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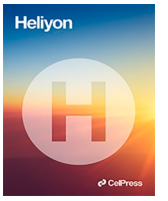

Research article

Development and validation of an MRI and clinicopathological factors prediction model for low anterior resection syndrome in anterior resection of middle and low rectal cancer

Zheng Wang [a,1], Chuanji Zhou [b,1], Linghou Meng [c,**], Xianwei Mo [c,*], Dong Xie [a], Xiaoliang Huang [c], Xinxin He [c], Shanshan Luo [c], Haiquan Qin [c], Qiang Li [a], Shaolv Lai [a]

[a] Medical Imaging Center, Guangxi Medical University Cancer Hospital, Nanning, Guangxi, China
[b] Department of Radiology, The Second Affiliated Hospital of Hainan Medical University, Haikou, China
[c] Department of Colorectal and Anal Surgery, Guangxi Medical University Cancer Hospital, Nanning, Guangxi, China

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ABSTRACT

Objective: To validate the predictive power of newly developed magnetic resonance (MR) morphological and clinicopathological risk models in predicting low anterior resection syndrome (LARS) 6 months after anterior resection of middle and low rectal cancer (MLRC).

Methods: From May 2018 to January 2021, 236 patients with MLRC admitted to two hospitals (internal and external validation) were included. MR images, clinicopathological data, and LARS scores (LARSS) were collected. Tumor morphology data included longitudinal involvement length, maximum tumor diameter, proportion of tumor to circumference of the intestinal wall, tumor mesorectal infiltration depth, circumferential margin status, and distance between the tumor and anal margins. Pelvic measurements included anorectal angle, mesenterial volume (MRV), and pelvic volume. Univariate and multivariate logistic regression was used to obtain independent risk factors of LARS after anterior resection Then, the prediction model was constructed, expressed as a nomogram, and its internal and external validity was assessed using receiver operating characteristic curves.

Results: The uni- and multivariate analysis revealed distance between the tumor and anal margins, MRV, pelvic volume, and body weight as significant independent risk factors for predicting LARS. From the nomogram, the area under the curve (AUC), sensitivity, and specificity were 0.835, 75.0 %, and 80.4 %, respectively. The AUC, sensitivity, and specificity in the external validation group were 0.874, 83.3 %, and 91.7 %, respectively.

Conclusion: This study shows that MR imaging and clinicopathology presented by a nomogram can strongly predict LARSS, which can then individually predict LARS 6 months after anterior resection in patients with MLRC and facilitate clinical decision-making.

Clinical relevance statement: We believe that our study makes a significant contribution to the literature. This method of predicting postoperative anorectal function by preoperative measurement of MRV provides a new tool for clinicians to study LARS.

* Corresponding author. Department of Colorectal and Anal Surgery, Guangxi Medical University Cancer Hospital, Nanning, Guangxi, China
** Corresponding author.
E-mail addresses: linghou_meng@163.com (L. Meng), mo_xianwei@126.com (X. Mo).
[1] Zheng Wang and Chuanji Zhou contribute equally to the article.

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Abbreviations

ADC	Apparent diffusion coefficient
AFP	Alpha fetoprotein
APR	abdominal perineal resection
AUC	Area under the receiver operating characteristic curve
CEA	Carcinoembryonic antigen
CA19-9	Carbohydrate antigen 19-9
CA125	Cancer antigen 125
CA153	Cancer antigen 153
CDTI	clock position of the deepest position of tumor invasion
CRM	Circumferential resection margin
C-index	Concordance index
DCE-MRI	Dynamic contrast-enhanced magnetic resonance imaging
DMRF	deepest tumor invasion and mesorectal fascia
DWI	Diffusion-weighted imaging
EMVI	extramural vascular invasion
ESMO	European Society of Medical Oncology
ICC	intraclass correlation coeffcients
ISR	intersphincteric resection
LARC	locally advanced rectal cancer
LARS	low anterior resection syndrome
LARSS	low anterior resection syndrome scores
LVI	Lymphovascular invasion
MRI	Magnetic resonance imaging
MLRC	middle and low rectal cancer
MAE	Mean absolute error
mrTstage	Magnetic resonance imaging T stage
MRV	mesenterial volume
NCCN	National Comprehensive Cancer Network
NCRT	Neoadjuvant chemoradiotherapy
NEX	Number of excitation
PNI	Perineural invasion
PVV	Pelvic volume
ROI	Region of interest
ROC	Receiver operating characteristic
T2WI	T2-weighted imaging
T1WI	T1-weighted imaging
TR	Repetition time
TE	Echo time
TME	total mesorectal excision
ULAR	ultra-low anterior resection

1. Introduction

With the continuous progress of surgical instruments and the popularization of total mesorectal resection (TME), the 5-year survival rate after middle and low rectal cancer (MLRC) surgery has reached about 70 % [1]. Preserving anal appearance and function section have become common requirements for patients' quality of life.Thus, tumor location is no longer a factor limiting radical anterior resection for low rectal cancer.

However, retaining the anus is not sufficient to retain normal fecal discharge function, especially after a previous anterior resection in MLRC patients with changes in pelvic floor structure, ampullectomy of the rectum, and sphincter and nerve tissue damage. The postoperative patients can present with a series of symptoms, such as increased defecation frequency, emergency defecation, difficulty in defecation, and urinary incontinence. Clinically referred to as low anterior resection syndrome (LARS) [2–4], the above symptoms seriously affect the survival and quality of life after surgery and cause a huge physical, psychological, and social burden. Therefore, the prediction of the occurrence and severity of postoperative LARS symptoms after anterior resection patients of MLRC may help reduce adverse factors related, reduce the risk of postoperative LARS, and improve the quality of life and survival [5–7]. In clinical practice, LARS assessment after anterior resection for MLRC mainly relies on the low anterior resection syndrome scores (LARSS) scale, which allows for the assessment of the severity of LARS, but only postoperatively. To date, the adverse factors of LARS can be predicted behind surgery [6–8]; however, preoperative predictions would help clinicians during the perioperative period to choose the

best-individualized treatment option [5,9,10].

Medical image evaluation is a trending topic in precision medicine. Medical imaging technology can provide a considerable amount of noninvasive information regarding pre-treatment evaluation and prediction of a curative effect to guide clinical practice, including treatment efficacy prediction, and post-treatment dynamic follow-up of rectal cancer patients. Medical imaging technology, including X-ray barium agent enterography, CT, MRI, and PET/CT. MRI is among the first choices for pre-treatment evaluation and is the standard preoperative imaging examination method for rectal cancer. However, few studies have investigated the relationship between quantitative imaging indicators of baseline MRI and LARS after anterior resection surgery in patients with MLRC. Previous clinical studies on LARS of MLRC after anterior resection have shown that the changes in new bowel volume, compliance, anal pressure, and perianal sphincter integrity are significant baseline imaging indicators to predict the severity of postoperative LARS [8, 11–13]. Recent studies have shown that surgeons cannot objectively predict the level of difficulty of laparoscopic surgery based only on preoperative MRIs. Further, pelvic volume assessment could provide an objective method for determining the refractory surgical pelvis [14,15]. Whether there are sensitive imaging indicators for LARS is an interesting topic [16,17]. If pre-surgical MRI could be used to predict LARS, such a model would deepen the understanding of LARS' adverse influencing factors and reduce its incidence and severity.

The objective of this study is to conduct a character preoperative consent procedure (1) to discover risk factors for preoperative bowel functional disorders. Based on the LARS score and (2), a predictive exemplar was developed where the elementary LARS can be made in clinical experience using personalized information for patient consent or during preoperative patient conversation.

