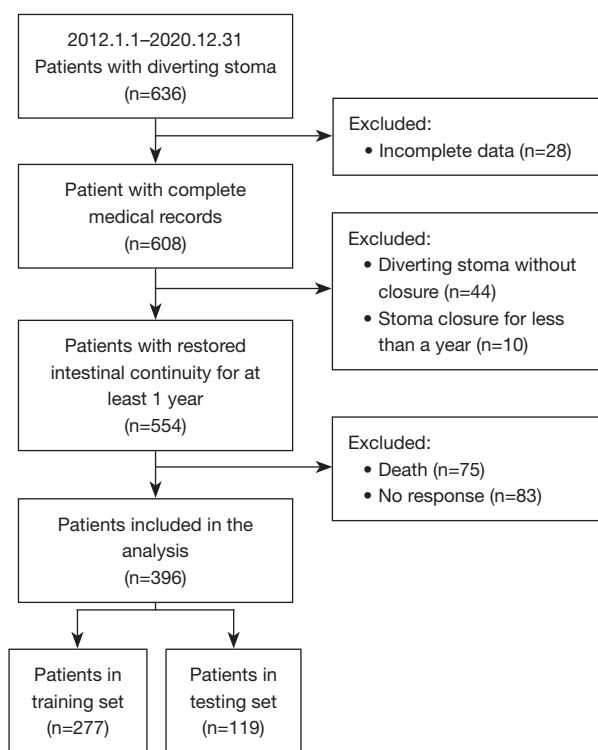


Figure 1 Flow chart of the screening of the patients.

major LARS was evaluated using the SHapley Additive exPlanations (SHAP) method (25,26). The SHAP method has proven to be a valuable tool for interpreting the predictions of machine learning models and can enhance our understanding of the underlying mechanisms that drive the model's predictions by estimating the contribution of each feature to the model prediction outcomes. Furthermore, the importance of each feature in the training set was assessed based on the contributions to the model output. By ranking the features according to their importance, we were able to identify the most influential factors in the prediction of major LARS.

Model utility

Decision curve analysis (DCA) was used to evaluate the potential clinical net benefits of the model under various thresholds and further verify the clinical application value (27). DCA examined the relative effects of false negatives (underdiagnosed major LARS) and false positives (misdiagnosed major LARS) on predictive outcomes in a range of threshold probabilities. This approach allows for

a more thorough comprehension of the clinical impact of a predictive model and can aid in guiding clinical decision-making.

Statistical analysis

Continuous variables are expressed as mean \pm standard deviation, whereas categorical variables are expressed as counts (percentage). One-way analysis of variance (ANOVA) or nonparametric Mann-Whitney U test was adopted to compare continuous variables between two groups. The χ^2 test was used to compare categorical variables between two groups. The tests were two-tailed and $P < 0.05$ was considered to indicate a statistically significant difference. Statistical analysis was performed using SPSS 27.0 (IBM Corp.) and the online tool Vassar Stats (<http://vassarstats.net/index.html>). All machine learning algorithms were implemented using Python version 3.9.7 (<https://www.python.org/>) and the Scikit-learn package version 0.24.2 (<https://scikit-learn.org>).

Results

Participants

The queue selection process is shown in *Figure 1*. The present study included 396 eligible patients diagnosed as mid-low rectal cancer, with an average anastomotic height of 3.6 cm (range, 1 to 10 cm). The age of the patients ranged from 26 to 82 years, with a mean age of 56 years; there were 154 female patients (38.9%). A total of 162 patients with diverting stoma developed major LARS within 1 year after diverting stoma closure, with an incidence of 40.9% (41.2% and 40.3% in the training and test set, respectively). The baseline characteristics of the two groups are shown in *Table 1*.

Model performance

In the training set, 14 clinicopathological factors were used as input features and major LARSs were used as the target to train the machine learning RF model. First, the probability of developing major LARS in patients with rectal cancer after stoma closure was calculated. These continuous probabilities generated by the RF algorithm were significantly correlated with the occurrence of major LARS in the training set (*Figure 2A*, $P < 0.001$) and the best cutoff value of the Youden index was 0.450 (*Figure 2B*).

Table 1 Comparison of the clinical characteristics in the training and test sets

Variables	Training cohort (n=277)	Test cohort (n=119)	P value
Age (years)	56.22±10.2	56.68±9.8	0.67
Male	164 (59.2)	78 (65.5)	0.14
BMI (kg/m ²)	22.83±2.8	23.12±2.9	0.35
Neoadjuvant	48 (17.3)	12 (10.1)	0.06
Hypertension	54 (19.5)	31 (26.1)	0.09
Diabetes	18 (6.5)	13 (10.9)	0.09
Tumor obstruction	8 (2.9)	7 (5.9)	0.12
Anastomotic height (cm)	3.61±1.61	3.62±1.56	0.95
Interval surgery-closing stoma (days)	147.44±112.4	144.40±134.6	0.81
ASA			0.06
1	43 (15.5)	22 (18.5)	
2	223 (80.5)	86 (72.3)	
3	11 (4.0)	11 (9.2)	
Operation time (min)	211.96±53.2	208.78±57.2	0.59
Specimen length (cm)	10.82±3.0	11.03±3.2	0.54
Tumor size (cm)	3.45±1.34	3.39±1.3	0.64
Stage			0.72
1	104 (26.3)	41 (34.5)	
2	84 (30.3)	35 (29.4)	
3	89 (32.1)	43 (36.1)	
LARS			0.48
Minor/no	163 (58.8)	71 (59.7)	
Major	114 (41.2)	48 (40.3)	

Data are presented as mean ± SD or n (%). BMI, body mass index; ASA, American society of Anesthesiologists classification; LARS, low anterior resection syndrome; SD, standard deviation.

