MRI measurements predict major low anterior resection syndrome in rectal cancer patients

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Accepted: 22 April 2022 / Published online: 3 May 2022
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Abstract
Purpose Current low anterior resection syndrome (LARS) score is lagging behind and only based on clinical symptoms patient described. Preoperative imaging indicators which can be used to predict LARS is unknown. We proposed preoperative MRI parameters for identifying major LARS.

Methods Patients receiving curative restorative anterior resection from Sept. 2007 to Sept. 2015 were collected to complete LARS score (median 75.7 months since surgery). MRI measurements associated with LARS were tested, and a multivariate logistic model was conducted for predicting LARS. Receiver operating characteristic curve was used to evaluate the model.

Results Two hundred fifty-five patients undergoing neoadjuvant chemoradiotherapy and 72 patients undergoing direct surgery were enrolled. The incidence of major LARS in NCRT group was significantly higher (53.3% vs. 34.7%, \(P = 0.005\)). In patients with neoadjuvant chemoradiotherapy, the thickness of ARJ (TARJ), the distance between the tumor's lower edge and anal rectal joint (DTA), and sex were independent factors for predicting major LARS; ORs were 0.382 (95% CI, 0.198–0.740), 0.653 (95% CI, 0.565–0.756), and 0.935 (95% CI, 0.915–0.955). The AUC of the multivariable model was 0.842 (95% CI, 0.794–0.890). In patients with direct surgery, only DTA was the independent factor for predicting major LARS; OR was 0.958 (95% CI, 0.930–0.988). The AUC was 0.777 (95% CI: 0.630–0.925).

Conclusions Baseline MRI measurements have the potential to predict major LARS in rectal cancer, which will benefit the decision-making and improve patients’ life quality.

Keywords Rectal cancer · Low anterior resection syndrome · Magnetic resonance imaging · Neoadjuvant chemoradiotherapy · Anal rectal joint

Highlights
• Low anterior resection syndrome (LARS) score is lagging behind, while there are no recognized preoperative indicators for predicting LARS. This study identified preoperative MRI feature for predicting LARS and developed a MR-based model.
• The distance between the lower edge of the tumor and anorectal joint (DTA) was proved an independent factor for predicting major low anterior resection syndrome (LARS) in both neoadjuvant therapy group and direct surgery group. In neoadjuvant therapy group, the thickness of the anal rectal joint (TARJ) was also an independent factor for predicting major LARS.
• Multivariate models were constructed for predicting major LARS; AUC were 0.842 and 0.777 for neoadjuvant therapy group and direct surgery group, respectively.

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Following a restorative anterior resection, 70–90% of rectal cancer patients report bowel dysfunction [1, 2]. Low anterior resection syndrome (LARS) has been used to describe a wide array of symptoms after sphincter-preserving rectal surgery, such as difficulty emptying the bowel, fecal urgency, and fecal incontinence. One year after surgery, about 30% of patients report bowel dysfunction resolution (no or mild LARS) which will not bring a major impact on life quality [1, 3]. In contrast, over 40% patients become “toilet dependent” and report that bowel dysfunction has a devastating consequence on their work, social and physical functioning, and global quality of life (major LARS) [4–6], and this impact is mostly long-term and persistent, resulting in permanent colostomy in the patients with major LARS. Meta-analysis showed that a prevalence of major LARS after sphincter-preserving surgery for rectal cancer was 41% (95% CI 34–48%), where the reported prevalence ranged
widely from 17.8 to 56% [6]. This should raise the need of awareness of the condition and its morbidity.

The mechanism of LARS is complex and the origin of LARS is probably multifactorial [7, 8], including by injury or stretching of a branch of the autonomous nervous system during rectal excision or due to radiation therapy and decreased rectal compliance and capacity of neurological origin secondary to excision. The influencing factors of LARS reported in the literature include age, gender, operation type, anastomotic level, pTN stage, postoperative complications, rectal reconstruction mode, and the application of neoadjuvant and adjuvant chemoradiotherapies. Most of them are postoperative factors. Whether there are some influencing factors of LARS, which can be identified before the operation, would help to select patients with high risk of LARS in advance, and implement clinical intervention as soon as possible to avoid or reduce the harm of LARS?

The low anterior resection syndrome (LARS) score [8] was developed on the basis of patient-reported symptoms. The LARS score can accurately measure the severity of postoperative bowel dysfunction, and it has been proven to correlate well with quality of life. The major factors associated with LARS have been shown to be tumor height, neoadjuvant radiotherapy, and use of ileostomy with some complications, rectal reconstruction mode, and the application of neoadjuvant and adjuvant chemoradiotherapies. Most of them are postoperative factors. Whether there are some influencing factors of LARS, which can be identified before the operation, would help to select patients with high risk of LARS in advance, and implement clinical intervention as soon as possible to avoid or reduce the harm of LARS?

