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*Observational Study*

**To explore the pathogenesis of anterior resection syndrome by MRI rectal defecography**

evaluate LARS by MRI rectal defecography

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**Abstract**

**BACKGROUND**

Over 90% of rectal cancer patients suffered low anterior resection syndrome (LARS) after sphincter preserving resection (SPR) surgery. At present, as a globally recognized evaluation method, the LARS score has many drawbacks and its subjectivity is too strong, which hinders the research and treatment of anterior resection syndrome.

**AIM**

To evaluate the anorectal function after operation of colorectal cancer by quantifying the index of MRI defecography and to explore the pathogenesis of LARS.

**METHODS**

The experimental model of 34 patients with anterior resection syndrome was established by LARS score, and a new LARS evaluation index was established by using the dynamic image of MRI defecography to verify the experimental model.

## RESULTS

In the LARS score model, there were 10 (29.41%) mild LARS and 24 (70.58%) severe LARS. The comparison of defecation rate between the two groups was  $(29.36 \pm 14.17) \%$  vs  $(46.83 \pm 18.62) \%$ ,  $P=0.004$ ; MIR-RC score:  $(3.63 \pm 1.96)$  vs  $(7.00 \pm 3.21)$ ,  $P=0.001$ . Both severe LARS and mild LARS had significant statistical significance in two different evaluation methods. There was a significant negative correlation between LARS score and MRI-RC score,  $P=0.000$ , and also has a negative correlation with the defecation rate,  $P=0.028$ .

## CONCLUSION

MRI defecography and standard LARS scoring method may have the same evaluation effect and can be used as an evaluation index to study the pathogenesis of LARS.

**Key Words:** Anterior resection syndrome; Colorectal cancer; Diagnostic evaluation system; MRI defecography; pathogenesis

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**Core Tip:** Currently, the evaluation of LARS symptoms in patients is solely reliant on subjective measures, such as questionnaires. There is a lack of a standardized and objective medical assessment index. Through our team's innovative application of MRI defecography to judge and quantify the compliance of neorectum after low rectal cancer surgery, we establish the objective diagnosis and severity evaluation criteria of LARS MRI defecography after rectal cancer operation, so that quantify the severity of LARS by objective clinical evaluation index, and promote the exploration of the pathogenesis of LARS.

## **INTRODUCTION**

Patients diagnosed with low rectal cancer who require sphincter preserving resection (SPR) are at a considerable risk of experiencing a notable decline in anorectal function following the surgical procedure. After long-term follow-up following sphincter preserving resection,<sup>1, 2</sup> over 90% of rectal cancer patients experienced suboptimal recovery of anorectal function, characterized by increased defecation frequency, higher incidence of encopresis, and incontinence of liquid or solid stools, collectively referred to as low anterior resection syndrome (LARS).<sup>3</sup> Postoperative intestinal dysfunction is a prevalent occurrence in patients with rectal cancer, with an incidence rate ranging from 70% to 90% of postoperative patients. Such dysfunction may manifest as periodic alterations in stool consistency, transitioning from dry and rigid to pasty, thereby significantly compromising the patients' quality of life.<sup>4</sup> This symptom has been a persistent source of distress for numerous patients, and its resolution without efficacious treatment measures has led to a cascade of physical and psychological ailments.<sup>5</sup> Efficiently enhancing the anorectal function of patients post-surgery is of utmost importance. Numerous studies on anal function have failed to provide a comprehensive explanation and precise evaluation of postoperative anorectal function impairment. Currently, the evaluation of LARS symptoms in patients is solely reliant on subjective measures, such as questionnaires. There is a lack of a standardized and objective medical assessment index, as well as an absence of an objective index for the systematic classification and grading of patients' symptoms.<sup>6</sup> Consequently, the scientific evaluation and analysis of diagnosis and treatment measures for patients with LARS are limited, leading to a dearth of scientific investigations on the prevention and treatment of LARS following anal preservation for rectal cancer. This, in turn, has resulted in the absence of effective objective evaluation criteria, thereby impeding the progress of research on LARS prevention and treatment over an extended period. Exploring defecography to assess and quantify the compliance of the neorectum after low rectal cancer surgery is a valuable approach to establishing objective diagnostic

criteria for LARS rectal MRI defecography, to explore the pathogenesis of LARS by imaging index.

