Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Exploratory machine learning analysis of factors associated with positive circumferential resection margins following transanal total mesorectal excision: a multicenter registry study

Pengyu Wei
Beijing Friendship Hospital
Cong Meng
Beijing Chuiyangliu Hospital
Yang Li
Beijing Friendship Hospital
Mingyang Ren
Nanchong Central Hospital
Hongyu Zhang
First Affiliated Hospital of Chongqing Medical University
Hong Zhang
Sheng Jing Hospital
Quan Wang
First Hospital of Jilin University
Weidong Tong
Daping Hospital
Qing Xu
Renji Hospital
Chi Chung Foo
Queen Mary Hospital
Yi Xiao
Peking Union Medical College Hospital
Chien-chih Chen
Koo Foundation Sun Yat-Sen Cancer Center
Hongwei Yao
Beijing Friendship Hospital
Zhongtao Zhang
zhangzht@ccmu.edu.cn

Beijing Friendship Hospital

Research Article

Keywords: Rectal cancer, Transanal total mesorectal excision, Circumferential resection margin, Machine learning, Predictive modelling

Posted Date: June 29th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9970346/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Additional Declarations: No competing interests reported.

Abstract

Purpose

Positive circumferential resection margin (CRM) is an important oncological quality indicator in rectal cancer surgery. This study aimed to explore factors associated with CRM positivity after transanal total mesorectal excision (taTME) using data from a multicenter registry.

Methods

Patients with rectal cancer who underwent primary taTME between 2017 and 2024 were identified from the Chinese TaTME Registry Collaborative. The primary outcome was pathological CRM positivity. Nine supervised machine learning algorithms were evaluated, including logistic regression, elastic net, decision tree, random forest, XGBoost, radial support vector machine, multilayer perceptron, LightGBM, and k-nearest neighbors. Model performance was assessed using the area under the receiver operating characteristic curve (AUC), and model interpretation was performed using SHapley Additive exPlanations.

Results

A total of 1,625 patients from 32 institutions were included, and the CRM positivity rate was 2.77%. In the validation cohort, the radial support vector machine model showed the highest apparent AUC of 0.84. SHAP analysis identified pathological N stage, threatened mesorectal fascia on preoperative MRI, and intersphincteric resection as the most influential variables.

Conclusion

This exploratory analysis identified clinically plausible factors associated with CRM positivity after taTME. Because the models included intraoperative and postoperative variables, they should not be interpreted as preoperative decision-support tools. Further studies using preoperative-only variables and external validation are required.

Introduction

Rectal cancer is one of the most common malignancies worldwide. Total mesorectal excision (TME), first described by Heald in 1982, has significantly improved oncological outcomes in rectal cancer surgery by ensuring complete removal of the mesorectal envelope[1].

Laparoscopic TME has become a standard surgical approach for rectal cancer[2–4]. However, performing laparoscopic TME in patients with a narrow pelvis, obesity, or bulky tumors can be technically challenging. These anatomical and tumor-related factors may increase the risk of incomplete mesorectal excision and positive circumferential resection margins (CRM) [5–7].

Transanal total mesorectal excision (taTME) was introduced as a “down-to-up” approach to overcome the limitations of conventional laparoscopic TME[8]. By providing improved visualization of the distal rectum and pelvic anatomy, taTME may facilitate more precise dissection in difficult cases[9–12]. Nevertheless, achieving negative CRM remains a key surgical objective, as positive CRM is strongly associated with local recurrence and worse survival outcomes[13, 14].

Accurate assessment of factors associated with CRM positivity is therefore clinically important. Previous registry-based work has used logistic regression to develop a CRM risk model after taTME and identified clinically plausible predictors, including threatened MRF, advanced tumor stage, and anterior tumor location, etc. [15].

Machine learning algorithms may complement conventional statistical approaches by modelling nonlinear relationships and supporting post hoc interpretation through methods such as SHapley Additive exPlanations (SHAP). However, their incremental value over standard clinical assessment and logistic regression requires cautious evaluation.

The Chinese TaTME Registry Collaborative (CTRC) is a nationwide multicenter database established in 2017 to collect real-world data on taTME procedures across China. Using this registry, the present study aimed to explore factors associated with CRM positivity by comparing multiple machine learning algorithms and identifying influential variables using SHAP-based interpretation. Because some candidate predictors were intraoperative or postoperative variables, this analysis was intended as exploratory modelling rather than a purely preoperative decision-support model.

Materials and Methods

This study was reported in accordance with the TRIPOD (Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis) reporting guideline[15]. A completed TRIPOD checklist is provided in the Supplementary Materials.

Source of data

This multicenter registry-based cohort study used data from the Chinese TaTME Registry Collaborative (CTRC), a nationwide web-based registry established in 2017 to collect real-world data on taTME procedures across China.

Centers performing taTME may voluntarily join the registry after review by a core expert committee, which evaluates institutional surgical experience, research capacity, and multidisciplinary support. Participating centers submit standardized clinical data through the registry platform.

The CTRC database includes patient demographics, preoperative evaluation, neoadjuvant therapy, intraoperative variables, pathological findings, postoperative outcomes, and follow-up. Key supporting materials, including MRI reports and pathological documentation, are uploaded when available, and questionable entries are verified with the reporting institution by the coordinating center.

Ethics

Ethical approval

for the CTRC registry and publication of its results was obtained from the Medical Ethics Committee of Beijing Friendship Hospital (Approval No. 2017-P2-181-01) and subsequently from the local ethics committees of all participating hospitals. As this study was a retrospective analysis of anonymized registry data, the institutional review board waived the requirement for informed consent.

Study population and primary outcome

The study population consisted of patients recorded in the CTRC database between November 15, 2017, and July 14, 2024. Patients were excluded if they had benign rectal disease, had undergone previous local excision, did not undergo anastomotic reconstruction of bowel continuity, underwent pure taTME (defined as a completely transanal procedure), or had unclear CRM records. No prospective sample size calculation was performed because this was a retrospective registry-based study including all eligible patients recorded in the CTRC database during the study period. The final sample size was therefore determined by data availability.

The primary outcome was positive CRM, defined as the presence of tumor cells or malignant lymph nodes within ≤ 1 mm of the CRM on histopathological examination. CRM status was determined according to pathological assessment at each participating institution; central pathological review was not performed.

Predictor variables

Twenty-one variables potentially associated with CRM status were considered. Demographic variables included sex, age, and body mass index (BMI). Tumor-related variables were primarily obtained from preoperative magnetic resonance imaging (MRI) and included anterior tumor location, clinical T stage, clinical N stage, threatened or involved mesorectal fascia (MRF), extramural vascular invasion (EMVI), and distance from the lower tumor edge to the anal verge. Preoperative MRI was defined as the MRI

assessment closest to surgery: the initial staging MRI for patients undergoing primary surgery and the post-treatment preoperative/restaging MRI for patients receiving neoadjuvant therapy.