2. Patients and methods

2.1. Patients

This retrospective study was approved by the Ethics Review Committee of hospital(Ethical review number: KY2024516), and all patients informed consent requirement was waived.The protocol was in accordance with the Declaration of Helsinki. The training group included patients diagnosed with rectal cancer in the Colorectal and Anal Surgery Department of the Cancer Hospital of Guangxi Medical University from May 2018 to January 2021. The external validation group was comprised of patients diagnosed with rectal cancer in the Colorectal and Anal Surgery Department of the Second Affiliated Hospital of Hainan Medical University during the same period. Baseline characteristics, including demographic data, laboratory findings, pretreatment MRI data, and pathological findings, were obtained from clinical records. The following inclusion/exclusion criteria were applied:

Inclusion criteria: (1) MLRC diagnosed by digital rectal examination and colonoscopy; (2) the patient underwent rectal MRI within

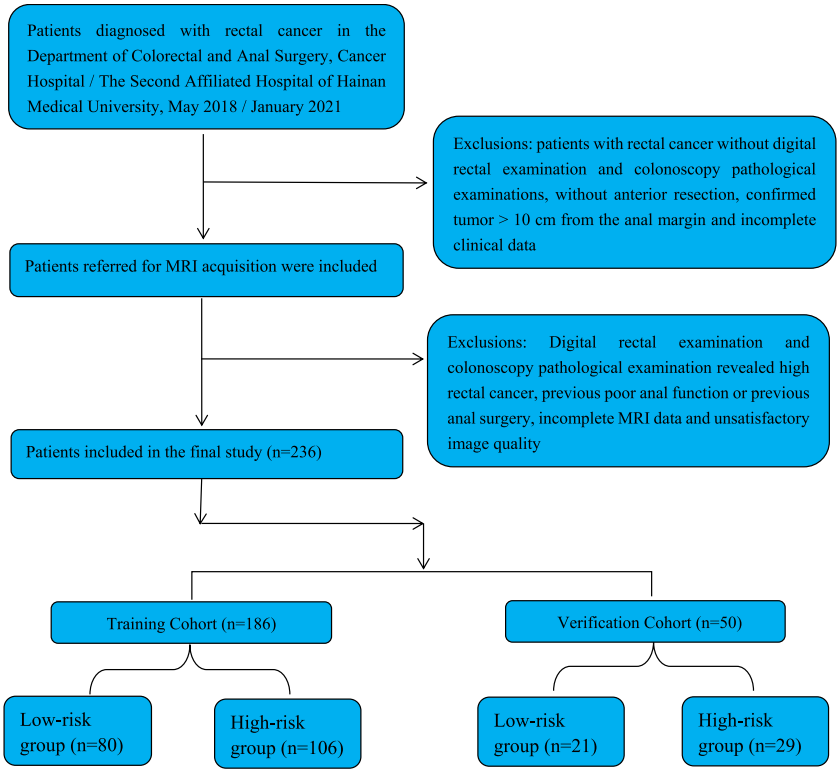

Fig. 1. Flowchart of the study population.

two weeks before surgery; (3) the patient did not any anti-tumor treatment before anterior resection,; (4) the clinical data were complete.

Exclusion criteria: (1) postoperative tumor confirmed >10 cm from anal margin, diagnosis of high rectal cancer, or accompanied by obvious bleeding, obstruction, perforation, and other conditions; (2) preoperative non-operative anti-tumor treatment, or failure to perform anterior resection; (3) previously poor anal function or previous anal surgery; (4) MRI incomplete or unsatisfactory image quality; (6) incomplete clinical, laboratory, or pathological data.

Using the above inclusion and exclusion criteria, 236 patients were included, with 186 in the colorectal and anal surgery department of Cancer Hospital of Guangxi Medical University (internal training cohort) and 50 in the colorectal and anal surgery department of The Second Affiliated Hospital of Hainan Medical University (external validation cohort). The training and validation cohort met the grouping criteria of 7:3 (Fig. 1).

2.2. Postoperative follow-up

All patients underwent anterior resection. To eliminate the influence of diet, postoperative pain, and other factors on patient defecation, the follow-up time, including telephone and outpatient visits, was 6 months after surgery. Patients requiring postoperative chemotherapy were followed up one week after the end of chemotherapy to eliminate the effects of chemotherapy on intestinal function as much as possible. The LARSS comprised five questions and a total score of 42; 0–20 was evaluated as no LARS, 21–29 as mild LARS, and 30–42 as severe LARS [18–20]. We divided the patients into the low- (0–29) and high-risk (30–42) of LARS groups.

2.3. MRI procedure and imaging analysis

The MRI field strengths, scanning sequence settings, and scanning parameter setups of the two research institutions were similar. MRI examination of rectal cancer patients was performed according to the following procedure: a DISCOVERY MR750W 3.0 T scanner with a 16-channel body phase-controlled front coil (GE Corporation, Boston, MA, USA) was used to acquire the MRIs. Full bowel preparation was required before the examination. The patients lay supine on the examination bed, using the advanced foot method. The symphysis pubis was used as the coil center, and the body phased array coil was placed before and after the patient's pelvic cavity so that the umbilicus was consistent with the center of the coil. The coil was taped in front of the pelvic cavity to bring it close to the pelvis and minimize abdominal breathing during the examination. At the end of the first scan phase, the contrast agent gadolinium was injected immediately through the cubital vein mass and then enhanced 20 s later in the second to sixth phases. The scan time of each phase was 1 min. After the injection, the tubes were washed with normal saline at the same flow rate. The MR scanning order and parameters are presented in Table 1 respectively Table 2.

2.4. MRI morphological measurements

2.4.1. Tumor morphology

The tumors were evaluated in multiple ways in the transverse, sagittal, coronal, or oblique positions, and the main observation sequences were T1WI, T2WI, and T1WI contrast-enhanced sequences, among which the cancer foci observed on T2WI were relatively clear. The morphological indices measured in this study were as follows and are summarized in Fig. 2.

Tumor location from anal verge: First, look for the lowest edge of the tumor on the sagittal section, and then measure the distance from the lower edge of the tumor to the anal margin along the central axis of the rectum. If the tumor invades the perianal region, the distance is 0. To improve readability, the "tumor location," namely, the distance between the lower tumor margin and the anal margin, was recorded(Fig. 2A).

Tumor length: Longitudinal involvement length of the tumor along the central axis of the intestinal lumen. If the tumor was discontinuous, its length was measured separately and added(Fig. 2B).

Tumor diameter: Maximum diameter of the tumor(Fig. 2C).

Tumor proportion of intestinal wall: Proportion of the tumor to the circumference of the intestinal wall divided into 4°: 0–25 %, 26–50 %, 51–75 %, 76–100 %(Fig. 2D).

Mesorectal extension depth(MED): Tumor mesorectal infiltration depth(Fig. 2E).

Circumferential resection margin(CRM): defined as the tumor edge, metastatic lymph node or cancer nodules <1 mm from the mesorectal fascia or invasion thickening, interruption, and enhancement(Fig. 2F).

Tumor volume: After calculating the length, width, and height of each pixel block in the ROI, the volume of a single-pixel block was obtained. Finally, the volume of all pixel blocks in the ROI was added to obtain the volume of the entire tumor.

Table 1
Guangxi Medical University Cancer Hospital Department of Radiology MR scanning order and parameters.

	TR	TE	Floor thickness	Spacing	Margin	Corner	Margin	Matrix	NEX	B value
T1WI	877 ms	11 ms	5 mm	1 mm	5 mm		28 cm	256 × 256	1	
T2WI	3720 ms	96 ms	5 mm	1 mm	5 mm		28 cm	256 × 256	1	
DWI	9000 ms	86 ms	3 mm	1 mm	0.3 mm		224 × 260	317 × 350	4	0、800/mm^2
DCE-MRI	4.0 ms	1.4 ms	2 mm	1 mm	0.2 mm	9°	317 × 350	203 × 320	2	

Table 2
The Second Affiliated Hospital of Hainan Medical University Haikou Department of Radiology MR scanning order and parameters.

	TR	TE	Floor thickness	Spacing	Margin	Corner	Margin	Matrix	NEX	B value
T1WI	877 ms	11 ms	5 mm	1 mm	5 mm		28 cm	256 × 256	1	
T2WI	3880 ms	97 ms	3 mm	0.3 mm	5 mm		28 cm	256 × 256	2	
DWI	11700 ms	86 ms	3 mm	0.3 mm	0.3 mm		224 × 260	317 × 350	4	0、1000/mm^2
DCE-MRI	4.39 ms	1.4 ms	3 mm	0 mm	0.2 mm	9°	317 × 350	203 × 320	1	