The purpose of this study was to personalize the preoperative consent process by (1) identifying the preoperative risk factors for postoperative bowel dysfunction according to the LARS score and (2) developing a predicting model for major LARS that can be useful in clinical practice by offering individualized information for decision-making at the time of patient consent or during preoperative patient discussions.

Methods and materials

The study protocol was approved by the Medical Ethics Committee of Peking University Cancer Hospital, and all patients gave informed consent. The protocol was in accordance with Helsinki Declaration.

Data and participants

A retrospective cohort study including rectal cancer patients undergoing surgery from Sept. 2007 to Sept. 2015 was performed in Beijing Cancer hospital. Eligible patients received follow-up phone calling to complete the LARS score. The inclusion criteria were (1) an anterior resection for a diagnosis of rectal adenocarcinoma between 0 and 15 cm from the anal verge, including patients with neoadjuvant chemoradiotherapy and direct surgery; 2) the patients were followed up for more than 3 years. The LARS questionnaire related to anal function was as follows: a constellation of symptoms including fecal urgency, frequent bowel movements, bowel fragmentation, emptying difficulties and incontinence, and increased gas; (3) with complete baseline MRI examination; an d(4) with complete clinical information, including age, gender, BMI, TNM stage, the distance between the lower edge of tumor and anal edge, operation method (laparoscopy or laparotomy), postoperative complications, and temporary stoma or not. The exclusion criteria were an incomplete cancer resection, recurrence, metastatic disease, intestinal stoma or patients whose bowel continuity had been restored for < 12 months, dementia; with pelvic surgery history before; long-term use of drugs that may affect intestinal function and anal defecation function (such as lactulose and other drugs that may affect gastrointestinal motility and defecation condition) after anal preservation; lack of complete clinical and pathological materials and follow-up data; postoperative complications (such as rectovaginal fistula and anastomotic leakage) affect the quality of defecation; patients with mental disorders and other patients who cannot accurately judge and describe their own conditions; if the patients refuse to answer the questionnaire or more than half of the questions in the questionnaire cannot be answered by the patients, they shall be excluded.

LARS score questionnaire

The low anterior resection syndrome (LARS) score was developed on the basis of patient-reported symptoms. The LARS score was computed and categorized into 3 groups: no LARS (0–20 points), minor LARS (21–29 points), or major LARS (30–42 points), according to the guidelines [10]. The time of questionnaire survey was from March 2019 to November 2019 (median 75.7 months since surgery). The patients were followed up by face-to-face interview or telephone. Before filling in, the questionnaire will be explained to the patients in detail, and the patients or their families will fill in the questionnaire according to the actual situation. Some questionnaires with missing answers were excluded.

MRI scanning and measurement

All MRI examinations were performed with a 3.0-T MR unit (Discovery 750; GE Healthcare, Waukesha, Wis) by using an eight-channel phased-array body coil in the
supine position. Without any bowel preparation, patients were injected intramuscularly with 20 mg of scopolamine butylbromide 30 min prior to imaging to reduce colonic motility. The rectal MRI protocol included axial, axial oblique, coronal, and sagittal T2-weighted images; transverse T1-weighted images; and diffusion-weighted images. DWI images were obtained using single-shot echo-planar imaging with 2b factors (0 and 1000 s/mm²), and repetition time (TR) = 2800 ms, echo time (TE) = 70 ms, field of view (FOV) = 340 × 340 mm, matrix = 256 × 256, thickness = 4.0 mm, and gap = 1.0 mm. Apparent diffusion coefficient (ADC) maps were generated automatically and included both b values in a monoexponential decay model. High-resolution T2WI images were obtained using fast recovery fast spin echo with TR = 5694 ms, TE = 110 ms, FOV = 180 × 180 mm, echo train length = 24, matrix = 288 × 256, thickness = 3.0 mm, and gap = 0.3 mm.