Treatment- and operation-related variables included neoadjuvant radiotherapy, previous pelvic therapies, expert supervision, simultaneous abdominal-perineal surgery, surgical approach, conversion to open surgery, ISR, and intraoperative difficulties during the abdominal or perineal phase. Pathological T stage and pathological N stage were included as postoperative variables. Because predictors were not all available at the same clinical timepoint, the model should be interpreted as exploratory rather than as a strictly preoperative prediction tool.

Data preprocessing

Age, BMI, and tumor distance from the anal verge were treated as continuous variables, and the remaining predictors as categorical variables. Data cleaning included checks for duplicates, outliers, and missing values. Missing data were handled using random forest-based multiple imputation with five imputations. To avoid data leakage, imputation was performed after splitting the dataset into training and validation cohorts; the imputation model was developed using the training data and applied within the validation workflow without using outcome information from the validation set for model training. Categorical variables were summarized as numbers and percentages, and continuous variables as means with standard deviations. Group differences were assessed using the chi-square test for categorical variables and the Mann-Whitney U test for continuous variables, with $p < 0.05$ considered statistically significant.

Model development and validation

For model development, grid search combined with five-fold cross-validation was used to optimize hyperparameters. Nine supervised algorithms were evaluated: logistic regression (LR), elastic net (ENET), decision tree (DT), random forest (RF), extreme gradient boosting (XGBoost), radial support vector machine (RSVM), multilayer perceptron (MLP), LightGBM, and k-nearest neighbors (KNN). Because CRM positivity was rare, stratified sampling was used to divide the dataset into training (70%) and validation (30%) cohorts while preserving the outcome distribution. Model performance was evaluated using AUC, accuracy, sensitivity, specificity, positive predictive value, negative predictive value, Matthews correlation coefficient, F-measure, and balanced accuracy. AUCs were reported with approximate 95% confidence intervals estimated using the Hanley–McNeil method based on the observed AUC and the numbers of positive and negative cases. Calibration was explored visually using grouped calibration plots; given the limited number of CRM-positive events, no definitive conclusions regarding calibration were made. The optimal classification threshold was determined using Youden's index as a conventional approach to balance sensitivity and specificity in this exploratory analysis. SHAP was used to quantify variable contributions to model output.

Statistical analysis

All statistical analyses were performed using R software version 3.5.3 (R Foundation for Statistical Computing, Vienna, Austria) in a fixed computational environment. The same software environment was used for model development, validation, and comparison across all algorithms.

Results

Study cohort

During the seven-year study period, a total of 2,526 patients were recorded in the CTRC database. After excluding 901 patients with benign disease, previous local excision, absence of anastomotic reconstruction, pure taTME procedures, or unclear CRM status, a final cohort of 1,625 patients was included in the analysis. Comparative data for the twenty-one potential predictors between CRM-positive and CRM-negative groups are presented in Table 1. The overall proportion of missing data was 11.69%, corresponding to 3,989 missing items among 34,125 data cells. Detailed information regarding missing data for individual variables is provided in the supplementary materials (**Figure S1**).

Table 1
Association between different potential risk factors of positive CRM in the development cohort.

n	level	overall	CRM-	CRM+	p-value
		1625	**1580**	**45**	
Gender (%)	Female	500 (30.77)	482 (30.51)	18 (40.00)	0.231
	Male	1125 (69.23)	1098 (69.49)	27 (60.00)	
Anterior tumor (%)	No	1062 (65.35)	1034 (65.44)	28 (62.22)	0.773
	Yes	563 (34.65)	546 (34.56)	17 (37.78)	
Clinical T-stage (%)	cT0	7 (0.43)	7 (0.44)	0 (0.00)	< 0.001
	cT1	42 (2.58)	42 (2.66)	0 (0.00)	
	cT2	321 (19.75)	317 (20.06)	4 (8.89)	
	cT3	1075 (66.15)	1050 (66.46)	25 (55.56)	
	cT4	171 (10.52)	155 (9.81)	16 (35.56)	
	cTx	9 (0.55)	9 (0.57)	0 (0.00)	
Clinical N-stage (%)	cN0	639 (39.32)	627 (39.68)	12 (26.67)	0.052
	cN1	485 (29.85)	474 (30.00)	11 (24.44)	
	cN2	410 (25.23)	393 (24.87)	17 (37.78)	
	cNx	91 (5.60)	86 (5.44)	5 (11.11)	
MRF (%)	Negative	1423 (87.57)	1397 (88.42)	26 (57.78)	< 0.001
	Positive	202 (12.43)	183 (11.58)	19 (42.22)	
EMVI (%)	Negative	1229 (75.63)	1203 (76.14)	26 (57.78)	0.008
	Positive	396 (24.37)	377 (23.86)	19 (42.22)	
Neoadjuvant radiotherapy (%)	No	1146 (70.52)	1116 (70.63)	30 (66.67)	0.682
	Yes	479 (29.48)	464 (29.37)	15 (33.33)	
Previous pelvic therapies (%)	No	1531 (94.22)	1490 (94.30)	41 (91.11)	0.561
	Yes	94 (5.78)	90 (5.70)	4 (8.89)	

Abbreviations: CRM, Circumferential Resection Margin; MRF, Mesorectal Fascia; EMVI, Extramural Vascular Invasion; ISR, Inter-sphincteric Resection; BMI, Body Mass Index

n	level	overall	CRM-	CRM+	p-value
		1625	**1580**	**45**	
Presence of expert supervision (%)	No	992 (61.05)	957 (60.57)	35 (77.78)	0.029
	Yes	633 (38.95)	623 (39.43)	10 (22.22)	
Abdominal/perineal surgery was performed simultaneously (%)	No	933 (57.42)	911 (57.66)	22 (48.89)	0.308
	Yes	692 (42.58)	669 (42.34)	23 (51.11)	
Surgical approach (%)	Laparoscopic	1570 (96.62)	1531 (96.90)	39 (86.67)	< 0.001
	robotic surgery	50 (3.08)	44 (2.78)	6 (13.33)	
	single-incision laparoscopic	5 (0.31)	5 (0.32)	0 (0.00)	
Conversion to open (abdominal phase) (%)	No	1607 (98.89)	1562 (98.86)	45 (100.00)	1
	Yes	18 (1.11)	18 (1.14)	0 (0.00)	
Intraoperative difficulties (abdominal phase) (%)	No	1569 (96.55)	1527 (96.65)	42 (93.33)	0.431
	Yes	56 (3.45)	53 (3.35)	3 (6.67)	
ISR (%)	No	1322 (81.35)	1292 (81.77)	30 (66.67)	0.018
	Yes	303 (18.65)	288 (18.23)	15 (33.33)	
Conversion to open (perineal phase) (%)	No	1593 (98.03)	1548 (97.97)	45 (100.00)	0.674
	Yes	32 (1.97)	32 (2.03)	0 (0.00)	
Intraoperative difficulties (perineal phase) (%)	No	1124 (69.17)	1092 (69.11)	32 (71.11)	0.903
	Yes	501 (30.83)	488 (30.89)	13 (28.89)	
Pathological T-stage (%)	pT0	118 (7.26)	118 (7.47)	0 (0.00)	0.002
	pT1	149 (9.17)	149 (9.43)	0 (0.00)	
	pT2	490 (30.15)	483 (30.57)	7 (15.56)	
	pT3	652 (40.12)	624 (39.49)	28 (62.22)	
	pT4	177 (10.89)	168 (10.63)	9 (20.00)	
	pTis	31 (1.91)	30 (1.90)	1 (2.22)	
	pTx	8 (0.49)	8 (0.51)	0 (0.00)	