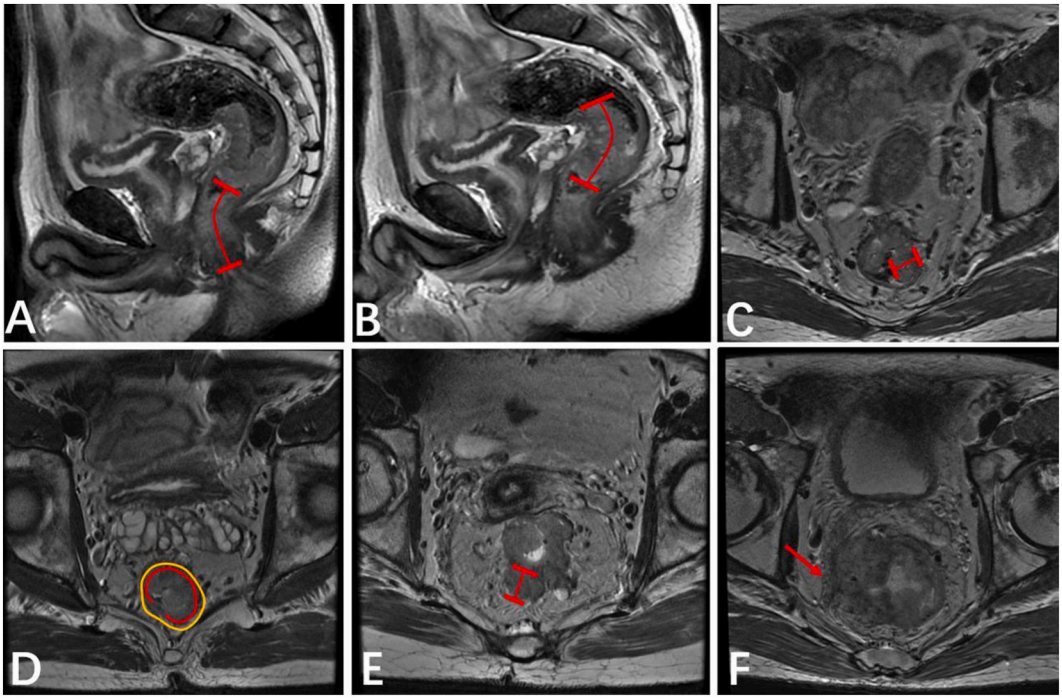

Fig. 2. Tumor morphology detected on magnetic resonance images. (A) Tumor location from anal verge. (B)Tumor length. (C) Tumor diameter. (D) Tumor proportion of intestinal wall. The red line outlines part of the tumor, and the yellow color represents the whole intestinal wall. (E) Mesorectal extension depth: (F) Circumferential resection margin (red arrow).

2.4.2. Pelvic measurements

The open-source software ITK-SNAP was used for volume outlining, resulting in a Region of Interest (ROI) model with a 3D volume. Subsequently, Python was employed for volume calculation. After loading the SimpleITK and Numpy packages, the outlined ROI was imported, and the length, width, and height of each pixel block within the ROI were calculated to determine the volume of a single pixel block. Finally, the volumes of all pixel blocks in the ROI were summed to obtain the overall volume of the ROI. The ROI was interpreted by two radiologists with more than 3 years of experience in diagnostic MRI for gastrointestinal diseases, who manually outlined the ROI of the rectal tumor at each level. The tumor area was defineddefned as a slightly higher signal on T2WI, which was different from the adjacent intestinal wall. The finalfnal decision was made by a senior radiologist with 8 years of experience in segmentation validation and calculating intraclass correlation coefficients (ICC).The morphological indices measured in this study were as follows and are summarized in Figs. 3 and 4.

Anorectal angle (ARA): between the long axis of the anal canal and the tangent of the posterior rectal wall(Fig. 3)

Mesorectal volume (MRV): a layer-by-layer outline strategy was utilized, where the upper boundary was set at the peritoneal reflection and the lower boundary was set at the disappearance of the mesorectal fascia. Additionally, the intestinal lumen, intestinal wall, pelvic floor muscles, and tumors were excluded from the outline (Fig. 4A.4B).

Pelvic volume (PVV): following the measurement method of the mesorectum volume, refers to the area of high fat signal within the true pelvis. The upper boundary of the outline is the line between the peritoneal back fold and the lower edge of the S1 vertebra, the lower boundary of the disappearance of the mesorectal fascia, the anterior boundary of the uterus or posterior edge of the prostate, and the posterior boundary of the sacrum. Notably, the intestinal tract, pelvic floor muscles, and tumors are not included within the outline range(Fig. 4C.4D.

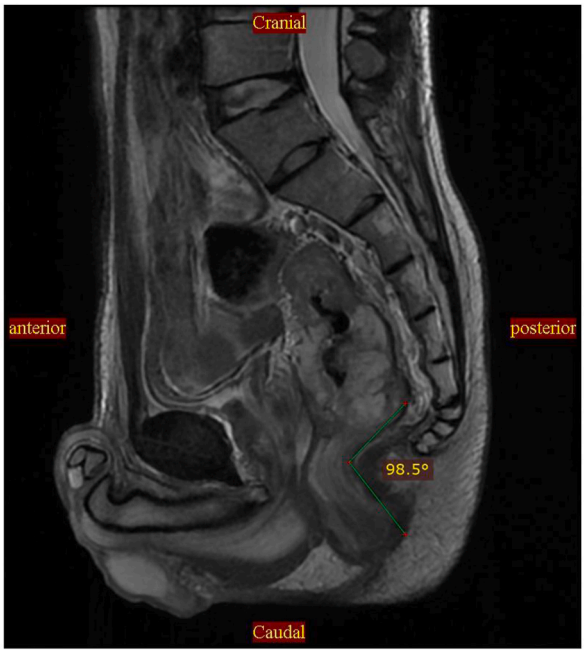

Fig. 3. Illustration of how the anorectal angle is measured in the sagittal plane on T2-weighted images: The reference line is drawn horizontally between the sacrum and the lower border of the pubic bone at the junction of the anus and rectum. The anorectal angle is measured on the sagittal plane of the T2-weighted image and is defined as the angle between two tangent lines: one tangent to the posterior wall of the anal canal and the other tangent to the posterior wall of the rectum.

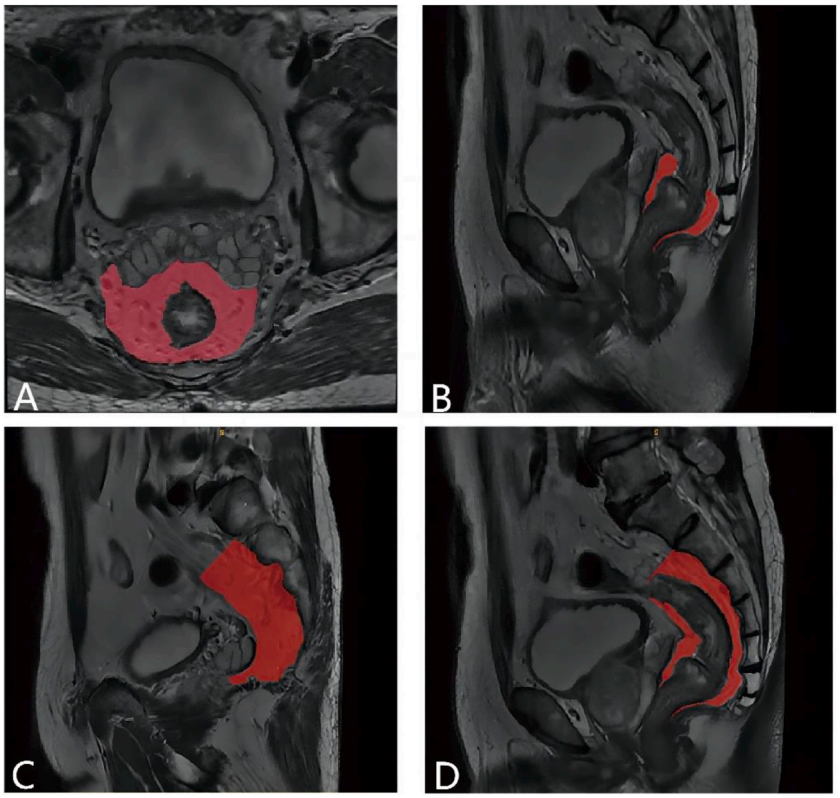

Fig. 4. The outline range of MRV in the transverse plane (A) and); sagittal plane (B); the outline range of PVV in the sagittal plane (C, D).

2.5. Statistical methods and prediction model nomograms

Statistical analyses were performed using SPSS 21.0 and R software (version 4.0.1, http://www.r-project.org). Image analysis was done using R software, GraphPad Prism 8.3.0, and Medcalc 18.2.1. Data were tested for normality and homogeneity of variance. Data that are (approximately) normally distributed are expressed as mean and standard deviation (mean ± SD). Comparisons between the groups were performed by using t-tests. Non-normally distributed data or data with variance inhomogeneity are expressed as the median and interquartile range (P25, P75). Multiple independent sample means were compared using a one-way ANOVA. Pairwise comparisons between the groups were made using Fisher's LSD method. Countable data are expressed as rates or percentages. Comparisons of two or more independent samples were conducted using the chi-square test or Fisher's exact probability method. The rank sum test was used for data without a normal distribution. Associations were analyzed using Pearson correlations, and the linear relationship between one continuous variable and multiple other variables was analyzed using logistic regression.

Variables with $P < 0.05$ in univariate analyses were used as candidates for multivariate logistic regression analysis. Stepwise backward regression was used to select LARS-independent predictor variables and establish a nomogram of the prediction model. Tolerance and variance inflation factors were used to assess the multicollinearity of the nomogram. The index of the receiver operating characteristic (ROC) was drawn to determine the cutoff value of the nomogram, and the area under the curve (AUC) was calculated to quantify the diagnostic efficacy of the nomogram. The calibration and fit of the nomogram were assessed by calibration curves and the Hosmer-Lemeshow test. The decision curve was created using the "dca.R" package. The statistical significance threshold was set at $P < 0.05$.