When the probability exceeded the Youden index, the patients were classified as major LARS group. The AUC and AUPRC were 0.781 and 0.728, respectively (Figure 2C,2D). In addition, the classification results based on this cut-off value are shown in Figure 2E. Figure 2F shows the sensitivity, specificity, PPV, NPV and accuracy of the model in the training set. The Brier score and C-index of the model were 0.20 and 0.75, respectively (Table 2). Compared with the LR model, the RF classifier exhibited superior performance across the multiple evaluation metrics in the training set, including AUC, AUPRC, Brier score, C-index, sensitivity, PPV, NPV and accuracy (Figure 3A,3B and Table

2; AUC 0.78 for RF versus 0.75 for LR; AUPRC 0.73 for RF versus 0.71 for LR; Brier 0.20 for RF versus 0.21 for LR; C-index 0.75 for RF versus 0.70 for LR; sensitivity 0.66 for RF versus 0.62 for LR; PPV 0.63 for RF versus 0.61 for LR; NPV 0.75 for RF versus 0.73 for LR; accuracy 0.70 for RF versus 0.68 for LR). These results demonstrated that the trained RF model showed good discrimination and calibration.

Model assessment

In the test set, the probabilities generated by the RF model

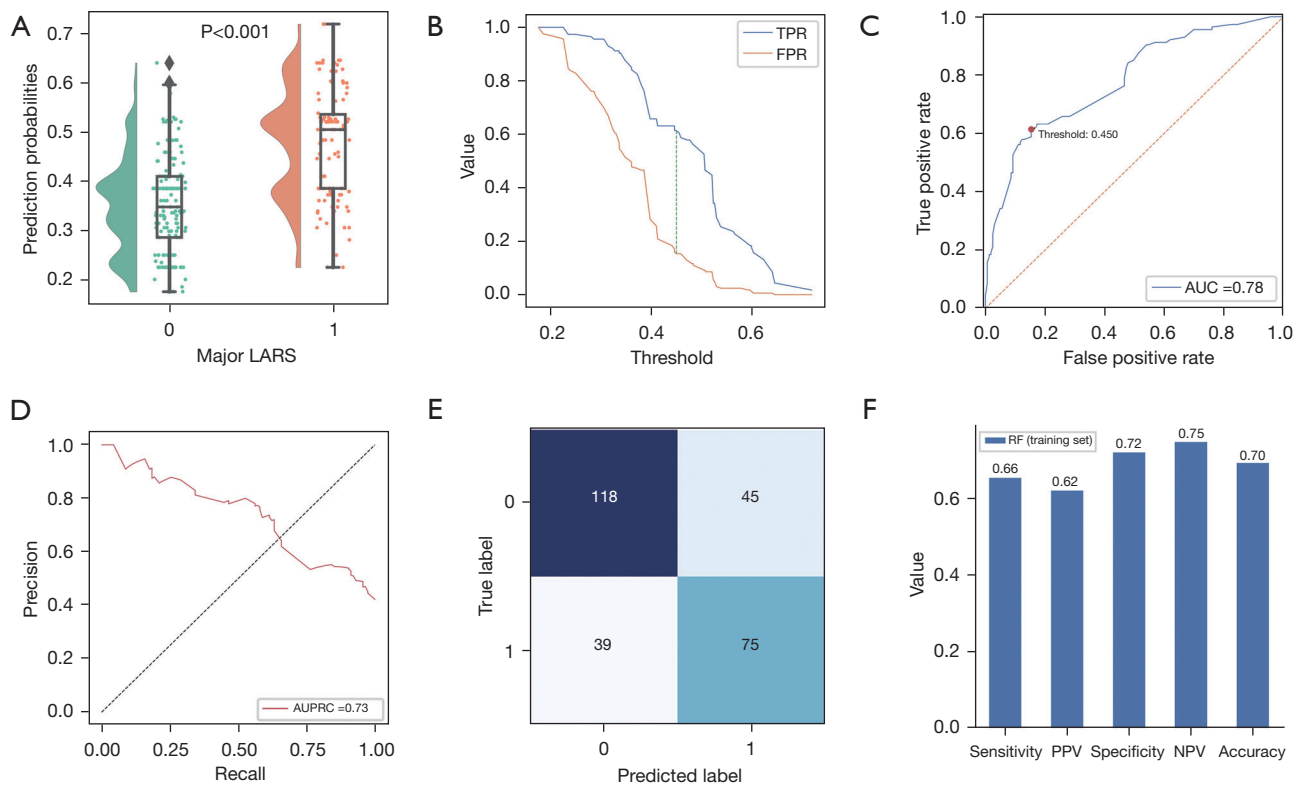


Figure 2 The performance of the model in the training set. (A) Comparison of predicted probabilities calculated using the RF model in patients with and without major LARS in the training set. (B) Changes of TPR and FPR at different thresholds in predicting major LARS. The green line represents the maximum value of TPR-FPR and the corresponding threshold is the Youden index. (C) Receiver operating characteristic curves of the RF model in the training set. The red dot denotes the Youden index. (D) The precision-recall curve of the model in the training set. (E) Confusion matrix of the optimization RF model. (F) Performance measurements of the model illustrated by sensitivity, PPV, specificity, NPV and accuracy. LARS, low anterior resection syndrome; TPR, true positive rates; FPR, false positive rates; AUC, area under the curve; AUPRC, area under the precision-recall curve; RF, random forest; PPV, positive predictive value; NPV, negative predictive value.