Abbreviations: CRM, Circumferential Resection Margin; MRF, Mesorectal Fascia; EMVI, Extramural Vascular Invasion; ISR, Inter-sphincteric Resection; BMI, Body Mass Index

n	level	overall	CRM-	CRM+	p-value
		1625	**1580**	**45**	
Pathological N-stage (%)	pN0	1097 (67.51)	1085 (68.67)	12 (26.67)	< 0.001
	pN1	377 (23.20)	360 (22.78)	17 (37.78)	
	pN2	151 (9.29)	135 (8.54)	16 (35.56)	
Age (mean (SD))		60.95 (11.15)	60.98 (11.14)	60.02 (11.76)	0.572
BMI (kg/m^2) (mean (SD))		23.82 (3.42)	23.84 (3.43)	23.18 (3.11)	0.2
Distance from the lower edge of the tumor to the anal verge (mm) (mean (SD))		49.40 (18.25)	49.33 (18.32)	51.77 (15.88)	0.377

Abbreviations: CRM, Circumferential Resection Margin; MRF, Mesorectal Fascia; EMVI, Extramural Vascular Invasion; ISR, Inter-sphincteric Resection; BMI, Body Mass Index

Among the 1,625 patients included in the study, 45 patients (2.77%) were found to have positive CRM on pathological examination. Patients in the CRM-positive group were more likely to have higher clinical T stage and were more frequently found to have MRF involvement or EMVI on preoperative MRI. In addition, these patients also exhibited higher pathological T stage and pathological N stage. Surgeries performed under expert supervision were associated with a lower risk of CRM positivity. Conversely, higher rates of CRM positivity were observed among patients undergoing robotic surgery and those who received ISR, as shown in Table 1.

Inter-center variation

Table 2 summarizes the total number of patients enrolled and the CRM-positive rates for each participating center. Statistical analyses demonstrated significant variation in CRM-positive rates across centers ($\chi^2 = 45.78$, $df = 19$, $p < 0.001$), suggesting heterogeneity among institutions. However, correlation analyses indicated no significant association between the CRM-positive rate and the total number of patients enrolled by each center. The Spearman correlation coefficient was − 0.354 ($p = 0.114$), and the Pearson correlation coefficient was − 0.311 ($p = 0.166$). Similarly, linear regression analysis showed that the number of patients enrolled by each center did not significantly influence the CRM-positive rate (regression coefficient = − 0.0003, $p = 0.166$, $R^2 = 0.097$).

Table 2
Total cases enrolled and CRM-positive numbers and proportions per medical center.

medical center	total number of enrolled patients	CRM-positive cases n (%)
1	264	16 (6.06)
2	178	2 (1.12)
3	144	0
4	131	4 (3.05)
5	115	3 (2.61)
6	101	1 (0.99)
7	95	2 (2.11)
8	89	8 (8.99)
9	81	0
10	72	5 (6.94)
11	69	3 (4.35)
12	63	0
13	47	0
14	33	0
15	24	0
16	23	0
17	22	1 (4.55)
18	14	0
19	11	0
20	9	0
21	7	0
22	6	0
23	6	0
24	5	0
25	5	0
26	3	0
27	2	0
28	2	0
29	1	0
30	1	0
31	1	0
32	1	0

Abbreviations: CRM, Circumferential Resection Margin

Model training and validation

The study population was randomly divided into a training set (70%) and a validation set (30%) using stratified random sampling. Baseline characteristics of the two datasets are summarized in **Table S1**. Nine machine learning algorithms were constructed. Performance metrics in the training and validation sets are presented in Table 3, and the parallel coordinate plot is shown in Fig. 1.

Table 3
Key performance parameters of each model in the training and validation sets.

Dataset	Model	Accuracy	Sensitivity	Specificity	PPV	NPV	Precision	Recall	F-measure	AUC (95% CI)
Training	LR	0.871	0.706	0.876	0.149	0.990	0.149	0.706	0.246	0.871 (0.794–0.948)
Training	ENET	0.640	0.824	0.635	0.065	0.992	0.065	0.824	0.120	0.802 (0.713–0.892)
Training	DT	0.900	0.382	0.916	0.123	0.980	0.123	0.382	0.186	0.660 (0.559–0.762)
Training	RF	0.931	0.941	0.930	0.294	0.998	0.294	0.941	0.448	0.984 (0.954-1.000)
Training	XGBoost	0.666	0.824	0.661	0.070	0.992	0.070	0.824	0.128	0.781 (0.688–0.874)
Training	RSVM	0.884	0.824	0.886	0.182	0.994	0.182	0.824	0.298	0.918 (0.854–0.982)
Training	MLP	0.613	0.971	0.602	0.070	0.998	0.070	0.971	0.130	0.871 (0.794–0.948)
Training	LightGBM	0.930	0.735	0.936	0.260	0.991	0.260	0.735	0.385	0.894 (0.823–0.965)
Training	KNN	0.803	1.000	0.797	0.132	1.000	0.132	1.000	0.233	0.930 (0.870–0.990)
Validation	LR	0.871	0.545	0.878	0.094	0.988	0.094	0.545	0.160	0.819 (0.666–0.973)
Validation	ENET	0.615	0.818	0.610	0.046	0.993	0.046	0.818	0.087	0.768 (0.603–0.934)
Validation	DT	0.883	0.182	0.899	0.040	0.979	0.040	0.182	0.066	0.512 (0.338–0.686)
Validation	RF	0.871	0.455	0.881	0.081	0.986	0.081	0.455	0.137	0.679 (0.502–0.856)
Validation	XGBoost	0.652	0.636	0.652	0.040	0.987	0.040	0.636	0.076	0.680 (0.503–0.857)
Validation	RSVM	0.863	0.636	0.868	0.100	0.990	0.100	0.636	0.173	0.842 (0.696–0.989)
Validation	MLP	0.594	0.727	0.591	0.039	0.989	0.039	0.727	0.075	0.756 (0.589–0.924)
Validation	LightGBM	0.912	0.455	0.922	0.119	0.987	0.119	0.455	0.189	0.639 (0.460–0.818)