3. Results

3.1. Data analysis of the training group

A total of 186 patients were included in the training group. Among them, 80 patients were in the low-risk group (0–29 points) according to the LARSS, and 106 in the high-risk group according to the LARSS (30–41 points). Twenty-nine indicators were included clinicopathological and Morphological indicators, including age, gender, height, weight, BMI, CEA, CA199, TNM, cancer nodules (tumor deposits), tumor differentiation, tissue type, tumor volume, P53, Ki67, perineural invasion (PNI), and lymphovascular invasion (LVI) status.

Univariate Cox regression produced one clinicopathological indicator (body weight) with a significant predictive value. After ROC analysis, the cutoff value was 53 kg, and a smaller weight was associated with a higher risk (HR: 1.971 (0.998–3.897)). Subsequently, this body weight was included in the multivariate Cox regression model. Body weight was significant ($P = 0.094$) and thus included in the LARS prediction model.

After Cox regression of the tumor morphological index, the only significant univariate variable was tumor location, with a cutoff value of 7.4 cm. The risk distance between the tumor location from anal verge (HR: 16.969) (8.175–35.221). In the multivariate Cox regression model, tumor location was significant ($P < 0.001$) and thus included in the LARS prediction model.

After Cox regression of the pelvic measurements, mesorectal volume and pelvic volume were significant univariate variables, with a cutoff value of 47.99 cm^3 and 282.6 cm^3, respectively. Smaller mesorectal and pelvic volumes were associated with a higher risk (HR: 3.444 (1.734–6.452) and HR: 2.939 (1.562-5-534), respectively). Both variables were then included in the multivariate Cox regression model. Mesorectal and pelvic volumes were significant ($P = 0.002$, $P = 0.001$, respectively). Therefore, mesorectal and pelvic volumes were included in the LARS prediction model. The result are presented in Table 3 respectively Table 4.

3.2. Construction and evaluation of the nomograms

Multivariate logistic regression analysis revealed body weight, tumor location, MRV, and PVV as independent influencing factors of LARS. After the "predict" function calculation, the constructed logistic regression model is 19.23 %, which indicates that the model has good predictive efficacy. The variance expansion factor values for each independent risk factor were: body weight: 1.01, tumor location: 1.02, MRV: 1.06, and PVV: 1.07. Each independent variance expansion factor is < 10, and the corresponding tolerance is > 0.1, indicating that the multiple correlations do not affect the estimate of least squares, meaning that the results of the logistic regression are credible. The C-index of the nomogram model was 0.899. The AUC under the ROC curve was 0.835, with a sensitivity of 75.0 % and a specificity of 80.4 %. The results of the calibration curve revealed that the observation estimated by the nomogram fell around the line 45 slope, and the mean absolute error (MAE) was 0.021, indicating that the nomogram is also well calibrated in the external validation group. In the quantitative evaluation of the calibration degree, we obtained a Brier score of 0.129, indicating that the nomogram prediction model has good calibration ability without overfitting. The morphological indices measured in this study were as follows and are summarized in Figs. 5 and 6.

3.3. Nomogram validation

Internal validation using the Bootstrap method (1000 iterations) revealed largely constant results across iterations. The corresponding calibration curve is shown in Fig. 6. The AUC in the external validation group was 0.874, with a sensitivity of 83.30 % and a specificity of 91.70 %. The MAE of the nomogram in the calibration curve was 0.035, indicating that the nomogram was well-calibrated in the validation group (Fig. 6). The Hosmer-Lemeshow test revealed $P = 0.150$, indicating that there was no overfitting.

Table 3
Clinicopathological and imaging characteristics of patients.

Characteristics	Min-Max	Median	Mean ± SD/n%	P Value*
Age (years, mean ± SD)	30–85	60	59.99±10.37	$P = 0.918$
Gender(%)				$P = 0.158$
Male			110(59.2 %)	
Female			76(40.8 %)	
Height (cm)	138–180	160.5	160.9±7.62	$P = 0.109$
Weight (kg)	39–85	58.7	59.0±8.89	$P = 0.049$*
BMI (kg/m^2)	14.71–32.44	22.53	22.6±2.96	$P = 0.283$
Triglycerides (mmol/L)	0.40–8.18	1.22	1.43±0.91	$P = 0.934$
≤1.7(Normal)			147(79.1 %)	
>1.7(Abnormal)			39(20.9 %)	
Total cholesterol (mmol/L)	1.97–10.08	4.97	5.07±1.15	$P = 0.182$
≤5.18(Normal)			108(58.1 %)	
>5.18(Abnormal)			78(41.9 %)	
LDL (mmol/L)	0.53–7.71	3.12	3.14±1.01	$P = 0.150$
≤3.12(Normal)			95(51.1 %)	
>3.12(Abnormal)			91(48.9 %)	
HDL (mmol/L)	0.35–2.41	1.22	1.26±0.35	$P = 0.486$
≥1.16(Normal)			110(59.2 %)	
<1.16(Abnormal)			76(40.8 %)	
MRV (cm^3)	6.81–94.03	39.58	41.80±17.39	$P < 0.019$*
PVV(cm^3)	102.6–438.4	256.10	260.97±44.18	$P = 0.017$*
Tumor length(cm, mean ± SD)	1.6–12.0	4.76	4.87±1.80	$P = 0.884$
Tumor location from anal verge (cm, mean ± SD)	0–15	6.98	7.09±3.17	$P < 0.001$*
ARA (°)	90.51–159.55	128.47	128.06±12.63	$P = 0.743$
MED(cm)	0–1.75	0.36	0.36±0.37	$P = 0.820$
Tumor diameter (cm, mean ± SD)	1.6–12.0	4.76	4.87±1.80	$P = 0.884$
Tumor volume(cm^3)	0.72–97.08	12.77	16.90±15.74	$P = 0.396$
CRM			173(93.1 %)	$P = 0.812$
Negative			13(6.9 %)	
Positive				
Tumor proportion of intestinal wall (%)			7(3.7 %)	$P = 0.125$
0–25 %			60(32.3 %)	
26–50 %			68(36.6 %)	
51–75 %			51(27.4 %)	
76–100 %				
Pathological T stage (%)			13(6.9 %)	$P = 0.568$
T1			63(33.9 %)	
T2			95(51.1 %)	
T3			15(8.1 %)	
T4				
Pathological N stage (%)			117(63.0 %)	$P = 0.924$
N0			19(10.2 %)	
N1a			14(7.5 %)	
N1b			15(8.1 %)	
N1c			11(5.9 %)	
N2a			10(5.3 %)	
N2b				
Tumor deposits (%)			154(82.7 %)	$P = 0.764$
Negative			32(17.2 %)	
Positive				
Tumor differentiation (%)			4(2.0 %)	$P = 0.124$
High			164(88 %)	
Moderate			18(10 %)	
Poor				
Tumor type (%)			59(31.9 %)	$P = 0.821$
Mass type			123(66.5 %)	
Ulcerative type			3(1.6 %)	
Infiltrating type				
P53 (%, mean ± SD)	0–99	40	43.68±38.43	$P = 0.678$
Ki67 (%, mean ± SD)	0–99	80	76.14±19.07	$P = 0.813$
LVI			135(72.5 %)	$P = 0.178$
Negative			51(27.5 %)	
Positive				
PNI			123(66.2 %)	$P = 0.364$
Negative			63(33.8 %)	
Positive				

(*continued on next page*)

Table 3 (*continued*)

Characteristics	Min-Max	Median	Mean ± SD/n%	P Value*
CEA(%)			122(65.5 %)	$P = 0.270$
≤5(Normal)			64(34.5 %)	
>5(Abnormal)				
CA199(%)			135(72.5 %)	$P = 0.309$
≤37(Normal)			51(27.5 %)	
>37(Abnormal)				
LARSS (%, mean ± SD)	11–41	30	29.82±5.48	
Low (0–29)			80(43.0 %)	
High (30–41)			106(57.0 %)	

Abbreviations: LDL, low-density lipoprotein; HDL, high-density lipoprotein; MRV, mesorectum volume; ARA, anorectal angle; MED, mesorectal extension depth; CRM, circumferential resection margin; LVI, lymphovascular invasion; PNI, perineural invasion; CEA, carcinoembryonic antigen; CA199, carbohydrate antigen-199; Tumor location from anal verge, the distance between the lower margin of the tumor and the anal margin; LARSS: low anterior resection syndrome scores.