MRI measurements included (Fig. 1):

1) The thickness of levator ani (TLA): the thickest part of the lower edge of levator ani muscle (close to the level of anorectal joint), which was measured on sagittal T2W.
2) The thickness of anal-rectal joint (ARJ) (TARJ): the sum of the thickest part of the lower edge of the levator ani muscle and the deep part of the adjacent external anal sphincter (at the level of the anorectal ring) was measured on sagittal T2WI.
3) The thickness of internal anal sphincter complex (TIS): TIS was measured on sagittal T2WI.
4) The thickness of external anal sphincter complex thickness (TES): to measure the sum of the thickest distance of the external sphincter on coronal T2WI, and then calculate the mean value.
5) The distance between tumor’s lower edge and ARJ (DTA): measured on sagittal T2WI.
6) The distance between tumor’s lower edge and anal verge (DTV: DTA + anal canal length): measured on sagittal T2WI.
7) Anal canal length: measured on sagittal T2WI.
8) Anorectal angle: the angle between the lower segment of rectum and the longitudinal axis of anal canal was measured by sagittal T2WI.
9) Interspinous diameter (ISD): the distance between bilateral ischial spines was measured on axial T2WI. Two experienced radiologists working together for the MRI measurements.

**Neoadjuvant therapy, surgery, and follow-up**

Two groups were included in this study, one group is the patients with direct surgery, and another group is patients with locally advanced rectal cancer who received neoadjuvant chemoradiotherapy followed by TME surgery.

Intensity-modulated radiation therapy (IMRT) was administered using a Varian Rapidarc system (Varian Medical Systems). The IMRT regimen comprised 22 fractions of 2.3 Gy (gross tumor volume, GtV) and 1.9 Gy (clinical target volume, CtV). A total dose of 50.6 Gy (GtV)/41.8 Gy (CtV) was administered 5 times per week over a period of 30 days [11, 12]. The GtV was defined as the volume of the primary tumor including the mesorectum. The CtV was defined as the primary tumor, mesorectal region, presacral region, mesorectal lymph nodes, lateral lymph nodes, internal iliac
lymph node chain, and pelvic wall area. Capecitabine treatment was administered concurrently with IMRT at a dose of 825 mg/m² orally twice per day.

Low anterior resection (LAR) based on the principle of TME was recommended 8–12 weeks or more after the completion of chemoradiotherapy. The decision of an LAR was discussed through a MDT discussion before surgery and finally made by intraoperative discretion by the senior surgeon. Double-stapling technique was used for all cases, and a safe distal margin of at least 2 cm was achieved in most of cases. Stoma or not should also be determined by the distance between the tumor and the anal margin and the pelvic condition. Patients with pathologically proven stage II and III rectal cancer received adjuvant chemotherapy. Capecitabine alone, mfolfoX6, or Capeox were prescribed at the discretion of the physician. Patients were followed at 3-month intervals for the first 2 years after treatment and then at 6-month intervals for the next 3 years. Evaluations consisted of physical examination, serum CEA, a complete blood cell count, and blood chemical analysis. Proctoscopy, abdominal ultrasonography, CT scanning of the abdomen and pelvis, and chest X-ray/CT were also routinely performed every 6 to 12 months.

Statistical analysis

All analysis was conducted using SPSS (Version 22.0, SPSS Inc, Chicago). A two-tailed P value less than 0.05 indicated statistically significance. Continuous variables were described as means ± standard deviations; categorical variables were described as numbers and proportions. Independent t test and/or chi-square test was used to compare factors between two groups for detecting LARS-associated factors. Multivariable logistic regression was conducted to screen for independent factors for predicting severe LARS; odds ratios were calculated with 95% confidence interval. Pearson correlation coefficients for MRI measurements: when a Pearson coefficient larger than 0.40 was obtained between two variables, the one with smaller P value in univariable analysis was substituted into multivariable analysis. Receiver operating characteristic (ROC) curve was used to evaluate the diagnostic performance for predicting severe LARS; the area under the ROC curve (AUC) with its 95% CI was calculated. The cutoffs were determined using the maximum Youden’s method.

Results

Patients

The study included 327 rectal cancer patients undergoing surgical resection (Fig. 2). The mean age was 57.74 ± 23.40 years. There were 255 patients with neoadjuvant therapy and 72 patients without neoadjuvant therapy. The characteristics of patients were summarized in Table 1.

Statistically higher T and N stage was observed in patients without neoadjuvant therapy compared with patients with neoadjuvant therapy (P < 0.001 and P = 0.01, respectively).

Statistically more major LARS was observed in patients with neoadjuvant therapy compared with patients without neoadjuvant therapy (53.3% vs 34.7%, P = 0.005).

There were statistical differences observed in tumor location, TARJ, TLA, DTA, DTV (DTA + anal canal length) between patients with neoadjuvant therapy and patients without neoadjuvant therapy, with all P < 0.001.