Dataset	Model	Accuracy	Sensitivity	Specificity	PPV	NPV	Precision	Recall	F-measure	AUC (95% CI)
Validation	KNN	0.785	0.727	0.786	0.073	0.992	0.073	0.727	0.132	0.225 (0.116–0.334)

In the training set, the AUC values were LR 0.8709, ENET 0.8025, DT 0.6602, RF 0.9838, XGBoost 0.7809, RSVM 0.9176, MLP 0.8711, LightGBM 0.8941, and KNN 0.9300. RF, RSVM, and KNN showed high apparent training discrimination, with AUC values exceeding 0.90. In the validation cohort, RSVM showed the highest apparent AUC of 0.842 (95% CI, 0.707–0.977), while LR showed comparable discrimination with an AUC of 0.819 (95% CI, 0.678–0.960). ROC curves for the validation set are shown in Fig. 2. Exploratory grouped calibration plots are presented in Fig. 3 and should be interpreted cautiously because of the small number of CRM-positive events and the absence of quantitative calibration metrics. Additional model figures are provided in the supplementary materials (**Figure S2-S10**).

Variable importance

Several algorithms showed discrepancies between training and validation performance, suggesting overfitting. For example, RF and KNN achieved high training AUC values but lower validation performance. RSVM showed relatively stable apparent performance across datasets and was therefore selected for exploratory SHAP interpretation. SHAP analysis quantified the contribution of individual predictors to model output (Fig. 4), identifying pathological N stage, MRF involvement, and ISR as the three most influential predictors of CRM positivity.

Discussion

In this multicenter registry-based study, we explored factors associated with CRM positivity following taTME using multiple machine learning algorithms. The model was not intended to replace preoperative multidisciplinary assessment or determine candidacy for taTME, but to provide an exploratory framework for understanding clinical, imaging, operative, and pathological variables associated with CRM positivity in a real-world registry. RSVM showed the highest apparent AUC in the validation cohort, while SHAP analysis identified pathological N stage, threatened MRF on preoperative MRI, and ISR as influential variables.

The overall CRM positivity rate in the present cohort was 2.77%, which is consistent with previously reported rates from large taTME registries. Data from the International TaTME Registry reported CRM positivity rates of approximately 2.4% to 4.0%, depending on study period and case mix[16, 17]. Similarly, previous reports from the CTRC have demonstrated CRM positivity rates of around 2.8% [18]. These findings suggest that the surgical quality and oncologic outcomes observed in this nationwide registry are broadly comparable to those reported in other large international cohorts.

Threatened MRF on preoperative MRI was one of the most important predictors, consistent with previous studies showing that MRI-assessed MRF involvement is a key determinant of CRM status[15, 18, 20]. Tumors close to or involving the MRF are inherently more challenging to resect with an adequate radial margin. Many variables identified as important, including threatened MRF, advanced tumor stage, EMVI positivity, low tumor location reflected by ISR, and reduced expert supervision, are clinically expected risk factors. Thus, the value of the present analysis lies not in discovering entirely novel predictors, but in quantitatively integrating these factors and estimating their relative contribution within a large multicenter registry. The analysis does not establish superiority over expert clinical judgment or conventional multidisciplinary assessment; future studies should directly compare model-based prediction with standard clinical evaluation, ideally using decision-curve analysis.

Pathological N stage was also identified as a highly influential variable in the predictive models. Advanced nodal disease may reflect more aggressive tumor biology and deeper tumor infiltration, which can increase the likelihood of tumor extension toward the MRF[19]. In addition, metastatic mesorectal lymph nodes located near the outer mesorectal boundary may directly contribute to CRM positivity even when the primary tumor itself does not invade the mesorectal fascia. This mechanism may partially explain cases in which CRM positivity occurs despite technically adequate mesorectal excision.

ISR also appeared among the most important variables associated with CRM positivity in the SHAP analysis. However, this finding should be interpreted with caution. ISR is typically performed for very low rectal tumors, where the mesorectum becomes thinner and surgical dissection becomes more technically demanding. In our cohort, patients undergoing ISR had significantly lower tumor locations compared with those undergoing conventional resections, suggesting that ISR may act primarily as a surrogate marker of low tumor location and increased anatomical complexity rather than an independent causal factor. Previous studies have reported that when matched for tumor height and stage, ISR does not have higher CRM positivity than abdominoperineal resection and is oncologically safe[20–22]. Therefore, our findings should not be interpreted as indicating that ISR itself increases the risk of CRM positivity.

Several algorithms showed high apparent training performance but reduced validation discrimination, especially RF and KNN, consistent with overfitting in a rare-outcome setting. RSVM showed relatively stable apparent performance across datasets, but this should not be interpreted as definitive superiority over other approaches, particularly because LR achieved comparable validation discrimination.

The low incidence of CRM positivity was both a favorable clinical finding and a major methodological challenge. With only 45 positive events and multiple candidate predictors, the events-per-predictor ratio was low, increasing the risk of overfitting and imprecise performance estimation. Because the validation cohort contained few CRM-positive events and the AUC confidence intervals were wide, small differences in AUC between models should not be overinterpreted. In addition, optimism-corrected performance estimates were not available. The models should therefore be regarded as exploratory and hypothesis-generating rather than definitive clinical prediction tools. The low event rate also affected the clinical interpretation of positive predictions. In the validation cohort, the PPV of the RSVM model was only 0.10, meaning that approximately 9 of every 10 patients classified as high risk would be false positives. This low PPV substantially limits the clinical utility of positive model predictions and reinforces that the model should not be used as a standalone tool for treatment escalation or surgical planning.

Another notable finding in our analysis was the significant variability in CRM positivity rates across participating centers. This heterogeneity likely reflects differences in surgical expertise, institutional experience with taTME, patient selection, and pathological assessment practices. Although we did not observe a significant association between center case volume and CRM positivity, other unmeasured factors—such as surgeon experience, learning curve effects, or differences in multidisciplinary management—may contribute to these variations. Because center-level effects were not explicitly modelled, residual confounding related to institutional practice cannot be excluded. Such heterogeneity is common in large multicenter registry studies and highlights the importance of continuous quality monitoring and standardized training in the adoption of technically demanding surgical techniques.