Table 4
Clinicopathological and Imaging Characteristics of Patients multivariate analysis.

Characteristics	Cutoff	Odds Ratio (95 % CI)	AUC(95 % CI)	Sensitivity	Specificity	*P* Value	Multivariate analysis
Weight (kg, high vs. low)	≤53	1.971(0.998–3.897)	0.571 (0.496–0.643)	33.0	80.0	$P = 0.094$	$P = 0.8259$
MRV (cm^3, high vs. Low)	≤47.99	3.444(1.734–6.452)	0.601 (0.527–0.672)	81.1	43.7	$P = 0.020$	$P = 0.0017$
Pelvic volume(cm^3, high vs. Low)	≤282.6	2.939(1.562-5-534)	0.604 (0.529–0.674)	77.4	46.2	$P = 0.014$	$P = 0.0001$
Tumor location from anal verge (cm, high vs. Low)	≤7.4	16.969 (8.175–35.221)	0.835 (0.773–0.885)	82.1	78.7	$P < 0.001$	$P = 0.0001$

Abbreviations: MRV, mesorectum volume; Tumor location from anal verge:the distance between the lower margin of the tumor and the anal margin.

In the decision curve, the abscissa represents a measure of patient or physician preference, and the ordinate represents the net benefit rate, indicating that the expected advantage of treatment equals the expected advantage of avoiding treatment.

3.4. Clinical application of the nomogram

Points for each predictor: body weight (>53 kg, 0 points; 53 kg, 40 points), tumor location (7.4 cm, 0 points; <7.4 cm, 77.5 points), MRV (>47.99 cm^3, 0 points; 47.99 cm^3, 47.5 points), PVV (>282.6 cm^3, 0 points; 282.6 cm^3, 90 points). The risk of low rectal cancer at baseline reflects the probability corresponding to the total score on the nomogram. For example, if the patient's weight is < 53 kg, the tumor location is 7.4 cm, the MRV is 47.99 cm^3, and the PVVis 282.6 cm^3, the possibility of LARS after anterior resection of MLRC patients is about 97 %.

4. Discussion

LARS is one of the more common complications after laparoscopic resection in patients with middle and low rectal cancer. Postoperative intestinal dysfunction is prevalent in patients with rectal cancer with an incidence rate ranging from 70 % to 90 %. Such dysfunction may manifest as periodic alterations in stool consistency, transitioning from dry and rigid to pasty, thereby significantly compromising quality of life. This study included several indicators of such patients, including clinical pathology, baseline MRI tumor morphology, and pelvic measurement indicators, analyzed the differences between different groups of LARS score, found out independent risk factors, and successfully constructed a nomogram prediction model, internal training and external validation confirmed that this model has good application value. The nomogram exerts a relatively good risk stratification ability during cancer treatment and is a very practical tool in clinical practice [17,18,21–23]. Several indicators, including imaging features, are rarely reported for the combined prediction of LARS after anterior laparoscopic resection of MLRC. Therefore, we constructed a nomogram by combining clinical pathology, baseline MRI tumor morphological indicators, and pelvic measurement indicators and used it to screen the high-risk population of LARS after anterior resection before MLRC patients to minimize and reduce the risk of postoperative LARS and improve the survival and quality of life after surgery.

We delineated the mesenteric volume layer by layer from high-resolution T2WI images of MLRC patients. The univariate analysis showed that mesenteric volume was an independent risk factor for postoperative LARS, with a cutoff value of 47.99. The smaller mesenteric volume predicted a high risk of LARS after anterior resection in MLRC patients with surgery, providing a reference for clinical research on LARS risk factors. With the gradual deepening of research in recent years, increasing attention has been paid to the value of mesorectum in the clinical diagnosis and prognosis of rectal cancer. Some scholars included clinically staged T3 rectal cancer patients undergoing radical surgery after neoadjuvant radiosurgery from January 2013 to September 2014 in the study. The distance

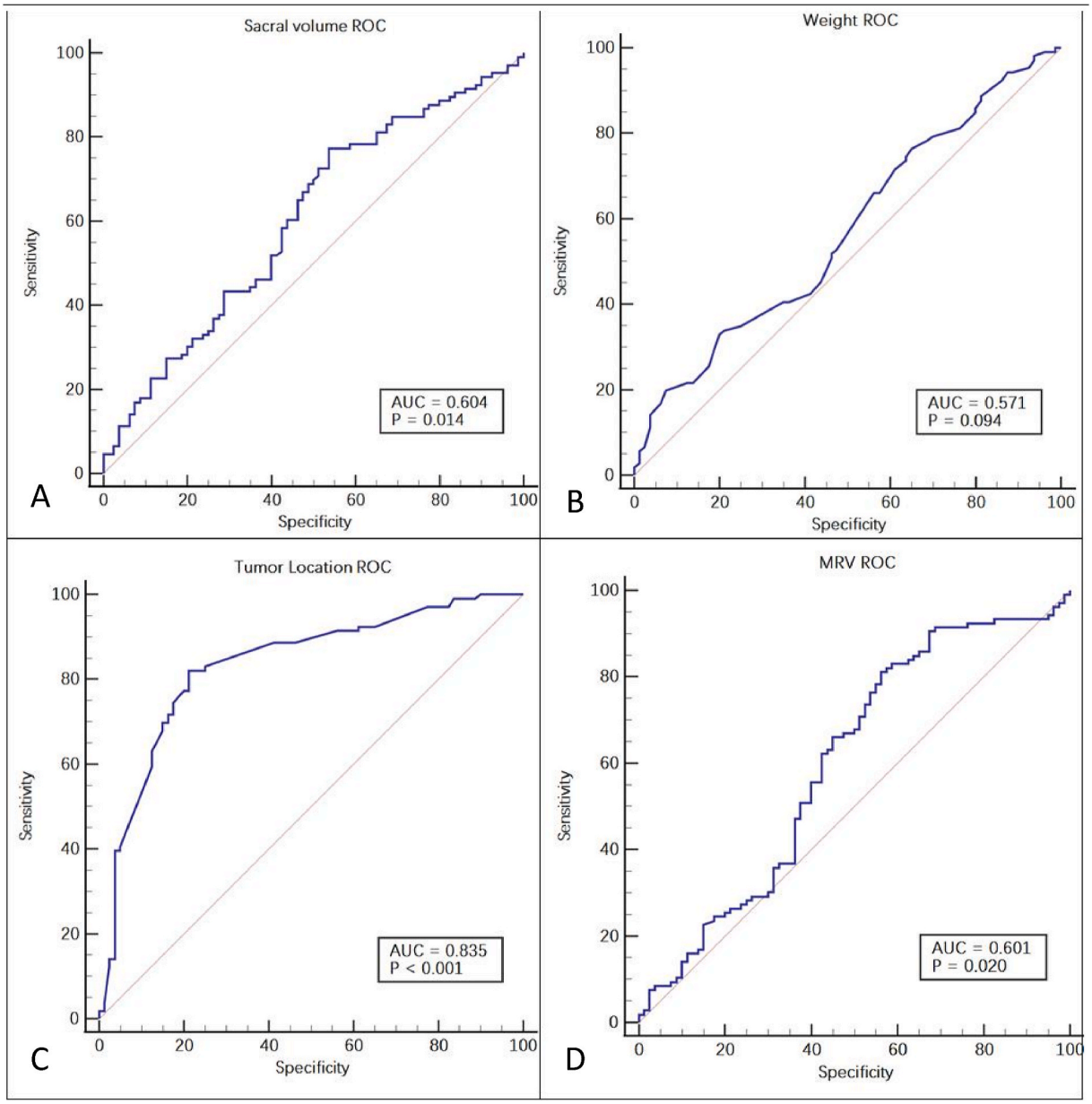

Fig. 5. The ROC curves of meaningful clinicopathological data and imaging signs of the LARS prediction model.

between the tumor invading the deepest tumor invasion and mesorectal fascia (DMRF) was measured at baseline, and the prognosis of patients was observed during the follow-up. In a total of 804 patients enrolled, 226 (28.1 %) progressed DMRF, clock position of the deepest position of tumor invasion(CDTI), and extramural vascular invasion (EMVI) were independent predictors of disease progression with a DMRF risk value of 7 mm [24,25]. Some scholars have pointed out that the mesorectal volume in the group with a good response to neoadjuvant radiotherapy in patients with locally advanced rectal cancer (LARC) was significantly greater than that in the group with a poor response. The mean MRV of the unresponsive group was 69.6 ± 31.0 ml in the well responsive group was 105.8 ±47.5 ml, and the group provided a better response place for NCRT treatment in rectal mesenteric adipose tissue in patients with neoadjuvant chemoradiotherapy (nCRT) of LARC patients [26].