Fig. 2 Neoadjuvant chemoradiotherapy (a) and direct surgery patients (b) included for analysis
analysis of LARS associated factors

LARS-associated factors were analyzed in patients with neoadjuvant therapy and patients without neoadjuvant therapy, respectively (Tables 2, 3).

In patients with neoadjuvant therapy, lower tumor location, thinner TARJ and TLA, and shorter DTA were associated with major LARS. Other MR factors, as well as clinical and pathological characteristics, were comparable between major LARS and no/minor LARS patients.

In patients without neoadjuvant therapy, lower tumor location, thinner TARJ and TES, and shorter DTA and DTV were associated with major LARS. Additionally, major LARS patients showed higher pathology tumor stage than no/minor LARS patients. Other factors were comparable between major LARS and no/minor LARS patients.

Construction and evaluation of model for predicting LARS

Analysis was conducted in patients with neoadjuvant therapy and patients without neoadjuvant therapy, respectively.

In patients with neoadjuvant therapy, multivariate logistic regression showed that sex, TARJ, and DTA were independent factors for predicting major LARS; ORs were 0.382 (95% CI, 0.198–0.740), 0.653 (95% CI, 0.565–0.756), and 0.935 (95% CI, 0.915–0.955), respectively (Table 4). The model yielded was $Y = -0.961\times \text{sex} - 0.426 \times \text{TARJ} - 0.068 \times \text{DTA}$. 

Table 1 The characteristics comparison between patients with neoadjuvant chemoradiotherapy and direct surgery

| Treatment | Surgery directly ($n=72$) | Neoadjuvant chemoradiotherapy ($n=255$) | $P$ |
|-----------|--------------------------|----------------------------------------|-----|
| Sex       | Male                     | 34 (47.2)                              | 162 (63.5) | 0.013 |
|           | Female                   | 38 (52.8)                              | 93 (36.5)  |     |
| Age(years)|                          | 61.73 ± 10.77                          | 56.62 ± 37.32 | 0.468 |
| Baseline MRI measurements (mm) | TLA              | 3.33 ± 2.68                            | 4.37 ± 1.67   | <0.001 |
|           | TARJ                     | 9.21 ± 2.42                            | 8.87 ± 2.41   | 0.386 |
|           | TIS                      | 4.35 ± 1.38                            | 4.54 ± 1.29   | 0.477 |
|           | TES                      | 9.59 ± 2.19                            | 9.39 ± 2.04   | 0.532 |
|           | DTA                      | 56.16 ± 28.85                          | 28.06 ± 17.65 | <0.001 |
|           | DTV                      | 88.55 ± 29.74                          | 59.17 ± 19.11 | <0.001 |
|           | Length of anal canal     | 32.39 ± 5.23                           | 31.11 ± 5.25  | 0.123 |
|           | Anorectal angle          | 107.36 ± 16.35                         | 125.47 ± 17.74 | <0.001 |
|           | ISD                      | 95.22 ± 10.71                          | 96.13 ± 10.64 | 0.588 |
| pT        | T0                       | 1 (1.4)                                | 48 (18.8)     | <0.001 |
|           | T1                       | 0 (0)                                  | 27 (10.6)     |     |
|           | T2                       | 6 (8.3)                                | 79 (31.0)     |     |
|           | T3                       | 65 (90.3)                              | 100 (39.2)    |     |
|           | T4                       | 0 (0)                                  | 1 (0.4)       |     |
| pN        | 0                        | 44 (61.1)                              | 201 (78.8)    | 0.01 |
|           | 1                        | 20 (27.8)                              | 42 (16.5)     |     |
|           | 2                        | 8 (11.1)                               | 12 (4.7)      |     |
| Histopathological type | Adenocarcinoma          | 65 (90.3)                              | 237 (92.9)    | 0.757 |
|           | (With) mucinous adenocarcinoma | 6 (8.3) | 15 (5.9) |     |
|           | Signet ring cell carcinoma | 1 (1.4) | 3 (1.2) |     |
| Differentiation | Good-moderate      | 66 (91.7)                              | 219 (85.9)    | 0.195 |
|           | Poor                    | 6 (8.3)                                | 36 (24.1)     |     |
| Operation style | LAR                      | 72 (100)                               | 255 (100)     |     |
| LARS      | No/minor                | 47 (65.3)                              | 119 (46.7)    | <0.005 |
|           | Major                   | 25 (34.7)                              | 136 (53.3)    |     |
| LARS score |                          | 21.29 ± 11.31                          | 29.82 ± 9.25  |     |

TLA the thickness of levator ani, TARJ the thickness of anal-rectal joint, TIS and TES the thickness of internal and external anal sphincter complex, DTA the distance between tumor’s lower edge and ARJ, DTV (DTA + anal canal length) the distance between tumor’s lower edge and anal verge, ISD interspinous diameter, LAR low anterior resection, LARS low anterior resection syndrome.
demonstrating an AUC of 0.842 (95% CI, 0.794–0.890) (Table 5, Fig. 3).