The relatively low proportion of patients receiving neoadjuvant chemoradiotherapy also deserves consideration. In many settings, threatened CRM on preoperative imaging is an important indication for neoadjuvant therapy. However, treatment patterns varied across centers and over time, and primary surgery may have been selected for technically resectable tumors even with locally advanced features. Such real-world variation may have influenced CRM positivity patterns and should be considered when interpreting generalizability.

Several limitations should be acknowledged. First, this retrospective registry-based study had few CRM-positive events, no external validation, no optimism-corrected performance estimates, and only exploratory calibration assessment without quantitative calibration metrics. Second, missing data were present, particularly for MRI-derived variables, although multiple imputation was used. Third, CRM assessment was institution-dependent rather than centrally reviewed, and center-level effects were not incorporated into the models. Fourth, detailed standardized post-neoadjuvant MRI response variables, such as ymrCRM and ymrTRG, were not uniformly available. Fifth, the cohort was derived exclusively from Chinese centers, which may limit generalisability to other populations. Sixth, analyses were conducted in a fixed R 3.5.3 environment, which ensured internal consistency but may limit compatibility with current package versions. Finally, not all predictors were available before surgery: pathological T and N stages were postoperative variables, and ISR and intraoperative difficulty reflected intraoperative decision-making and technical complexity. Therefore, the current model should be interpreted as an exploratory analysis of factors associated with CRM positivity rather than as a preoperative surgical planning tool. Future studies should develop preoperative-only models using larger event numbers and independent external validation cohorts.

Despite these limitations, the study provides an exploratory, registry-based description of factors associated with CRM positivity after taTME. Its main value lies in confirming, within a large Chinese multicenter registry, the relative importance of clinically

plausible factors rather than establishing a deployable prediction tool. Whether machine learning-based modelling adds clinically meaningful value beyond standard multidisciplinary assessment remains uncertain and should be tested in future studies using preoperative-only variables and external validation.

In conclusion, exploratory machine learning models identified factors associated with CRM positivity after taTME in a nationwide multicenter registry. Threatened MRF on preoperative MRI, pathological nodal stage, and surgical complexity reflected by ISR were influential variables. Because the models included intraoperative and postoperative predictors and lacked external validation, they should not be considered preoperative decision-support tools. Further studies using exclusively preoperative predictors, larger numbers of CRM-positive events, and independent validation are required before clinical application.

Abbreviations

PPV, positive predictive value; NPV, negative predictive value; AUC, area under the receiver operating characteristic curve; CI, confidence interval; LR, logistic regression; ENET, elastic net; DT, decision tree; RF, random forest; XGBoost, extreme gradient boosting; RSVM, radial support vector machine; MLP, multilayer perceptron; KNN, k-nearest neighbors. AUC 95% CIs were estimated using the Hanley-McNeil method based on the observed AUC and the numbers of positive and negative cases in each cohort.

Declarations

Disclosures

Dr. Pengyu Wei, Cong Meng, Yang Li, Prof. Mingyang Ren, Hongyu Zhang, Hong Zhang, Quan Wang, Weidong Tong, Qing Xu, Chi Chung Foo, Yi Xiao, Chien-chih Chen, Hongwei Yao, and Zhongtao Zhang have no conflicts of interest or financial ties to disclose.

Funding:

This work was supported by grants from the Noncommunicable Chronic Diseases-National Science and Technology Major Project (2024ZD0520306); Program of Clinical Center for Colorectal Cancer of Capital Medical University (1192070313); Beijing Hospitals Authority Clinical Medicine Development of special funding support (ZLRK202302).

Author Contribution

P.W. drafted the manuscript, acquired data, and contributed to data interpretation; C.M. performed data analysis, prepared figures, and assisted in manuscript drafting; Y.L. critically reviewed and revised the manuscript, and supervised the CTRC database including data collection and liaison; H.Y. and Z.Z. critically reviewed and revised the manuscript, and initiated and led the CTRC database; All other authors contributed substantially to case registration (each registering >100 cases) and actively participated in national taTME academic conferences to promote regional development. All authors have approved the final version and meet the ICMJE authorship criteria.

Acknowledgement

Assistance with the study: The authors would like to express their gratitude to the following collaborators who contributed to the development and maintenance of the CTRC database: Zhongtao Zhang, Hongwei Yao, Chien-chih Chen, Gang Yu, Mingyang Ren, Xuanhua Yang, Hongyu Zhang, Qing Xu, Lei Gu, Quan Wang, Weihua Tong, Weidong Tong, Yi Xiao, Guole Lin, Yuanguang Chen, Hong Zhang, Yanan Wang, Aiwen Wu, Shuhua Li, Yong Li, Deqing Wu, Zhanlong Shen, Zhicong Fu, Feng Gao, Zhongshi Xie, Jianfeng Gong, Weidong Xiao, Yuhui Yang, Dan Ma, Dehai Xiong, Xuedong Xu, Qingtong Zhang, Jianbin Xiang, Jiagang Han, Xinxiao Li, Minhua Zheng, Guoqiang Su, Jingwang Ye, Jun You, Gang Liu, Jinlin Du, Peng Li, Yuru Zhang, Jun Li, Hao Zhang, Bo Feng, Ning Chen, Miao Wu, Yuan Gao, Jun Li, Yongbo An, Zenan Jin, Bowen Xu, Yishan Liu, Yang Li, Pengyu Wei.

Data availability

The CTRC registry contains patient-level data and is not publicly available. Deidentified data and analysis code may be available from the corresponding author upon reasonable request and institutional approval.