were significantly associated with major LARS (Figure 4A). The model achieved satisfactory performance, with AUC and AUPRC of 0.74 (95% CI: 0.70–0.79) and 0.69, respectively (Figure 4B,4C). In addition, the model had a Brier score and C-index of 0.21 and 0.70, respectively (Table 2). The classification results of the model are shown in Figure 4D. Sensitivity (0.67; 95% CI: 0.51–0.79), specificity (0.66; 95% CI: 0.54–0.77), PPV (0.57; 95% CI: 0.43–0.70) and NPV (0.75; 95% CI: 0.62–0.84) and accuracy (0.66; 95% CI: 0.57–0.75) are shown in Figure 4E and Table 2. The concordance between the model's predictions results and the observed values was evaluated by plotting calibration curves (Figure 4F). Briefly, in the test set, the RF model still showed good discrimination and calibration.

Feature importance

Figure 5A illustrates the relationship between each patient characteristic and the major LARS, as determined by the feature importance analysis. To evaluate the impact of individual patient features on major LARS, we employed the SHAP value method and assigned importance values to each feature, as presented in Figure 5B. Moreover, in Figure 5C, the ranking of feature importance is presented, emphasizing the salient patient characteristics correlated with major LARS. The analysis identified the interval (days) between stoma creation and closure, neoadjuvant therapy, and BMI as the foremost three significant patient characteristics. Figure S1 further illustrates the disparities in the intervals

Table 2 Performance of the RF model in training set and test set

Variables	Training set (n=277)		Test set (n=119)
	RF	LR	
Sensitivity (95% CI)	0.66 (0.56–0.74)	0.62 (0.53–0.71)	0.67 (0.51–0.79)
Specificity (95% CI)	0.72 (0.65–0.79)	0.72 (0.65–0.79)	0.66 (0.54–0.77)
PPV (95% CI)	0.63 (0.53–0.71)	0.61 (0.52–0.70)	0.57 (0.43–0.70)
NPV (95% CI)	0.75 (0.68–0.82)	0.73 (0.66–0.80)	0.75 (0.62–0.84)
Accuracy (95% CI)	0.70 (0.64–0.75)	0.68 (0.62–0.74)	0.66 (0.57–0.75)
AUC (95% CI)	0.78 (0.74–0.83)	0.75 (0.70–0.79)	0.74 (0.70–0.79)
AUPRC	0.73	0.71	0.69
Brier	0.20	0.21	0.20
C-index	0.75	0.70	0.72

RF, random forest; LR, logistic regression; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; AUC, area under the receiver operating characteristic curve; AUPRC, area under the precision-recall curve; C-index, concordance index.

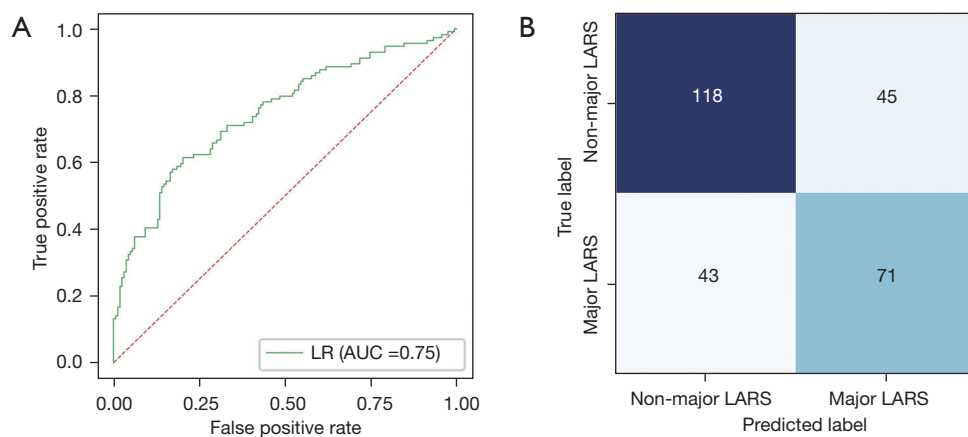


Figure 3 The performance of the LR in the training set. (A) Receiver operating characteristic curves of the LR model. (B) Confusion matrix for classification of major LARS using the LR model. LR, logistic regression; AUC, area under the curve; LARS, low anterior resection syndrome.

between stoma creation and closure within the major and non-major LARS cohorts, as well as the variations in neoadjuvant therapy status and BMI. Additionally, the intervals between stoma creation and closure were stratified into three distinct categories: ≤ 30 , >30 to <60 , and ≥ 60 days. In our study population, there was no statistically significant difference in the incidence of major LARS after the diverting stoma closure between the ≤ 30 and >30 to <60 days groups ($P=0.30$). Nevertheless, the incidence of major LARS after the diverting stoma closure was significantly higher within the ≥ 60 days group compared to the >30 to

<60 days group ($P<0.001$), as showed in [Figure S2](#).