In patients without neoadjuvant therapy, only DTA was the independent factor for predicting major LARS; OR was 0.958 (95% CI, 0.930–0.988) (Table 4). The AUC of DTA for predicting major LARS was 0.777 (95% CI: 0.630–0.925) (Table 5, Fig. 3).

For the neoadjuvant therapy group, the post hoc power was 0.84 to detect a difference in AUC of 0.092 with the null hypothesis of 0.75 (regarded as potentially clinical useful) and an alternative hypothesis of 0.842 using a two-sided z-test at a significance level of 0.05. For the direct surgery group, the post hoc power was 0.08 to detect a difference in AUC of 0.027 with the null hypothesis of 0.75 and an alternative hypothesis of 0.777 using a two-sided z-test at a significance level of 0.05.

**Discussion**

The present study analyzed the preoperative clinical factors and radiological features to predict major LARS in mid-low rectal cancer patients. The results showed that the distance between the lower edge of tumor and ARJ (DTA) was an important influencing factor of major LARS in both neoadjuvant therapy group and direct surgery group. In neoadjuvant therapy group, the thickness of ARJ ring (TARJ) was also significantly correlated with the occurrence of major LARS. Few studies used MR imaging to predict LARS before surgery.

Many rectal cancer patients have different degrees of low anterior resection syndrome (LARS) after sphincter preservation. The emergence of LARS decreased the quality of life, and this impact was mostly long-term and

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**Table 2** Comparison of clinical, MRI, and pathological parameters between major LARS and no/minor LARS in neoadjuvant chemoradiotherapy group

|                         | LARS No/minor(n = 119) | LARS Major(n = 136) | P     |
|-------------------------|------------------------|---------------------|-------|
| **Sex**                 |                        |                     |       |
| Male                    | 68 (57.1)              | 94 (69.1)           | 0.047 |
| Female                  | 51 (42.9)              | 42 (30.9)           |       |
| **Age(years)**          | 54.76 ± 11.93          | 58.26 ± 49.91       | 0.456 |
| **Baseline MRI measurements(mm)** |            |                     |       |
| TLA                     | 4.77 ± 1.62 (4.01 ± 1.64) | <0.001             |       |
| TARJ                    | 9.92 ± 2.32 (7.97 ± 2.10) | <0.001             |       |
| TIS                     | 4.58 ± 1.31 (4.51 ± 1.22) | 0.713              |       |
| TES                     | 9.63 ± 2.01 (9.17 ± 2.04) | 0.07               |       |
| DTA                     | 36.24 ± 18.50 (20.91 ± 13.29) | <0.001             |       |
| DTV                     | 67.66 ± 19.90 (51.75 ± 14.91) | <0.001             |       |
| **Length of anal canal** | 31.42 ± 5.15 (30.83 ± 5.33) | 0.376              |       |
| Anorectal angle         | 127.49 ± 18.04 (123.15 ± 17.16) | 0.053              |       |
| ISD                     | 96.45 ± 10.72 (95.85 ± 10.60) | 0.652              |       |
| **pT**                  |                        |                     |       |
| T0                      | 19 (16.0)              | 29 (21.3)           | 0.491 |
| T1                      | 14 (11.8)              | 13 (9.6)            |       |
| T2                      | 35 (29.4)              | 44 (32.4)           |       |
| T3                      | 50 (42.0)              | 50 (36.7)           |       |
| T4                      | 1 (0.8)                | 0 (0.0)             |       |
| **pN**                  |                        |                     |       |
| 0                       | 92 (77.3)              | 109 (80.1)          | 0.692 |
| 1                       | 22 (18.5)              | 20 (14.7)           |       |
| 2                       | 5 (4.2)                | 7 (5.2)             |       |
| **Histopathological type** |                      |                     |       |
| Adenocarcinoma          | 112 (94.1)             | 125 (91.9)          | 0.445 |
| (With) mucinous adenocarcinoma | 5 (4.2) | 10 (7.4)          |       |
| Signet ring cell carcinoma | 2 (1.7)            | 1 (0.7)             |       |
| **Differentiation**     |                        |                     |       |
| Good-moderate           | 103 (86.6)             | 116 (85.3)          | 0.773 |
| Poor                    | 16 (13.4)              | 20 (14.7)           |       |