Our mesentery volume measurement was obtained by observing the whole mesentery range and layer by layer, and this is one of the advantages of the research method; it can capture the whole mesentery information, not limited to a slice or a level, thus considering the integrity of the mesangial, this is more than a single level measuring mesentery area capture information, can dig out more valuable predictive information. This study found that MLRC patients with more MRV had relatively low postoperative LARS scores. The mesorectum is distributed around the middle and lower segment of the rectum, and its main component is adipose tissue, which is firmly wrapped by the mesenteric fascia. It shows an inverted cone structure on the pelvic MRI conventional T 1 WI and T 2 WI

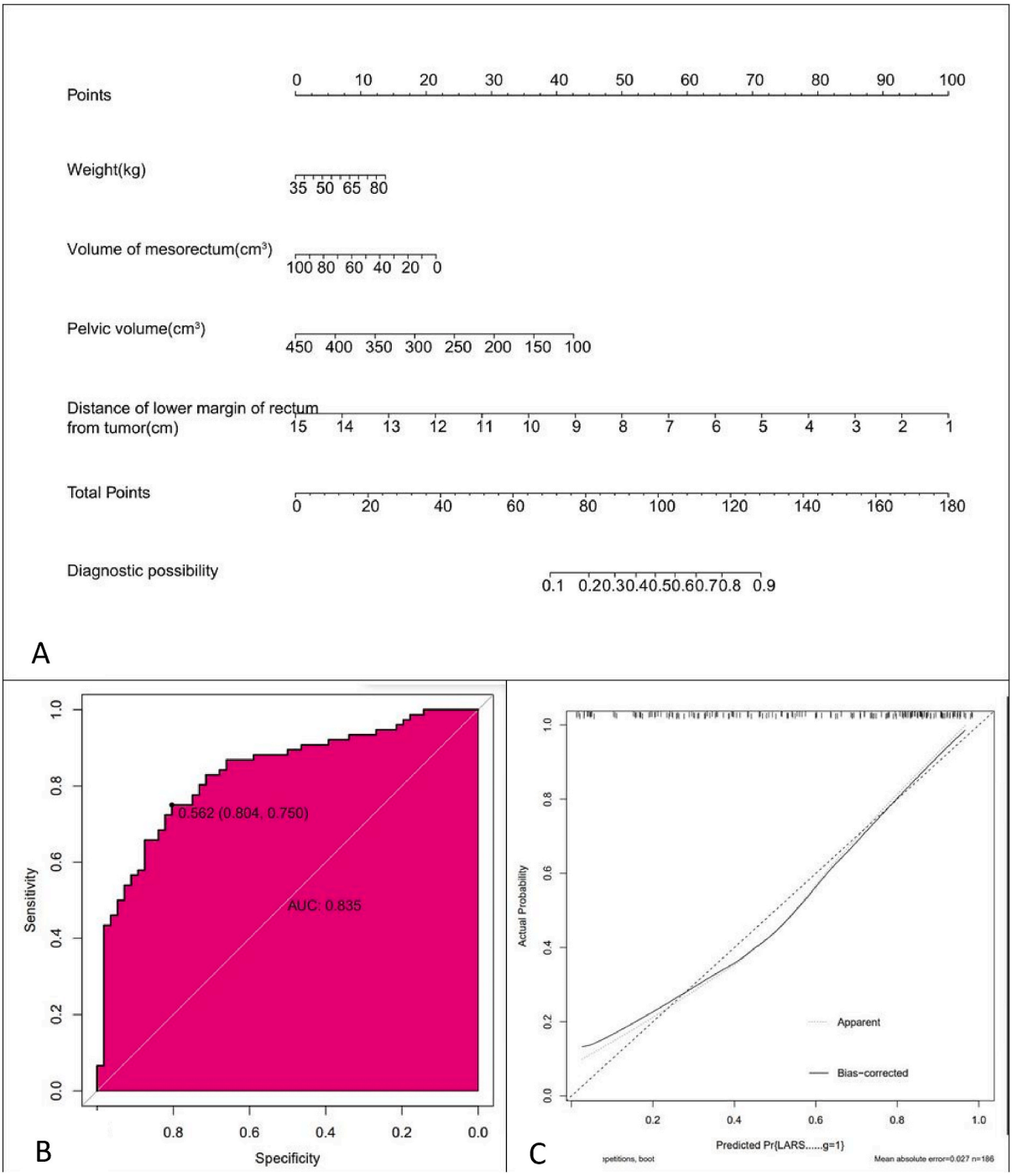

Fig. 6. Nomogram of meaningful tumor markers and imaging signs of MLRC patients LARS prediction efficacy (A) The training group ROC curve of the nomogram (B) The training group calibration curve of the nomogram (C).

sequences, similar to the high signal fat, and low signal vascular and lymphatic shadows can be seen inside. Our analysis of the above results is related to the physiological characteristics and tissue repair of the mesorectum the main component of the mesorectum is adipose tissue, and many adipose tissues in the human body have neuroendocrine activity under the regulation of neurohumoral factors [27]. In mesorectal patients with large volumes of MLRC anterior resection, the body's fat compensatory mechanism will be activated, and other parts of the adipose tissue (such as subcutaneous fat and visceral adipose tissue) under the regulation of nerve humoral factors will be more decomposition into free fatty acids in the blood, for the rectum around the adipose tissue provides material basis [33,34]. At the same time, in the process of tissue repair, the formation of anterior sacral soft tissue wounds after

anterior resection will release more tissue damage repair factors, and the above tissue repair factors will accelerate the continuous deposition of free fatty acids around the anastomosis and the reconstructed "rectum", forming similar mesenteric-like adipose tissue [28].

In previous pelvic studies, the measurement of the pelvic has received considerable attention. With the continuous development of measurement techniques in recent years, surgeons have used MRI images to measure the pelvic volume preoperatively, which predicts the surgical difficulty in pelvic surgery and provides an objective research method to elucidate the difficulty of pelvic surgery further [32]. However, the relationship between pelvic measures and postoperative adverse events in rectal cancer patients is unknown [29–31]. Surgeons have long used MRI pelvic measurements to predict the difficulty of pelvic surgery, increasing their confidence in the success of the surgery. Our study also found that: preoperative MRI measurement of pelvic volume is one of the factors affecting the LARS after anterior resection in patients with MLRC, the above reasons may be various: (1) The MLRC pelvic volume is relatively small, when the surgeon performs a low anterior resection, the mesorectum and free anterior sacral space to the surgical wound space in the course of tissue repair, the proliferof scar tissue makes the "new rectum" more likely to adhere widely to the anterior sacrum, and both sides of the pelvic wall in a narrow space, reducing the intestinal tube compliance and the ability to control defecation [36,37]; (2) Patients with relatively small MLRC have relatively small operating space which increases the difficulty of the surgery, affecting the functional recovery of all postoperative organs, increasing the chance of complications in the surgical area, and making the post-operative tissue repair more difficult, at the same time, with the increased opportunity of aseptic inflammation, there is an increased chance of developing LARS and the severity of LARS increases accordingly [35]; (3) After low anterior resection in MLRC patients with relative pelvic volume, the sigmoid colon and part of the small intestine was altered, the part of the sigmoid colon that replaced the original rectum, became the "new rectum". However, it does not have the volume and physiological curvature of the normal rectum and the storage space and storage capacity of feces decreased significantly. When a part of the small intestine moves down to occupy the pelvic space, it further compresses the contraction and peristalsis space of the "new rectum" to reduce its compliance, further reducing the ability of the new rectum to control fecal excretion. The above possible reasons will allow us to explore LARS's pathogenesis and predisposing factors [40,41].

In addition, measuring the distance from the lower tumor margin to the anal margin as an independent risk factor for LARS is a generally accepted. In Paku's study, the lower tumor margin of less than 7.4 cm from the anal margin was an independent risk factor for developing LARS after surgery. Miacci et al. [11] also reported similar results with less than 6.5 cm from the anal margin. Some scholars pointed out that tumor height and anastomotic height are also risk factors for postoperative LARS in patients with colorectal cancer [38]. Similarly, in this study, we used the anal margin as the starting point and accurately measured the distance from the lower edge of the tumor to the anal margin along. The obtained risk value was 7.4 cm. The closer the distance from the lower margin to the anal margin, the higher the risk of LARS after surgery (HR: 16.969,95%CI: 8.17535.22). In rectal cancer patients after TME with laparoscopic sphincter preservation, the results further confirmed that neoadjuvant radiotherapy and tumor location were independent risk factors for LARS after surgery [15]. Thus, the tumor location is low, surgical anastomosis position corresponds down, and the surgical wounds is in the process of tissue repair. Anastomosis and surrounding tissue collagen fiber excessive hyperplasia and scar contracture more easily to anal canal adhesion, making the compliance of the anal tube, reduce the ability to control defecation, increased defecation frequency, LARS is more obvious [39]. The findings of this study similarly support this. It is believed that LARS is associated with low anastomosis in rectal cancer resection but not with the transanal approach.