Clinical application value

Finally, the DCA results indicated that our model had good clinical application value, as shown in [Figure 5D](#). Specifically, within the threshold probability range of 0.2–0.8, patients would benefit from comparing all or no treatments using the model. The DCA results provide evidence that our model can be a helpful tool for personalized treatment decision-making within this range

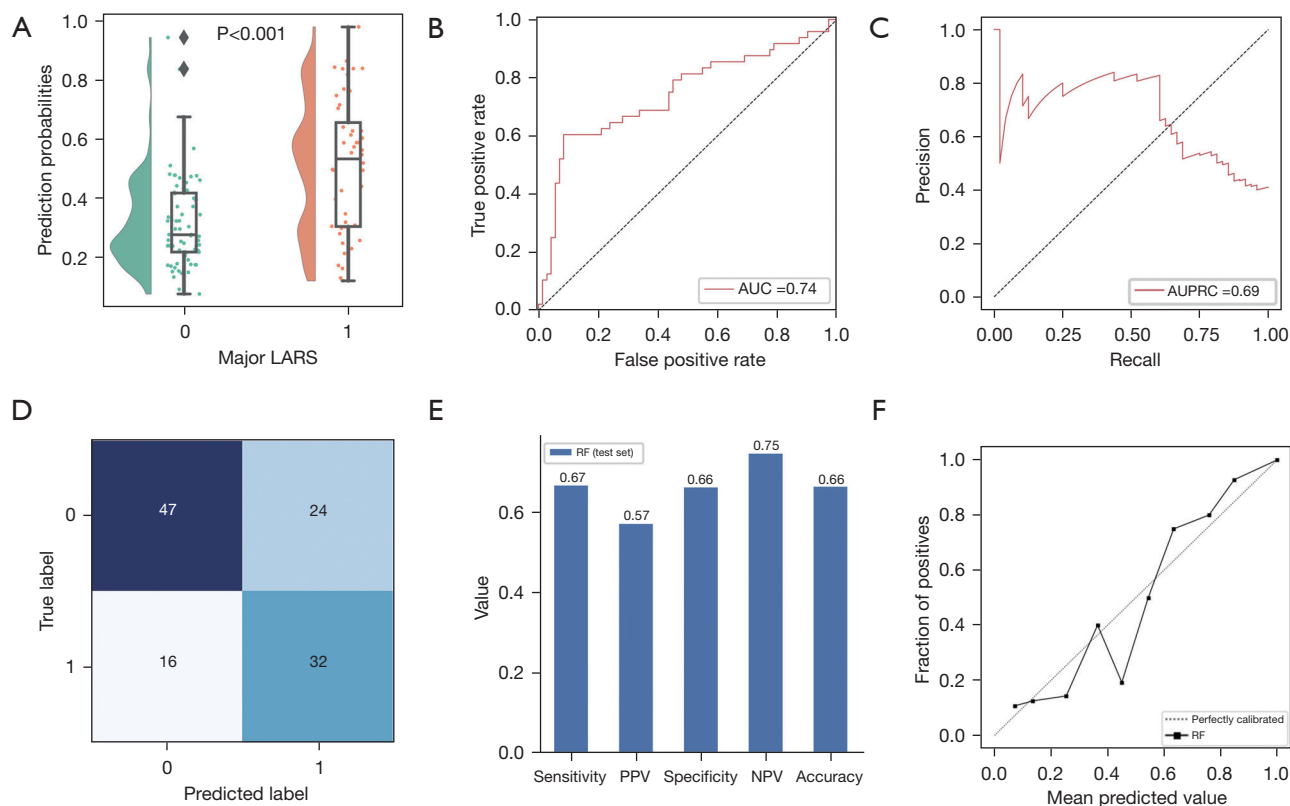


Figure 4 The performance of the model in the test set. (A) Comparison of predicted probabilities calculated using the RF model in patients with and without major LARS in the test set. (B) Receiver operating characteristic curves of the RF model in the test set. (C) The precision-recall curve of the model in the test set. (D) Confusion matrix for classification of major LARS using the RF model. (E) Performance measurements of the model illustrated by sensitivity, PPV, specificity, NPV and accuracy. (F) Calibration curves of the model developed by 10-fold cross-validation. LARS, low anterior resection syndrome; AUC, area under the curve; AUPRC, area under the precision-recall curve; RF, random forest; PPV, positive predictive value; NPV, negative predictive value.

in patients with rectal cancer who are considering stoma closure.

Discussion

The present study constructed a predictive model for major LARS after diverting stoma closure based on a supervised machine-learning RF classifier. Thirteen clinicopathological features were imputed to predict the risk probability of major LARS in patients with rectal cancer after stoma closure. The model demonstrated good discrimination, calibration and clinical application value. Furthermore, the study identified the top five crucial features affecting the predictive results of the model, including the interval between creation and stoma closure, neoadjuvant therapy, BMI, the length of removed bowel, and age.