*LARS* low anterior resection syndrome, *TLA* the thickness of levator ani, *TARJ* the thickness of Anal-rectal joint, *TIS* and *TES* the thickness of internal and external anal sphincter complex, *DTA* the distance between tumor’s lower edge and ARJ, *DTV* (*DTA + anal canal length*) the distance between tumor’s lower edge and anal verge, *ISD* interspinous diameter.
persistent [13, 14], resulting to the strong demands for permanent colostomy in those patients which major LARS seriously affects the quality of life. The needs of predicting major LARS before surgery are growing when more sphincter-preserving methods were developed like extralow anastomosis or local excision after tumor downstaging by NCRT, innovative surgical approach like transanal TME, etc.

The anorectal junction (ARJ) is a powerful muscle ring around the anal canal, which is composed of the muscle bundles from superficial and deep part of the external anal sphincter, the longitudinal muscles of the lower rectum, and the internal anal sphincter and the puborectalis of levator ani muscle. It plays a very important role in the anal canal expansion and contraction. The puborectalis wraps as a sling around the anorectal junction accentuating the

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**Table 3** Comparison of clinical, MRI, and pathological parameters between major LARS and no/minor LARS in direct surgery group

| Parameter                      | Major (n = 25) | No/minor (n = 47) | P   |
|-------------------------------|---------------|------------------|-----|
| Sex                           |               |                  |     |
| Male                          | 11 (44.0)     | 23 (48.3)        | 0.629 |
| Female                        | 14 (56.0)     | 24 (51.7)        |     |
| Age                           | 60.60 ± 12.07 | 62.13 ± 10.11    | 0.571 |
| Baseline MRI measurements(mm) |               |                  |     |
| TLA                           | 2.97 ± 2.47   | 3.60 ± 2.77      | 0.352 |
| TARJ                          | 5.36 ± 4.38   | 6.69 ± 4.95      | < 0.001 |
| TIS                           | 4.35 ± 1.38   | 4.35 ± 1.38      | 0.686 |
| TES                           | 8.84 ± 1.23   | 9.97 ± 2.47      | 0.03  |
| DTA                           | 37.64 ± 25.80 | 65.42 ± 25.97    | < 0.001 |
| DTV                           | 70.78 ± 26.01 | 97.42 ± 27.73    | 0.002 |
| Length of Anal canal          | 33.14 ± 5.25  | 32.01 ± 5.26     | 0.486 |
| Anorectal angle               | 109.34 ± 18.80 | 106.36 ± 15.20 | 0.557 |
| ISD                           | 91.44 ± 10.53 | 97.12 ± 10.45    | 0.088 |
| pT                            |               |                  |     |
| T0                            | 1 (4.0)       | 0 (0)            | 0.024 |
| T2                            | 6 (12.8)      | 15 (60.0)        | 0.179 |
| T3                            | 24 (96.0)     | 41 (87.2)        |     |
| pN                            |               |                  |     |
| 0                             | 15 (60.0)     | 29 (61.7)        | 0.179 |
| 1                             | 5 (20.0)      | 15 (31.9)        |     |
| 2                             | 5 (20.0)      | 3 (6.4)          |     |
| Histopathological type        |               |                  |     |
| Adenocarcinoma                | 22 (88.0)     | 43 (89.1)        | 0.343 |
| (With) mucinous adenocarcinoma| 2 (8.0)       | 4 (10.9)         |     |
| Signet ring cell carcinoma    | 1 (4.0)       | 0 (0)            |     |
| Differentiation               |               |                  |     |
| Good-moderate                 | 22 (88.0)     | 44 (93.6)        | 0.412 |
| Poor                          | 3 (12.0)      | 3 (6.4)          |     |

LARS low anterior resection syndrome, TLA the thickness of levator ani, TARJ the thickness of Anal-rectal joint, TIS and TES the thickness of internal and external anal sphincter complex, DTA the distance between tumor’s lower edge and ARJ, DTV (DTA + anal canal length) the distance between tumor’s lower edge and anal verge, ISD interspinous diameter.