## **MATERIALS AND METHODS**

### **Study**

### **Population**

The research cohort comprised 34 patients, ranging in age from 18 to 76 years, who had been diagnosed with low rectal cancer and had undergone total mesorectal excision (TME) and one-stage intestine anastomosis within 12 mo prior to their enrollment. Patients diagnosed with rectal cancer that is amenable to surgical resection, and whose tumors are situated below the S2 Level with a lower margin within 5cm of the dentate line. The preoperative rectal MRI measurement of the mean distance between the lower border of the tumor and the anal margin is  $(4.12 \pm 1.04)$  cm. The pathological classification of the observed condition is adenocarcinoma. The diagnosis of T1-3, negative MRF or EMVI was determined through rectal MRI. Participants were excluded if they had distant organ metastases, severe cardiac or pulmonary medical disease, gastrointestinal dysfunction or motility disorders; or metabolic, neurogenic or endocrine disease known to cause colonic motility disorders. Patients with anastomotic leakage or requiring multiple dilations of the anastomotic stricture were excluded. The present study recruited a control group consisting of 26 healthy volunteers, aged between 18 and 60 years, who underwent MRI defecography at the hospital where the research was conducted. The control group exhibited regular bowel patterns, characterized by a frequency of three bowel movements per day to one bowel movement every three days, and were devoid of any gastrointestinal symptoms. The medical records, follow-up data, and postoperative pathology of the patients were comprehensive. The patients were duly informed and provided their consent by signing the informed consent form, subsequently returning to the hospital for the LARS questionnaire and MRI defecography imaging assessment post-surgery. The treatment process was consistently overseen by the same surgical team, ensuring uniformity in all procedures and follow-ups.

The evaluation of neorectal defecation frequency and MRI-Rectal compliance through MRI defecography

Prior to the examination, a standard bowel cleansing protocol was implemented and the bladder was voided 30 minutes prior to the procedure. The patient assumed a supine position with the head advanced, both arms elevated, and the knees elevated to induce flexion in the lower limbs, followed by the administration of static and dynamic MRI scans of the rectum. The United Imaging 1.5T superconducting MRI served as the examination tool. The pelvic examination site was equipped with an abdominal phased-array coil, and the initial scan conducted was the resting sagittal T2WI. Subsequently, the transverse-axis T2WI, which was perpendicular to the long axis of the anal canal, and the oblique coronal T2WI, which was parallel to the long axis of the anal canal, were scanned in the median sagittal position. Prior to the injection of the ultrasonic coupling agent, a pre-determined amount of 150-250 mL was weighed and then administered through the anal canal. The sagittal localization image was rescanned, and the FIESTA sequence dynamic defecography scan was performed in the median sagittal position, and the patient was instructed to forcefully evacuate the bowel until it was emptied and do anal lift, then perform a single-excitation fast spin-echo sequence T2WI image scan, and the resting and maximum force evacuation images were taken in the median sagittal position dynamic MRI real-time image, which took 68 s. Finally, the transverse axis of T2WI was scanned; if necessary, the coronal dynamic Valsalva maneuver scan images. The scan layer thickness was 15mm, interval 0mm, matrix 272×85, FOV 250×250. The couplant that was discharged from the patient was gathered and re-weighed, and subsequently, the ratio between the mass of the discharged couplant and the mass of the injected couplant was determined as the defecation rate.