Creating a diverting stoma to protect anastomosis is

considered standard practice by most rectal surgeons after anterior resection or low anterior resection for rectal cancer, especially in patients with middle and low rectal cancer (28). Recent analysis has shown an increase in the proportion of diverting stomas due to an increase in sphincter-preserving surgery (29). Snijders *et al.* (30) found that the proportion of diverting stomas increased from 57% in 1999 to 70% in 2010 and creating diverting stomas significantly reduced the incidence of symptomatic anastomotic leakage and the associated mortality (31,32). However, bowel dysfunction after stoma closure in patients with rectal cancer is common and significantly impacts the quality of life because diverting stoma interrupts intestinal function, leading to diverting colitis (33). Taylor and Bradshaw (15) found that patients with rectal cancer have frequent intestinal movement, urgency and fecal fragmentation and incontinence after diverting stoma closure. Changes in bowel function restrict

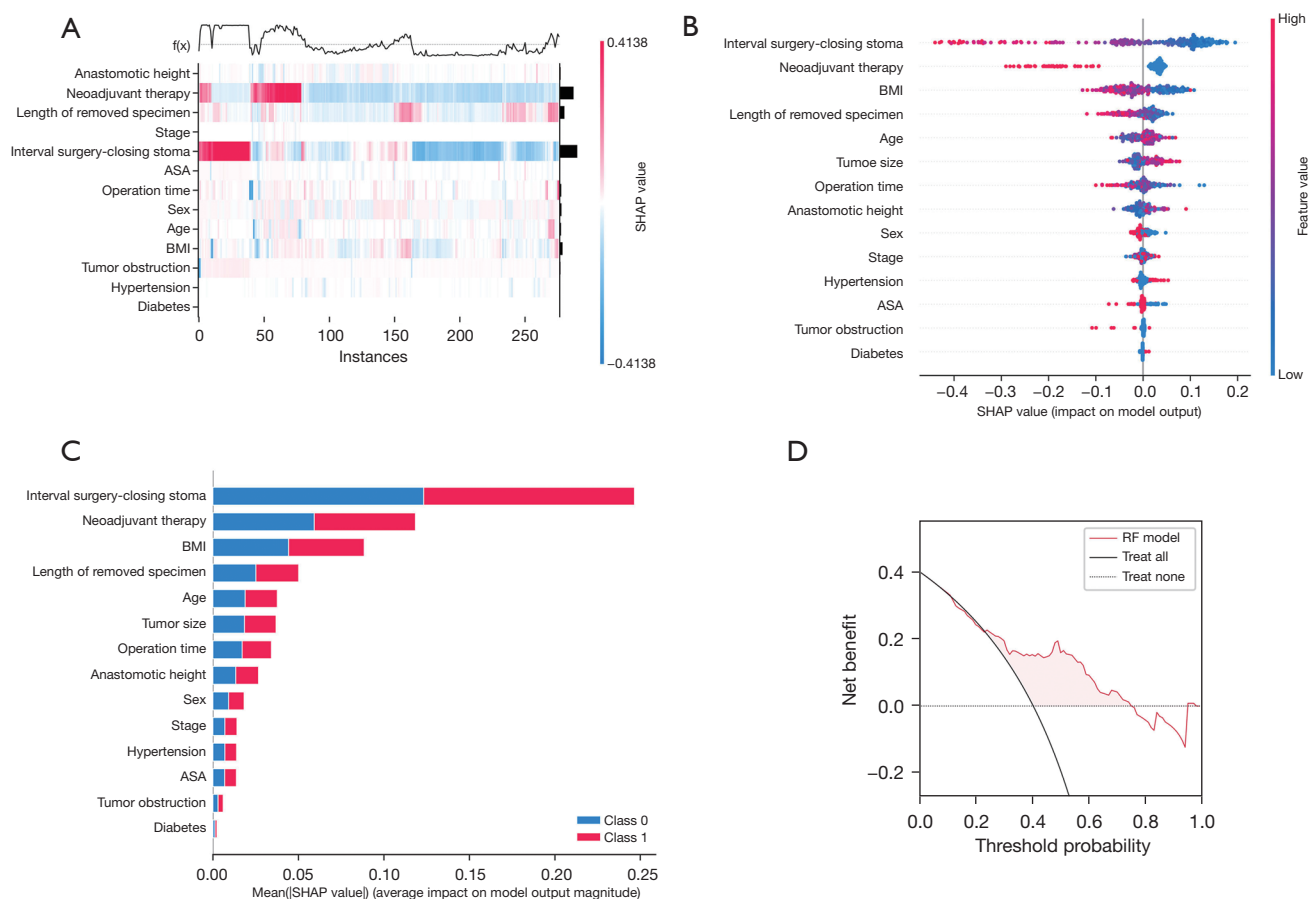


Figure 5 Feature importance and decision curve analysis. (A) Correlation heatmaps of patients' characteristics in the training set. The larger the red area the greater the correlation with the results of the RF model predicting major LARS. (B) Feature importance plot for the RF model. The blue and red points in each row depict nodules with low and high values of the relevant characteristic, respectively, while the x-axis displays the SHAP value, showing the effect on the model. (C) Ranking the importance of features in predicting major LARS in the RF model. (D) The decision curve analysis of the model in the test set. ASA, American Society of Anesthesiologists; BMI, body mass index; SHAP, SHapley Additive exPlanations; LARS, low anterior resection syndrome; RF, random forest.

the daily life and work routine of the patients, affecting their mental and physical health and thus altering their expectations after diverting stoma closure. Jansen *et al.* (34) reported that bowel dysfunction damaged the quality of life of the patient within 1 year after stoma closure. Similarly, Engel *et al.* (35) pointed out in a 4-year prospective study that bowel dysfunction, such as diarrhea, urgency and fecal incontinence, significantly impacted the quality of life of postoperative patients with rectal cancer.