References

1. Heald RJ, Husband EM, Ryall RD (1982) The mesorectum in rectal cancer surgery–the clue to pelvic recurrence? Br J Surg 69(10):613–616. 10.1002/bjs.1800691019
2. Kang SB, Park JW, Jeong SY, Nam BH, Choi HS, Kim DW et al (2010) Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): short-term outcomes of an open-label randomised controlled trial. Lancet Oncol 11(7):637–645. 10.1016/S1470-2045(10)70131-5
3. Bonjer HJ, Deijen CL, Abis GA, Cuesta MA, van der Pas MH, de Lange-de Klerk ES et al (2015) A randomized trial of laparoscopic versus open surgery for rectal cancer. N Engl J Med 372(14):1324–1332. 10.1056/NEJMoa1414882
4. Jiang WZ, Xu JM, Xing JD, Qiu HZ, Wang ZQ, Kang L et al (2022) Short-term Outcomes of Laparoscopy-Assisted vs Open Surgery for Patients With Low Rectal Cancer: The LASRE Randomized Clinical Trial. JAMA Oncol 8(11):1607–1615. 10.1001/jamaoncol.2022.4079
5. Russell MC, You YN, Hu CY, Cormier JN, Feig BW, Skibber JM et al (2013) A novel risk-adjusted nomogram for rectal cancer surgery outcomes. JAMA Surg 148(8):769–777. 10.1001/jamasurg.2013.2136
6. Warrier SK, Kong JC, Guerra GR, Chittleborough TJ, Naik A, Ramsay RG et al (2018) Risk Factors Associated With Circumferential Resection Margin Positivity in Rectal Cancer: A Binational Registry Study. Dis Colon Rectum 61(4):433–440. 10.1097/DCR.0000000000001026
7. Cecil TD, Taffinder N, Gudgeon AM (2006) A personal view on laparoscopic rectal cancer surgery. Colorectal Dis. ;8 Suppl 3:30 –2. 10.1111/j.1463-1318.2006.01068.x
8. Sylla P, Rattner DW, Delgado S, Lacy AM (2010) NOTES transanal rectal cancer resection using transanal endoscopic microsurgery and laparoscopic assistance. Surg Endosc 24(5):1205–1210. 10.1007/s00464-010-0965-6
9. de Lacy FB, van Laarhoven J, Pena R, Arroyave MC, Bravo R, Cuatrecasas M et al (2018) Transanal total mesorectal excision: pathological results of 186 patients with mid and low rectal cancer. Surg Endosc 32(5):2442–2447. 10.1007/s00464-017-5944-8
10. Veltcamp Helbach M, Deijen CL, Velthuis S, Bonjer HJ, Tuynman JB, Sietses C (2016) Transanal total mesorectal excision for rectal carcinoma: short-term outcomes and experience after 80 cases. Surg Endosc 30(2):464–470. 10.1007/s00464-015-4221-y
11. Persiani R, Biondi A, Pennestri F, Fico V, De Simone V, Tirelli F et al (2018) Transanal Total Mesorectal Excision vs Laparoscopic Total Mesorectal Excision in the Treatment of Low and Middle Rectal Cancer: A Propensity Score Matching Analysis. Dis Colon Rectum 61(7):809–816. 10.1097/DCR.0000000000001063
12. Park SC, Sohn DK, Kim MJ, Chang HJ, Han KS, Hyun JH et al (2018) Phase II Clinical Trial to Evaluate the Efficacy of Transanal Endoscopic Total Mesorectal Excision for Rectal Cancer. Dis Colon Rectum 61(5):554–560. 10.1097/DCR.0000000000001058
13. Galvez A, Biondo S, Trenti L, Espin E, Kraft M, Farres R et al (2023) Prognostic Value of the Circumferential Resection Margin After Curative Surgery for Rectal Cancer: A Multicenter Propensity Score-Matched Analysis. Dis Colon Rectum 66(7):887–897. 10.1097/dcr.0000000000002294
14. Birbeck KF, Macklin CP, Tiffin NJ, Parsons W, Dixon MF, Mapstone NP et al (2002) Rates of circumferential resection margin involvement vary between surgeons and predict outcomes in rectal cancer surgery. Ann Surg 235(4):449–457. 10.1097/00000658-200204000-00001
15. Collins GS, Reitsma JB, Altman DG, Moons KG (2015) Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. BMJ 350:g7594. 10.1136/bmj.g7594
16. Penna M, Hompes R, Arnold S, Wynn G, Austin R, Warusavitarne J et al (2017) Transanal Total Mesorectal Excision: International Registry Results of the First 720 Cases. Ann Surg 266(1):111–117. 10.1097/SLA.0000000000001948

17. Roodbeen SX, de Lacy FB, van Dieren S, Penna M, Ris F, Moran B et al (2019) Predictive Factors and Risk Model for Positive Circumferential Resection Margin Rate After Transanal Total Mesorectal Excision in 2653 Patients With Rectal Cancer. Ann Surg 270(5):884–891. 10.1097/SLA.0000000000003516
18. Yao H, An Y, Zhang H, Ren M, Chen CC, Xu Q et al (2021) Transanal Total Mesorectal Excision: Short-term Outcomes of 1283 Cases from a Nationwide Registry in China. Dis Colon Rectum 64(2):190–199. 10.1097/DCR.0000000000001820
19. Lau S, Kong J, Bell S, Heriot A, Stevenson A, Moloney J et al (2021) Transanal mesorectal excision: early outcomes in Australia and New Zealand. Br J Surg 108(2):214–219. 10.1093/bjs/znaa098
20. Du Q, Yang W, Zhang J, Qiu S, Liu X, Wang Y et al (2024) Oncologic outcomes of intersphincteric resection versus abdominoperineal resection for lower rectal cancer: a systematic review and meta-analysis. Int J Surg 110(4):2338–2348. 10.1097/js9.0000000000000205
21. Wang GC, Chen JX, Pan HF, Ye K, Guo YC, Huang Y (2025) Long-term efficacy and short-term outcomes of intersphincteric resection vs abdominoperineal resection in patients with ultra-low rectal cancer. World J Gastroenterol 31(29):110004. 10.3748/wjg.v31.i29.110004
22. Shin JK, Kim HC, Lee WY, Yun SH, Cho YB, Huh JW et al (2022) Sphincter-saving surgery versus abdominoperineal resection in low rectal cancer following neoadjuvant treatment with propensity score analysis. Surg Endosc 36(4):2623–2630. 10.1007/s00464-021-08558-z

Figures

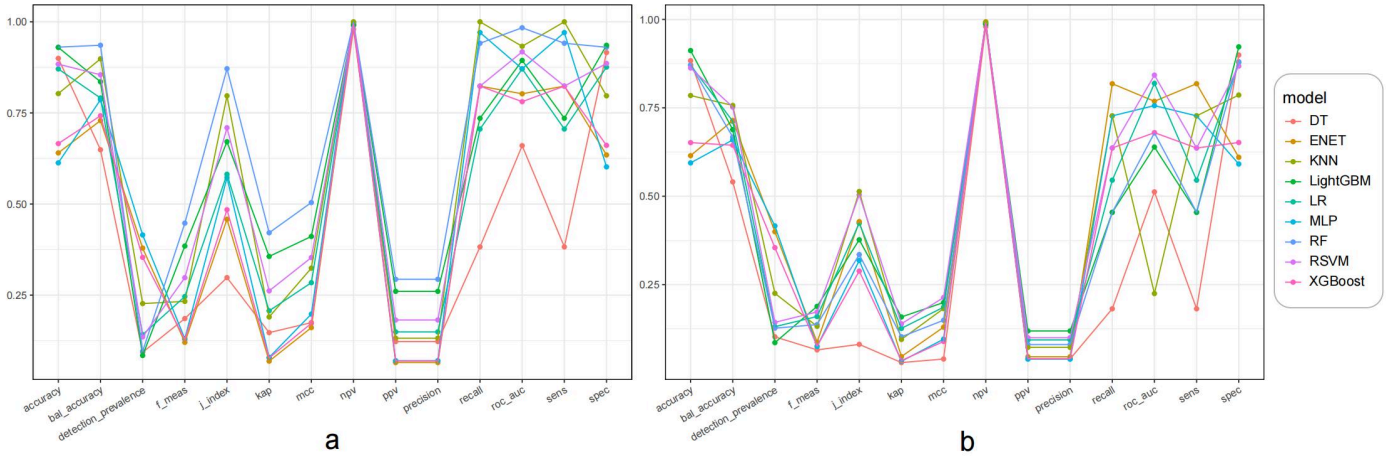


Figure 1

Parallel coordinate plots showing performance parameters for each model. (a) training set, (b) validation set.