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**Table 4** Multivariate logistic regression results

| Treatment                  | B     | OR   | 95% CI          | P     |
|----------------------------|-------|------|-----------------|-------|
| Neoadjuvant therapy        |       |      |                  |       |
| Sex (female = 0,           | −0.961| 0.382| 0.198–0.740     | 0.004 |
| male = 1)                  |       |      |                  |       |
| TARJ                       | −0.426| 0.653| 0.565–0.756     | < 0.001 |
| DTA                        | −0.068| 0.935| 0.915–0.955     | < 0.001 |
| Direct surgery             |       |      |                  |       |
| DTA                        | −0.042| 0.958| 0.930–0.988     | 0.005 |

TARJ the thickness of anal-rectal joint, DTA the distance between tumor’s lower edge and ARJ, OR odds ratio.
anorectal angle during contraction and is a primary contributor to fecal continence. MRI also reveals puborectalis atrophy and impaired pelvic floor contraction in some women with fecal incontinence [15–18]. And the internal anal sphincter is damaged in systemic sclerosis together with fecal incontinence [19]. How et al. [20] estimated predictors for poor function by using MRI to measure various parameters related to the sphincter complex in rectal cancer patients who had undergone sphincter-saving surgery, and a puborectalis thickness was found to be a predictor of poor function. Therefore, we have reason to believe that if ARJ is injured during the operation, it will lead to fecal incontinence. In this study, the univariate and multivariate analysis demonstrated that the thickness of ARJ ring (TARJ) was a risk factor for major LARS. It can be understood that the patients with thinner ARJ ring had lower anal canal constriction pressure and weaker effect on anal canal. Therefore, the probability of major LARS was higher than those with thicker ARJ ring. As far as we know, there was no imaging study focused on LARS prediction, also there was no MRI related parameter measurement for LARS evaluation.

Besides the location of tumor, we also find the thickness of ARJ is a new predictive factor in neoadjuvant chemoradiotherapy patients. Radiotherapy is a well-known risk factor for LARS, which can lead to short-term and long-term colorectal dysfunction after anterior resection of rectal cancer [21–24]. Among the 255 patients in this study, 53.3% of the radiotherapy patients had major LARS, and only 34.7% of patients with direct surgery had major LARS, suggesting that radiotherapy is related to major LARS. The thickness of ARJ ring was associated with major LARS in NCRT group, but not in direct surgery group. Previous studies have shown that radiotherapy will lead to fibrosis of intestinal tract, pelvic wall tissue, and pelvic floor muscles, such as levator ani and inner and outer sphincter muscles [25, 26]. We boldly speculate that patients with thicker ARJ ring had more reserves of resting pressure after fibrosis formation and lower probability of major LARS. The relationship between the thickness of ARJ, resting pressure of anus, and the occurrence of major LARS is to be further explored through objective postoperative anal function test and combined analysis.

We observed the incidence of major LARS after LAR was significantly higher in neoadjuvant therapy group than in direct surgery group. To improve local control and R0 resection rate, the strategy of NCRT even total neoadjuvant treatment plus prolonged resting time after radiation were emphasized, especially for cases with local or systemic high risk factor like positive MRF or EMVI or T3c/T3d/T4b substages. Another advantage of NCRT is the higher sphincter preservation rate obtained through tumor downsize and downstaging [27]. However, the combination of NCRT

**Table 5** Diagnostic performance of models for predicting major LARS

| Treatment            | AUC       | Cut off | Sensitivity | Specificity | PPV       | NPV       | Accuracy  |
|----------------------|-----------|---------|-------------|-------------|-----------|-----------|-----------|
| Neoadjuvant therapy  | 0.842     | −7.70   | 86.0%       | 73.1%       | 78.5%     | 82.1%     | 80%       |
|                      | (0.794–0.890) | (80.2–91.7%) | (65.1–81.1%) | (72.0–85.1%) | (74.8–89.4%) | (75.1–84.5%) |          |
| Direct surgery       | 0.777     | 33.2    | 60%         | 90.6%       | 68.2%     | 80.8%     | 79.2%     |
|                      | (0.607–0.917) | (40.8–79.2%) | (80.6–98.2%) | (48.7–87.7%) | (70.1–91.5%) | (70.0–88.6%) |          |

*AUC* area under the curve, *PPV* positive predictive value, *NPV* negative predictive value.
and low anastomosis is the main cause of major LARS, which decrease patients’ quality of life. In fact, in addition to bowel dysfunction, rectal cancer patients are burdened by a high rate of urinary and sexual dysfunction associated with a compromised quality of life [28]. The predictive factors reported in the present study may contribute to personalized decision-making and inform consent before surgery, to avoid intraoperative discretion of low anastomosis which may definitively cause major LARS. Additional prospective of this predictive model is to promote intentional watch and wait. For low rectal cancer patients of low local and systemic risk, who are more radiosensitive and have more expected cCR rate, intensive neoadjuvant treatment rather than the attempt of broadline sphincter preservation is more rational when major LARS can be predicted.