Given the decline in patient expectations after diverting stoma closure (36), it is crucial to inform patients of the risk of postoperative bowel dysfunction before diverting stoma closure. Although several previous studies have attempted to develop predictive models for LARS following rectal

cancer surgery, these models have only a moderate ability to discriminate major LARS due to various methodological limitations. For example, Paku *et al.* (37) established a nomogram model to predict major LARS based on the traditional LR algorithm, but the model did not include patients after diverting stoma closure. The pre-operative LARS score tool developed and externally validated by Battersby *et al.* (38) to predict bowel dysfunction following restorative rectal cancer resection was also based on the traditional regression algorithm. However, Essangri *et al.* (39) observed that when applied to other populations, this tool showed a Kendall coefficient of 0.433 and a Kappa coefficient of 0.327, which indicated weak concordance. Moreover, the comparison of the predicted and actual LARS

scores, by category and degree of agreement, resulted in only 18.09% perfect agreement for major LARS. In summary, the moderate discriminatory accuracy of these models is attributable to the conventional regression algorithm's dependence on a linear correlation between prediction variables and predicted outcomes (39), which may not hold true for multidimensional clinical variables (16).

The current study developed a machine learning algorithm that accurately predicts the risk of major LARS in patients with rectal cancer after stoma closure (AUC, 0.75; 95% CI: 0.69–0.79). Patients with diverting stomas should benefit from the model, according to DCA. The predictive factors included in the model were reported in previous literature, such as the interval between the creation and stoma closure, neoadjuvant therapy, anastomotic height, age, sex, and BMI (40–42). In addition, our model identified several pre-operative variables that were significantly associated with post-operative bowel function recovery. These variables include the length (cm) of the removed bowel, pathological stage of tumor, ASA classification, hypertension, diabetes, operation time, tumor obstruction and tumor size. Of these variables, the interval between the creation and stoma closure was the most important predictor of post-operative bowel function recovery. The distance between the anastomosis and the anal margin was included because a diverting stoma was always performed in patients with mid-low rectal cancer who have risk factors for anastomotic leakage. The model's clinical utility was evaluated, and the DCA indicated that the trained model would be helpful in clinical practice. The predictive model may improve patient outcomes by facilitating more informed and personalized surgical decision-making, reducing the risk of postoperative complications, and ultimately improving patient satisfaction.

The present study features several limitations. First, like for any other single-center retrospective observational study, information and selection biases may exist. Second, the model needs to be validated by external datasets at different times and locations. Third, assessing the surgical impact on the anal sphincter and pelvic plexus, including the degree of damage, presented challenges. Additionally, obtaining precise data on patients' self-administered medications to improve bowel function, along with dosages and compliance with pelvic floor rehabilitation exercises, proved to be significantly challenging. Finally, the generalization ability of the model may need to be improved. Our study only included patients with colorectal cancer who underwent prophylactic stoma closure, which

may limit the applicability of the predictive model to other patient populations. Although the model included 14 predictors, these may still be a relatively small number. To overcome these limitations, a multicenter prospective study will be performed to further evaluate the clinical impact of using the present model. Additionally, further dedicated prospective studies are required to explicitly elucidate the relationship between diverting stoma, LARS, and the timing of closure.

Conclusions

In conclusion, our study successfully developed a machine learning model that can predict major LARS in rectal cancer patients before diverting stoma closure. The model demonstrated reliability and has the potential to aid patients in making informed decisions about diverting stoma closure. The personalized estimates provided by the model can help clinicians guide patients in their surgical management and improve their understanding of the potential outcomes. Moreover, this model can be used to identify patients at high risk of poor bowel function recovery, enabling clinicians to provide targeted post-operative care to improve their outcomes.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE

uniform disclosure form (available at <https://jgo.amegroups.com/article/view/10.21037/jgo-23-1019/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by Ethics Committee of the Tongji Hospital, Huazhong University of Science and Technology (No. TJ-IRB20230364). The requirement for informed consent was waived due to the retrospective nature of the study.