Although more clinicopathological factors were included in our study, it was unexpected that only body weight remained significant after multivariate analysis. The direct relationship between body weight and LARS and body weight is relatively rarely studied in the current clinical studies. The current study mainly focuses on the different operations of rectal cancer and patients' weight on postoperative LARS. Zhang B al[40. [][]study results show that for ultra-low rectal cancer patients, abdominal perineal resection (APR) postoperative body measurements and nutritional status recovery are better than ultra-low anterior resection (,ULAR); such study results may indirectly reflect the APR surgery patients postoperative LARS chance, where the symptoms are relatively mild. Therefore, it can help colorectal surgeons to choose more suitable surgical methods for rectal cancer patients with different body measurements and ultra-low nutritional status, and better apply the surgical methods for ultra-low rectal cancer patients. Some studies show that for patients with low rectal cancer, compared with patients after ULAR surgery, the ultra-low patients with intersphincteric resection(ISR) rectal cancer had a worse bowel control ability. The incidence of LARS was more than twice in low rectal cancer patients performing ISR [41]. In addition to the above indicators, the ratio of mesentery and pelvic volumes and the significance of BMI in this study is also not highlighted. The kind of connection between them and optimizing these indicators before surgery is worthy of further investigation. Adjusting the above indicators to achieve a relatively reasonable state, reducing the risk of LARS, and reducing the severity of LARS after low anterior resection in MLRC patients are problems worth considering.

A nomogram is a visualization tool used to optimize statistical models for the accuracy of individual predictions. From the nomogram, the area under the curve (AUC)in the internal validation group, sensitivity, and specificity were 0.835, 75.0 %, and 80.4 %, respectively. The AUC, sensitivity, and specificity in the external validation group were 0.874, 83.3 %, and 91.7 %, respectively. However, the factors included in this study were simpler, and we used only preoperative MR imaging data and clinicopathological data to construct the nomogram, which can save examination time and cost and be more conducive to the rational utilization and allocation of medical resources. The results of this study suggest that our nomogram can be used to assist clinical decision-making in achieving individualized and precise treatment.And health education should be strengthened to make patients fully understand LARS. Post-operative rehabilitation treatment, pelvic foor function training, and follow-up should be guided.

This study has some limitations. First, the incidence and severity of postoperative LARS symptoms were mainly evaluated based on the clinical course and LARS score scale, meaning that the evaluations were partly subjective. Second, this study extracted image omics information only from single T2WI sequences. Although T2WI is considered to have the best display effect, the information provided is

relatively limited. Future MRI studies with multiple sequences and multi-parameter MRI, such as combined functional imaging sequences, should be performed to overcome these issues. Morphological assessments using T2WI sequences were a major focus of pelvic MRI studies. Unlike unenhanced scans, the enhanced images provide better histological contrast for measurement and boundary delineation and contain more information about tumor heterogeneity. Their combination improves the prediction ability. Finally, we performed MRI measurements using static images, in which some organs in the pelvic cavity have some degree of uncertainty. Even if the space occupied by the rectal and surrounding anatomical areas is relatively fixed and not susceptible to individual, behavioral, and other factors, miscalculations may occur during the measurement. There is no consistent measurement method nor a fixed reference point for rectal and surrounding structural measurements. Therefore, knowledge and experience differences between investigators may lead to varying outcomes. The stability of MRI image boundary delineation and the accuracy of quantitative, software-based analysis still requires further investigation.

5. Conclusion

The etiology of LARS is complex, its clinical manifestations vary, and there is a lack of targeted treatment and preventive measures, which affects the quality of life of patients. This study provides a novel prediction model using non-invasive, surgical MRI-based tumor morphology and pelvic measurement features, which improves the prognostic ability of clinical pathology and tumor morphology to better predict the occurrence and severity of postoperative complications of the disease. The developed nomogram successfully classified MLRC patients into both high- and low-risk groups, contributing to risk stratification and the necessary preoperative interventions. This study provides important insights for precision intervention and a new perspective for clinicians to study LARS, such as the etiological mechanisms of LARS and regenerative medicine. It facilitates the formulation of perioperative treatment decisions for anterior resection in MLRC patients and provides a new reference basis to effectively reduce the incidence and severity of LARS with continuous research and the development of techniques. We believe that colorectal surgery will have a positive and far-reaching impact on addressing a range of complex issues.

Data availability

The authors confirm that all data underlying the findings are fully available without restriction. All relevant data are within the paper and its supporting information files.

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CRediT authorship contribution statement

Zheng Wang: Writing – review & editing, Validation, Supervision, Investigation, Funding acquisition, Conceptualization. **Chuanji Zhou:** Writing – original draft, Visualization, Software, Methodology, Investigation, Data curation, Conceptualization. **Linghou Meng:** Supervision, Resources. **Xianwei Mo:** Writing – review & editing, Visualization, Supervision, Funding acquisition. **Dong Xie:** Supervision, Resources. **Xiaoliang Huang:** Resources, Investigation. **Xinxin He:** Validation, Investigation. **Shanshan Luo:** Validation, Investigation. **Haiquan Qin:** Investigation. **Qiang Li:** Investigation. **Shaolv Lai:** Investigation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] N. Wilkinson, Management of rectal cancer, Surg Clin North Am 100 (3) (2020) 615–628, https://doi.org/10.1016/j.suc.2020.02.014.
[2] T.H. Nguyen, R.V. Chokshi, Low anterior resection syndrome, Curr. Gastroenterol. Rep. 22 (10) (2020) 48, https://doi.org/10.1007/s11894-020-00785-z.

[3] L.K.F. Temple, Expert commentary on low anterior resection syndrome, Dis. Colon Rectum 62 (12) (2019) 1423–1424, https://doi.org/10.1097/DCR.0000000000001531.

[4] C. Keane, N.S. Fearnhead, L.G. Bordeianou, et al., International consensus definition of low anterior resection syndrome, Dis. Colon Rectum 63 (3) (2020) 274–284, https://doi.org/10.1097/DCR.0000000000001583.

[5] E. Pape, P. Pattyn, A. Van Hecke, et al., Impact of low anterior resection syndrome (LARS) on the quality of life and treatment options of LARS - a cross sectional study, Eur. J. Oncol. Nurs. 50 (2021) 101878, https://doi.org/10.1016/j.ejon.2020.101878.

[6] L.M. Jimenez-Gomez, E. Espin-Basany, L. Trenti, et al., Factors associated with low anterior resection syndrome after surgical treatment of rectal cancer, Colorectal Dis. (2017), https://doi.org/10.1111/codi.13901. Published online ahead of print, 2017 Sep. 29.

[7] R. Didailler, Q. Denost, P. Loughlin, et al., Antegrade enema after total mesorectal excision for rectal cancer: the last chance to avoid definitive colostomy for refractory low anterior resection syndrome and fecal incontinence, Dis. Colon Rectum 61 (6) (2018) 667–672, https://doi.org/10.1097/DCR.0000000000001089.

[8] F. Pucciani, A review on functional results of sphincter-saving surgery for rectal cancer: the anterior resection syndrome, Updates Surg 65 (4) (2013) 257–263, https://doi.org/10.1007/s13304-013-0220-5.

[9] K. Afshari, K. Smedh, P. Wagner, A. Chabok, M. Nikberg, Risk factors for developing anorectal dysfunction after anterior resection, Int. J. Colorectal Dis. 36 (12) (2021) 2697–2705, https://doi.org/10.1007/s00384-021-04024-3.

[10] J.A.G. van der Heijden, S.M. Qaderi, R. Verhoeven, et al., Transanal total mesorectal excision and low anterior resection syndrome, Br. J. Surg. 108 (8) (2021) 991–997, https://doi.org/10.1093/bjs/znab056.

[11] F.L.C. Miacci, C.R. Guetter, P.H. Moreira, et al., Predictive factors of low anterior resection syndrome following anterior resection of the rectum. Síndrome da ressecção anterior do reto: Fatores preditivos, Rev. Col. Bras. Cir. 46 (6) (2020) e20192361, https://doi.org/10.1590/0100-6991e-20192361.

[12] T. Juul, H. Elfeki, P. Christensen, S. Laurberg, K.J. Emmertsen, P. Bager, Normative data for the low anterior resection syndrome score (LARS score), Ann. Surg. 269 (6) (2019) 1124–1128, https://doi.org/10.1097/SLA.0000000000002750.