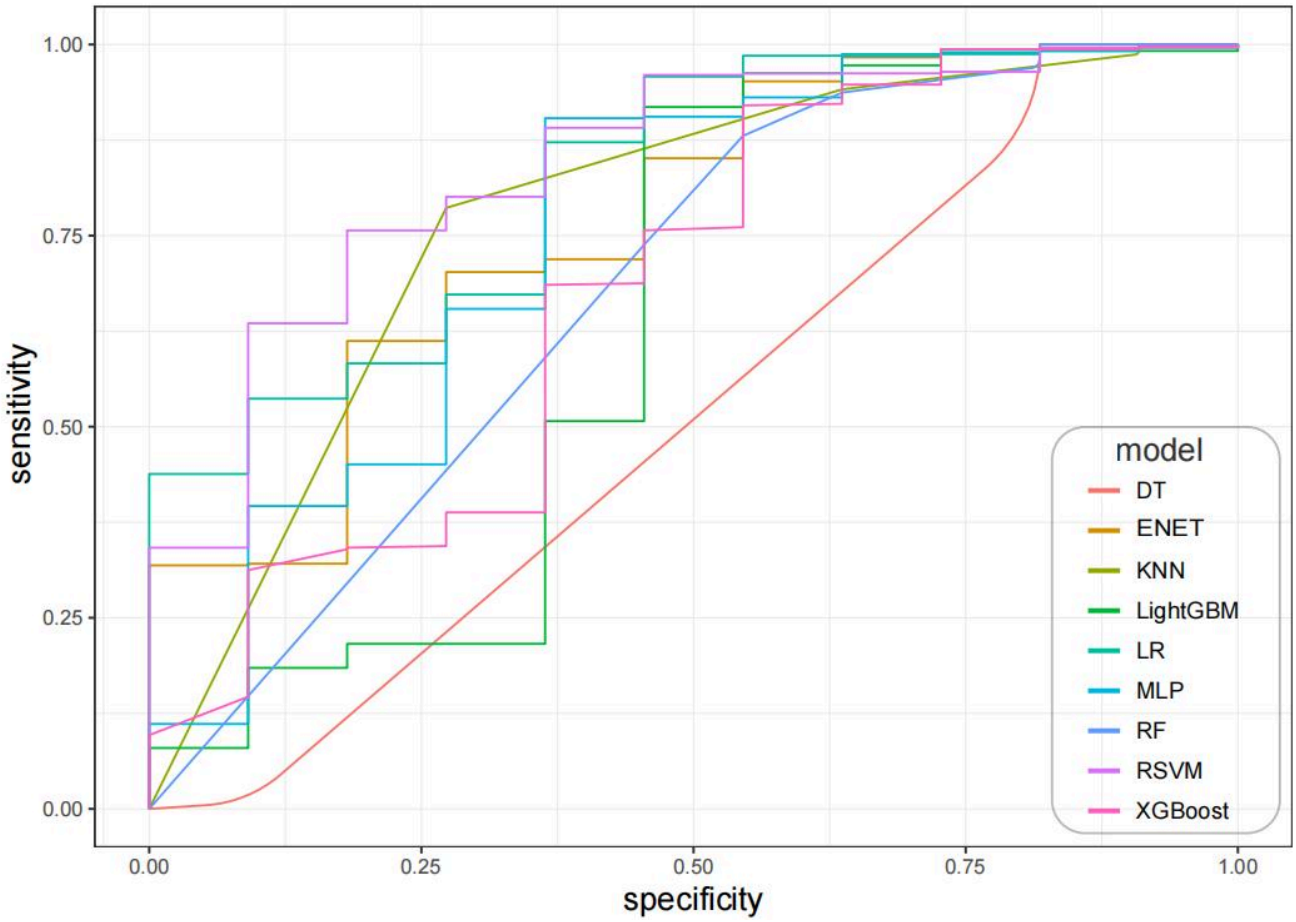


Figure 2

Receiver operating characteristic (ROC) curves for the nine models in the validation set.