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References

1. Myrseth E, Nymo LS, Gjessing PF, et al. Diverting stomas reduce reoperation rates for anastomotic leak but not overall reoperation rates within 30 days after anterior rectal resection: a national cohort study. *Int J Colorectal Dis* 2022;37:1681-8.
2. Schlesinger NH, Smith H. The effect of a diverting stoma on morbidity and risk of permanent stoma following anastomotic leakage after low anterior resection for rectal cancer: a nationwide cohort study. *Int J Colorectal Dis* 2020;35:1903-10.
3. Tsujinaka S, Suzuki H, Miura T, et al. Diagnosis, Treatment, and Prevention of Ileostomy Complications: An Updated Review. *Cureus* 2023;15:e34289.
4. Omar M, Tarek A, Abdeslam B, et al. Risk factors of acute renal failure in patients with protective ileostomy after rectal cancer surgery. *BMC Surg* 2023;23:107.
5. Rud CL, Baunwall SMD, Bager P, et al. Patient-Reported Outcomes and Health-Related Quality of Life in People Living With Ileostomies: A Population-Based, Cross-Sectional Study. *Dis Colon Rectum* 2022;65:1042-51.
6. Babakhanlou R, Larkin K, Hita AG, et al. Stoma-related complications and emergencies. *Int J Emerg Med* 2022;15:17.
7. Keane C, Sharma P, Yuan L, et al. Impact of temporary ileostomy on long-term quality of life and bowel function: a systematic review and meta-analysis. *ANZ J Surg* 2020;90:687-92.
8. Ge Z, Zhao X, Liu Z, et al. Complications of preventive loop ileostomy versus colostomy: a meta-analysis, trial sequential analysis, and systematic review. *BMC Surg* 2023;23:235.
9. Denost Q, Sylla D, Fleming C, et al. A phase III randomized trial evaluating the quality of life impact of a tailored versus systematic use of defunctioning ileostomy following total mesorectal excision for rectal cancer-GRECCAR 17 trial protocol. *Colorectal Dis* 2023;25:443-52.
10. Tsunoda A, Tsunoda Y, Narita K, et al. Quality of life after low anterior resection and temporary loop ileostomy. *Dis Colon Rectum* 2008;51:218-22.
11. Park J, Angenete E, Bock D, et al. Cost analysis in a randomized trial of early closure of a temporary ileostomy after rectal resection for cancer (EASY trial). *Surg Endosc* 2020;34:69-76.
12. Alves A, Panis Y, Lelong B, et al. Randomized clinical trial of early versus delayed temporary stoma closure after proctectomy. *Br J Surg* 2008;95:693-8.
13. Emmertsen KJ, Laurberg S. Low anterior resection syndrome score: development and validation of a symptom-based scoring system for bowel dysfunction after low anterior resection for rectal cancer. *Ann Surg* 2012;255:922-8.
14. Keane C, Fearnhead NS, Bordeianou LG, et al. International Consensus Definition of Low Anterior Resection Syndrome. *Dis Colon Rectum* 2020;63:274-84.
15. Taylor C, Bradshaw E. Tied to the toilet: lived experiences of altered bowel function (anterior resection syndrome) after temporary stoma reversal. *J Wound Ostomy Continence Nurs* 2013;40:415-21.
16. Rajkomar A, Dean J, Kohane I. Machine Learning in Medicine. *N Engl J Med* 2019;380:1347-58.
17. Mitsala A, Tsalikidis C, Pitiakoudis M, et al. Artificial Intelligence in Colorectal Cancer Screening, Diagnosis and Treatment. *A New Era. Curr Oncol* 2021;28:1581-607.
18. Shao S, Liu L, Zhao Y, et al. Application of Machine Learning for Predicting Anastomotic Leakage in Patients with Gastric Adenocarcinoma Who Received Total or Proximal Gastrectomy. *J Pers Med* 2021;11:748.
19. Shao S, Zhao Y, Lu Q, et al. Artificial intelligence assists surgeons' decision-making of temporary ileostomy in

- patients with rectal cancer who have received anterior resection. *Eur J Surg Oncol* 2023;49:433-9.
20. Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. *Nat Med* 2019;25:44-56.
 21. Hou XT, Pang D, Lu Q, et al. Validation of the Chinese version of the low anterior resection syndrome score for measuring bowel dysfunction after sphincter-preserving surgery among rectal cancer patients. *Eur J Oncol Nurs* 2015;19:495-501.
 22. Nguyen TH, Chokshi RV. Low Anterior Resection Syndrome. *Curr Gastroenterol Rep* 2020;22:48.
 23. Afshari K, Smedh K, Wagner P, et al. Risk factors for developing anorectal dysfunction after anterior resection. *Int J Colorectal Dis* 2021;36:2697-705.
 24. Yang W, Jiang J, Schnellinger EM, et al. Modified Brier score for evaluating prediction accuracy for binary outcomes. *Stat Methods Med Res* 2022;31:2287-96.
 25. Nohara Y, Matsumoto K, Soejima H, et al. Explanation of machine learning models using shapley additive explanation and application for real data in hospital. *Comput Methods Programs Biomed* 2022;214:106584.
 26. Rodríguez-Pérez R, Bajorath J. Interpretation of machine learning models using shapley values: application to compound potency and multi-target activity predictions. *J Comput Aided Mol Des* 2020;34:1013-26.
 27. Vickers AJ, van Calster B, Steyerberg EW. A simple, step-by-step guide to interpreting decision curve analysis. *Diagn Progn Res* 2019;3:18.
 28. Hamabe A, Ito M, Nishigori H, et al. Preventive effect of diverting stoma on anastomotic leakage after laparoscopic low anterior resection with double stapling technique reconstruction applied based on risk stratification. *Asian J Endosc Surg* 2018;11:220-6.
 29. Grupa VEM, Kroon HM, Ozmen I, et al. Current practice in Australia and New Zealand for defunctioning ileostomy after rectal cancer surgery with anastomosis: Analysis of the Binational Colorectal Cancer Audit. *Colorectal Dis* 2021;23:1421-33.
 30. Snijders HS, van den Broek CB, Wouters MW, et al. An increasing use of defunctioning stomas after low anterior resection for rectal cancer. Is this the way to go? *Eur J Surg Oncol* 2013;39:715-20.
 31. Gadan S, Brand JS, Rutegård M, et al. Defunctioning stoma and short- and long-term outcomes after low anterior resection for rectal cancer—a nationwide register-based cohort study. *Int J Colorectal Dis* 2021;36:1433-42.
 32. Yang S, Lin Y, Zhong W, et al. Impact of ileostomy on postoperative wound complications in patients after laparoscopic rectal cancer surgery: A meta-analysis. *Int Wound J* 2023. [Epub ahead of print]. doi: 10.1111/iwj.14493.
 33. Dilke S, Segal J, Tozer PJ, et al. Diversion colitis: aetiology, diagnosis and treatment. A systematic review. *GastroHep* 2020;2:266-71.
 34. Jansen L, Herrmann A, Stegmaier C, et al. Health-related quality of life during the 10 years after diagnosis of colorectal cancer: a population-based study. *J Clin Oncol* 2011;29:3263-9.
 35. Engel J, Kerr J, Schlesinger-Raab A, et al. Quality of life in rectal cancer patients: a four-year prospective study. *Ann Surg* 2003;238:203-13.
 36. Siassi M, Hohenberger W, Lösel F, et al. Quality of life and patient's expectations after closure of a temporary stoma. *Int J Colorectal Dis* 2008;23:1207-12.
 37. Paku M, Miyoshi N, Fujino S, et al. Development and evaluation of a Japanese prediction model for low anterior resection syndrome after rectal cancer surgery. *BMC Gastroenterol* 2022;22:239.
 38. Battersby NJ, Bouliotis G, Emmertsen KJ, et al. Development and external validation of a nomogram and online tool to predict bowel dysfunction following restorative rectal cancer resection: the POLARS score. *Gut* 2018;67:688-96.
 39. Essangri H, Majbar MA, Benkabbou A, et al. Do we have enough Foreknowledge to predict the low anterior resection syndrome (LARS) score preoperatively? *Colorectal Dis* 2020;22:1445.
 40. Hughes DL, Cornish J, Morris C, et al. Functional outcome following rectal surgery—predisposing factors for low anterior resection syndrome. *Int J Colorectal Dis* 2017;32:691-7.
 41. Nicotera A, Falletto E, Arezzo A, et al. Risk factors for Low Anterior Resection Syndrome (LARS) in patients undergoing laparoscopic surgery for rectal cancer. *Surg Endosc* 2022;36:6059-66.
 42. Liang Z, Zhang Z, Wu D, et al. Effects of Preoperative Radiotherapy on Long-Term Bowel Function in Patients With Rectal Cancer Treated With Anterior Resection: A Systematic Review and Meta-analysis. *Technol Cancer Res Treat* 2022;21:15330338221105156.