[13] K.S. Ng, R. Russo, M.A. Gladman, Colonic transit in patients after anterior resection: prospective, comparative study using single-photon emission CT/CT scintigraphy, Br. J. Surg. 107 (5) (2020) 567–579, https://doi.org/10.1002/bjs.11471.

[14] P. Ihnát, I. Slívová, L. Tulinsky, L. Ihnát Rudinská, J. Máca, I. Penka, Anorectal dysfunction after laparoscopic low anterior rectal resection for rectal cancer with and without radiotherapy (manometry study), J. Surg. Oncol. 117 (4) (2018) 710–716, https://doi.org/10.1002/jso.24885.

[15] J.P. Burke, Low anterior resection syndrome - "braking" our focus with the pelvis, Colorectal Dis. 23 (2) (2021) 339–340, https://doi.org/10.1111/codi.15548.

[16] N. Horvat, C. Carlos Tavares Rocha, B. Clemente Oliveira, I. Petkovska, M.J. Gollub, MRI of rectal cancer: tumor staging, imaging techniques, and management, Radiographics 39 (2) (2019) 367–387, https://doi.org/10.1148/rg.2019180114.

[17] R.G.H. Beets-Tan, D.M.J. Lambregts, M. Maas, et al., Magnetic resonance imaging for clinical management of rectal cancer: updated recommendations from the 2016 European Society of Gastrointestinal and Abdominal Radiology (ESGAR) consensus meeting, Eur. Radiol. 28 (4) (2018) 1465–1475, https://doi.org/10.1007/s00330-017-5026-2.

[18] A.M.A. Al-Saidi, S.J. Verkuijl, S. Hofker, M. Trzpis, P.M.A. Broens, How should the low anterior resection syndrome score be interpreted? Dis. Colon Rectum 63 (4) (2020) 520–526, https://doi.org/10.1097/DCR.0000000000001561.

[19] K.J. Emmertsen, S. Laurberg, 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. 255 (5) (2012) 922–928, https://doi.org/10.1097/sla.0b013e31824f1c21.

[20] A. Annicchiarico, J. Martellucci, S. Solari, M. Scheiterle, C. Bergamini, P. Prosperi, Low anterior resection syndrome: can it be prevented? Int J Colorect Dis 36 (12) (2021) 2535–2552, https://doi.org/10.1007/s00384-021-04008-3.

[21] Q. Qin, B. Huang, W. Cao, et al., Bowel dysfunction after low anterior resection with neoadjuvant chemoradiotherapy or chemotherapy alone for rectal cancer: a cross-sectional study from China, Dis. Colon Rectum 60 (7) (2017) 697–705, https://doi.org/10.1097/DCR.0000000000000801.

[22] P. Ihnát, P. Vávra, J. Prokop, A. Pelikán, L. Ihnát Rudinská, I. Penka, Functional outcome of low rectal resection evaluated by anorectal manometry, ANZ J. Surg. 88 (6) (2018) E512–E516, https://doi.org/10.1111/ans.14207.

[23] H. Qin, L. Meng, Z. Huang, et al., A study on the clinical application of greater omental pedicle flap transplantation to correct anterior resection syndrome in patients with low rectal cancer, Regen Ther 18 (2021) 146–151, https://doi.org/10.1016/j.reth.2021.05.003.

[24] X. Zhang, Q. Lu, X. Guo, et al., Better prognostic determination of cT3 rectal cancer through measurement of distance to mesorectal fascia: a multicenter study, Chinese Journal of Cancer Research = Chung-kuo yen cheng yen chiu 33 (5) (2021) 606–615, https://doi.org/10.21147/j.issn.1000-9604.2021.05.07.

[25] X.Y. Zhang, X.T. Li, Y.J. Shi, et al., Correlation between the distance to mesorectal fascia and prognosis of cT3 rectal cancer: results of a multicenter study from China, Dis. Colon Rectum 65 (3) (2022) 322–332, https://doi.org/10.1097/DCR.0000000000002167.

[26] O. Dilek, H. Akkaya, C. Parlatan, et al., Can the mesorectal fat tissue volume be used as a predictive factor in foreseeing the response to neoadjuvant chemoradiotherapy in rectum cancer? A CT-based preliminary study, Abdom Radiol (NY) 46 (6) (2021) 2415–2422, https://doi.org/10.1007/s00261-021-02951-x.

[27] K.P. Robb, L. Juignet, Martin P. Morissette, et al., Adipose stromal cells enhance decellularized adipose tissue remodeling through multimodal mechanisms, Tissue Eng Part A 27 (9–10) (2021) 618–630, https://doi.org/10.1089/ten.TEA.2020.0180.

[28] K.C.L.R. Buzatti, A. Petroianu, S. Laurberg, et al., Validation of low anterior resection syndrome score in Brazil with Portuguese, Ann Coloproctol (2022), https://doi.org/10.3393/ac.2022.00136.0019 [published online ahead of print, 2022 May 13].

[29] J.S.Y. Hong, M.S. De Robles, C. Brown, K.G.M. Brown, C.J. Young, M.J. Solomon, Can MRI pelvimetry predict the technical difficulty of laparoscopic rectal cancer surgery? Int. J. Colorectal Dis. 36 (12) (2021) 2613–2620, https://doi.org/10.1007/s00384-021-04000-x.

[30] J.S. Hong, K.G.M. Brown, J. Waller, C.J. Young, M.J. Solomon, The role of MRI pelvimetry in predicting technical difficulty and outcomes of open and minimally invasive total mesorectal excision: a systematic review, Tech. Coloproctol. 24 (10) (2020) 991–1000, https://doi.org/10.1007/s10151-020-02274-x.

[31] P. Tripathi, Y. Hai, Z. Li, Y. Shen, X. Hu, D. Hu, Morphometric assessment of the mesorectal fat in Chinese Han population: a clinical MRI study, Sci. Prog. 104 (2) (2021) 368504211016214, https://doi.org/10.1177/00368504211016214.

[32] L. Lorenzon, F. Bini, F. Landolfi, et al., 3D pelvimetry and biometric measurements: a surgical perspective for colorectal resections, Int J Colorect Dis 36 (5) (2021) 977–986, https://doi.org/10.1007/s00384-020-03802-9.

[33] S.D. Allen, V. Gada, D.M. Blunt, Variation of mesorectal volume with abdominal fat volume in patients with rectal carcinoma: assessment with MRI, Br. J. Radiol. 80 (952) (2007) 242–247, https://doi.org/10.1259/bjr/66311683.

[34] R.K. Zwick, C.F. Guerrero-Juarez, V. Horsley, M.V. Plikus, Anatomical, physiological, and functional diversity of adipose tissue, Cell Metab 27 (1) (2018) 68–83, https://doi.org/10.1016/j.cmet.2017.12.002.

[35] J. Knol, D.S. Keller, Total mesorectal excision technique-past, present, and future, Clin Colon Rect Surg 33 (3) (2020) 134–143, https://doi.org/10.1055/s-0039-3402776.

[36] S. Cinti, Adipose organ development and remodeling, Compr. Physiol. 8 (4) (2018) 1357–1431, https://doi.org/10.1002/cphy.c170042.

[37] S. Bell, P. Malouf, N. Johnson, et al., Pelvic fat volume reduction with preoperative very low energy diet (VLED): implications for rectal cancer surgery in the obese, Tech. Coloproctol. 23 (9) (2019) 887–892, https://doi.org/10.1007/s10151-019-02074-y.

[38] L. Ye, M. Huang, Y. Huang, K. Yu, X. Wang, Risk factors of postoperative low anterior resection syndrome for colorectal cancer: a meta-analysis, Asian J. Surg. 45 (1) (2022) 39–50, https://doi.org/10.1016/j.asjsur.2021.05.016.

[39] L. Meng, H. Qin, Z. Huang, et al., Analysis of presacral tissue structure in LARS and the prevention of LARS by reconstruction of presacral mesorectum with pedicled greater omentum flap graft, Tech. Coloproctol. 25 (12) (2021) 1291–1300, https://doi.org/10.1007/s10151-021-02521-9.

[40] B. Zhang, K. Zhao, Y.J. Zhao, et al., Variation in rectoanal inhibitory reflex after laparoscopic intersphincteric resection for ultralow rectal cancer, Colorectal Dis. 23 (2) (2021) 424–433, https://doi.org/10.1111/codi.15444.

[41] M. Morihiro, K. Koda, K. Seike, H. Miyauchi, M. Miyazaki, Characteristic findings on defecography according to reconstruction method and defecatory disorder following sphincter-saving surgery for rectal cancer, Int. J. Colorectal Dis. 23 (9) (2008) 883–892, https://doi.org/10.1007/s00384-008-0485-1.