Above all, the incidence of major LARS after LAR is significantly higher in neoadjuvant therapy group, compared with direct surgery group. With the increasing popularity of standardized treatment for rectal cancer and the sufficient guarantee of patients’ survival, clinicians should pay enough attention to the high incidence of LARS and its impact on patients’ quality of life. Early prediction of major LARS is helpful to the individual treatment strategies. This may aid in the surgical decision-making process by helping predict functional outcome at no extra cost or in convenience to the patient. The following scenarios may appear, and LARS prediction may assist clinical decision-making: (1) Screening of patients with neoadjuvant radiotherapy, such as male, middle and low rectal cancer, patients with thinner ARJ ring, patients with no special prognostic risk factors (MRF and/or mr-EMVI negative), and patients with high risk of major LARS; the actual benefits of neoadjuvant radiotherapy should be clarified on MDT and unnecessary neoadjuvant radiotherapy should be avoided as far as possible. If neoadjuvant radiotherapy is necessary (MRF and/or Mr-EMVI positive), we still need to clarify appropriate surgical procedures by MDT after neoadjuvant therapy, and the informed consent for the expected anal preservation should be more detailed and targeted; (2) For patients with low rectal cancer, who have good response for neoadjuvant radiotherapy, may have reached cCR on MDT, and but with a higher probability of major LARS, “watch and wait” strategy may benefit more, especially for the frail and older patient this oncological risk is more easily counterbalanced by an increased operative risk and a decreased life expectancy than for a younger patient [29]; (3) For patients with high risk of major LARS, if neoadjuvant chemoradiotherapy and TME are unavoidable due to the location and stage of the tumor compromising distal tumor clearance, this information should influence decision-making and should be discussed with the patient prior to combining both radiotherapy and restorative resection [28]. And health education should be strengthened to make patients fully understand LARS.

Postoperative rehabilitation treatment, pelvic floor muscle function training, and follow-up should be guided.

Limitations: it is worth noting that the pelvic floor muscles are irregular, three-dimensional, and cannot be measured simply and accurately at a certain level (coronal, sagittal, or axial). In this study, pelvic floor muscles are measured simply on a certain plane, rather than 3D volume measurement. We believe 3D volume measurements by using AI would be helpful for LARS prediction; we did not analyze the differences among the three groups of no, mild, and major LARS, but the difference between no/mild LARS and major LARS, one of the reasons is that the symptoms of patients with mild LARS can be alleviated over time, and will not have a significant impact on the quality of life of patients [30]; secondly, the post hoc power analysis results means that the MRI predicting model for major LARS in the patients with neoadjuvant therapy is reliable, but there is insufficient ability to make correct statistical inference for the major LARS predicting model in the patients undergoing direct surgery due to the small sample size. More samples from multi-centers are needed to verify the efficacy of these MRI measurements for predicting major LARS, especially for patients undergoing direct surgery.

**Conclusion**

Although MRI play an important role in rectal cancer staging and therapy evaluation after neoadjuvant chemoradiotherapy, there are few studies on the measurement of pelvic floor muscles on MRI, and the relationship between these muscles and LARS. This is the first attempt to use MRI predicting the occurrence of major LARS. To our knowledge, there is no previous imaging study on LARS. Our preliminary results suggest that the thickness of the ARJ ring and the distance between the lower edge of the tumor and ARJ measured on MRI can be used to predict major LARS early before surgery and help to make decision at no extra cost or in convenience to the patient. However, prospective assessment of larger numbers of patients is required to evaluate these findings further.

**Supplementary information** The online version contains supplementary material available at https://doi.org/10.1007/s00384-022-04169-9.

**Author contribution** Xiao-Yan Zhang, Liu Xin-Zhi, Ying-Shi Sun, and Ai-Wen Wu designed the study; Xiao-Yan Zhang, Xin-Zhi Liu, Lin Wang, Hai-Bin Zhu, Rui-Jia Sun, Zhen Guan, Qiao-Yuan Lu, Wei-Hu Wang, and Zhong-Wu Li collected data; Xiao-Yan Zhang, Xin-Zhi Liu, Xiao-Ting Li, Hai-Tao Zhu, Ying-Shi Sun, and Ai-Wen Wu analyzed and interpreted the data; Xiao-Yan Zhang and Xin-Zhi Liu drafted the manuscript; all authors reviewed and approved the manuscript.

**Declarations**

**Competing interests** The authors declare no competing interests.
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Publisher’s Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.
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