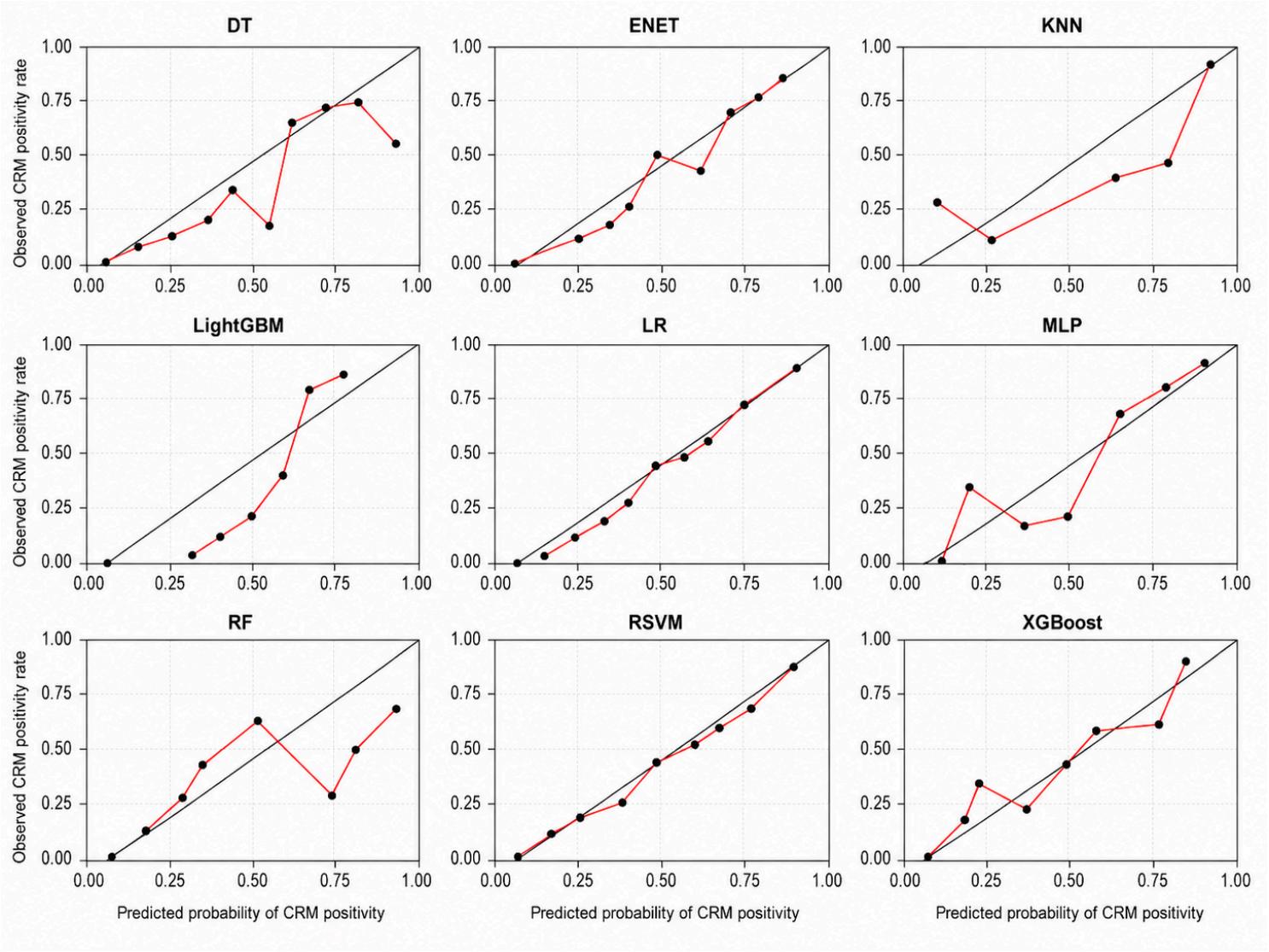


Figure 3

Exploratory grouped calibration plots of the nine prediction models. The x-axis represents the mean predicted probability of CRM positivity, and the y-axis represents the observed CRM positivity rate across grouped predictions. The diagonal line indicates perfect calibration. Both axes are presented on a 0–1 probability scale. Because of the limited number of CRM-positive events and the absence of quantitative calibration metrics, these plots should be interpreted as exploratory rather than definitive calibration assessment. CRM, circumferential resection margin.

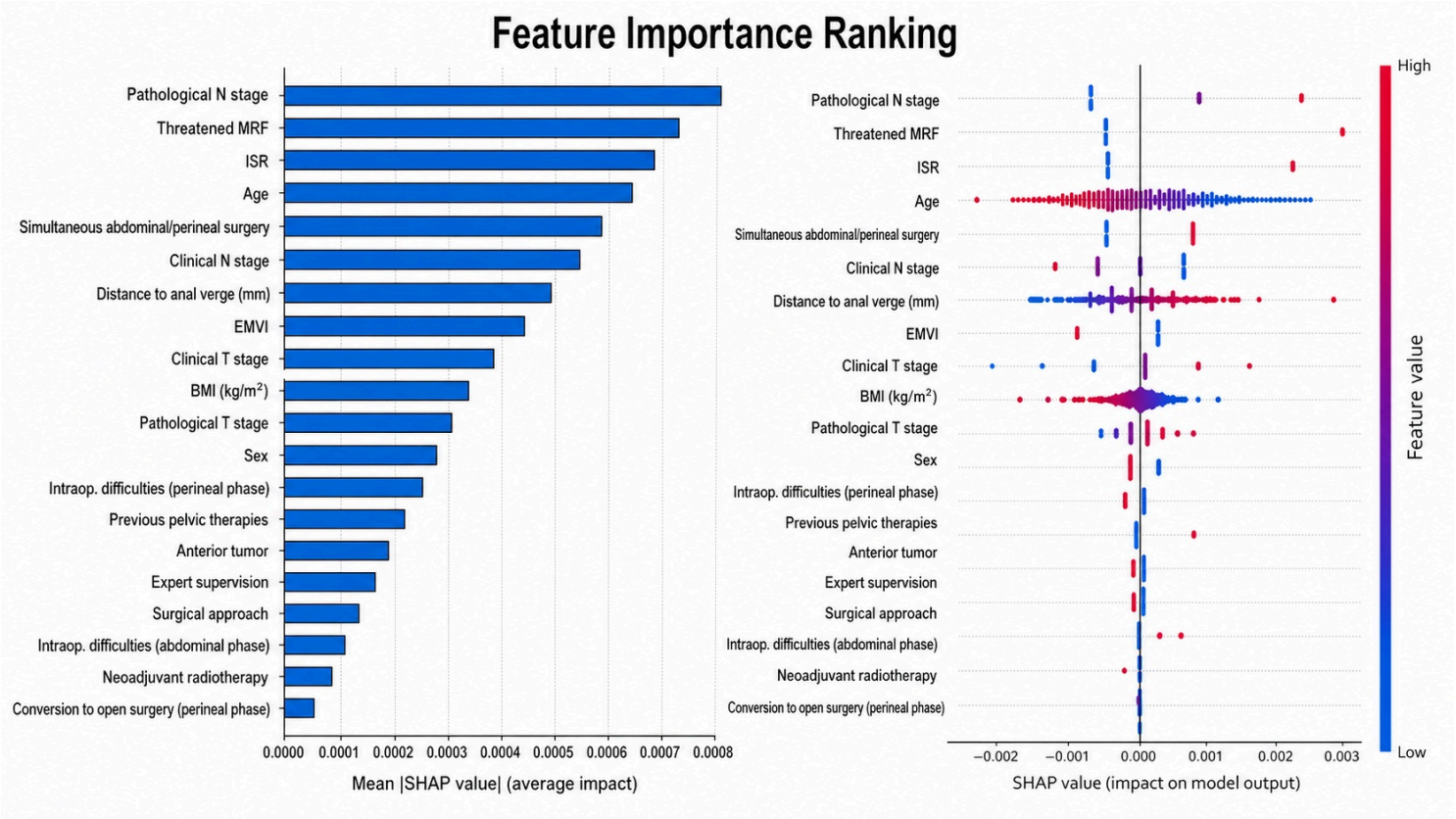


Figure 4

SHAP-based feature importance analysis for CRM positivity prediction using the RSVM model. The left panel shows the mean absolute SHAP value of each variable, representing its average impact on model output. The right panel shows the SHAP summary plot, in which each point represents an individual patient. The horizontal axis indicates the SHAP value, and the color gradient represents feature value from low to high. Full clinical variable names or standard abbreviations are displayed to improve interpretability. CRM, circumferential resection margin; RSVM, radial support vector machine; SHAP, SHapley Additive exPlanations; MRF, mesorectal fascia; EMVI, extramural vascular invasion; ISR, intersphincteric resection.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryMaterials.docx
- TRIPODchecklist.pdf