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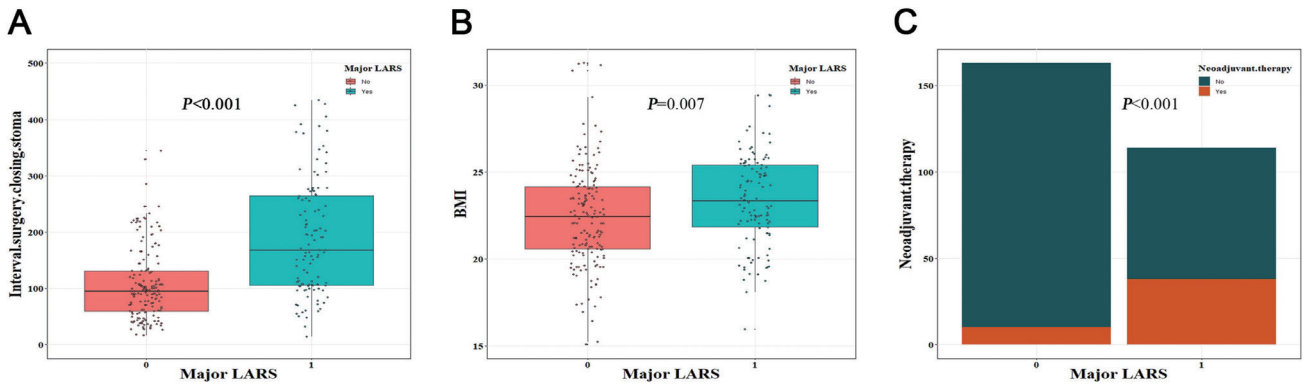


Figure S1 Comparison of the interval time of closure after primary surgery, BMI, and neoadjuvant therapy status between major LARS and non-major LARS groups in the training set. (A) The interval time of closure after primary surgery (mean time of 107 days for non-major LARS groups versus 205 days for major LARS groups; $P < 0.001$). (B) BMI (mean BMI of 22.4 kg/m² for non-major LARS groups versus 23.4 kg/m² for major LARS groups; $P = 0.007$). (C) Neoadjuvant therapy status (10 for non-major LARS groups versus 38 for major LARS groups; $P < 0.001$). LARS, low anterior resection syndrome; BMI, body mass index.

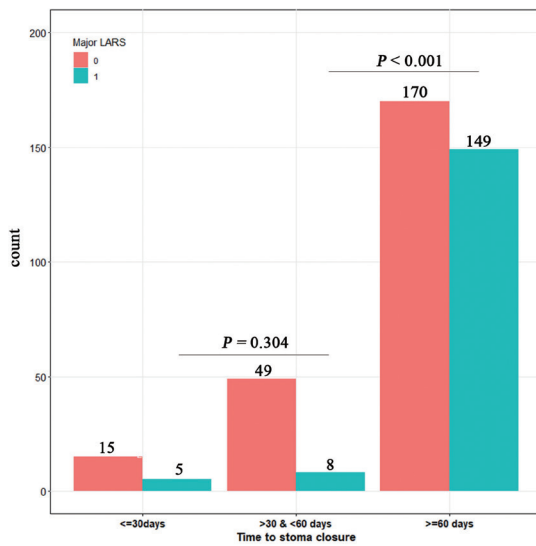


Figure S2 Relationship between the timing of stoma closure and major LARS. LARS, low anterior resection syndrome.