The rectal compliance was assessed using the five-line partition scoring method, and the dynamic images were captured. Six diameters perpendicular to the midline of the intestinal canal were made along the sacral intervertebral space, and the midline and vertical line of the intestinal canal were divided into five regions. Each region is represented by the letters A, B, C, D and E respectively, and each region is defined as 2

points. The intestinal wall motion of each region is observed during force exclusion. The score of the area can be defined when there is a significant swing of the intestinal wall during defecation (Figure 1 and 2).



a

b

**Figure 1: Rectal compliance was assessed by five-line partition scoring**

(a) The shape of the wall of the intestine in the area where the bowel is at rest; (b) The continuous contraction and relaxation of the intestinal wall in the area where the contrast agent passes through the intestine.



**Figure 2: The utilization of magnetic resonance imaging (MRI) scanning for the acquisition of both dynamic and static rectal images**

The method of follow-up  
The study recorded an average follow-up time of 18 mo for anal defecation, during which the subjective index of the severity of low anterior resection syndrome after operation was obtained using the Low Anterior Resection Syndrome Score (LARSS) developed by Danish scholar Emmert-sen in 2012.<sup>7</sup> A lower score is indicative of milder symptoms, while a higher score is associated with more severe symptoms. For instance,

a score ranging from 0-20 is indicative of mild LARS, while a score ranging from 21-29 suggests moderate LARS, and a score ranging from 30-42 indicates severe LARS (Figure3).

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**Figure 3: The Low Anterior Resection Syndrome Score (LARS score)**

Statistical analysis

The statistical analysis involved the utilization of SPSS 26 to analyze all data. The measurement data for both the experimental and control groups were presented as mean±standard deviation ( $\bar{X} \pm S$ ). The comparison between groups was conducted using the independent sample t test, while the correlation analysis in the experimental group was performed using Pearson correlation analysis. Statistical significance was determined when  $P \leq 0.05$ .

Biostatistics statement

The statistical methods of this study were reviewed by Linghou Meng, Bingyu Yang,

Qingzhou Song, Guohai Yang, Changlin Mo, Zheng Wang from Guangxi Medical University Cancer Hospital.

## **RESULTS**

Using the LARS score as the primary metric for assessment, the LARS scores of each patient in the experimental cohort were consistently monitored at 6 and 12 mo post-surgery. The LARS score was  $(37.02 \pm 3.43)$  vs  $(32.58 \pm 4.91)$ ,  $P=0.00$ . The MRI defecation rate and MIR-RC score were utilized to analyze the experimental results of 34 patients in the experimental group at various time points. The MRI defecation rate was  $(39.47 \pm 0.15)\%$  vs  $(35.53 \pm 0.17)\%$ ,  $P=0.411$ ; MIR-RC score:  $(4.41 \pm 2.40)$  vs  $(4.82 \pm 2.92)$ ,  $P=0.165$ . The statistical analysis of Table 1 indicates that there is no significant difference in the  $P$  values obtained from the two evaluation methods. Despite a decrease in the LARS score, the actual anorectal function has not been accurately assessed.

The average MIR-RC score and defecation rate of 26 healthy subjects in the control group were  $(8.88 \pm 0.90)$  and  $(61.19 \pm 0.86)\%$ , respectively. The MIR-RC score and MRI defecation rate were compared between the experimental group and normal subjects. The results indicated a statistically significant difference between the two groups, with the experimental group exhibiting lower scores for both MIR-RC  $(4.82 \pm 2.92$  vs  $8.88 \pm 0.90)$ ,  $P=0.000$ , and MRI defecation rate  $(35.53 \pm 0.17)\%$  vs  $(61.19 \pm 0.86)\%$ ,  $P=0.007$ . These findings suggest that there is a notable difference in neorectal function between postoperative patients and normal subjects, as presented in Table 2. Based on the LARS score findings, the cohort of 34 patients was stratified into two subgroups, namely the severe LARS group ( $n = 24$ ) and the mild LARS group ( $n = 10$ ). The results indicate a statistically significant difference in defecation rates between the two groups, with rates of  $(29.36 \pm 14.17)\%$  and  $(46.83 \pm 18.62)\%$  for Severe group and Mild group respectively ( $P=0.004$ ). Additionally, the MIR-RC score was found to be significantly lower in Severe group  $(3.63 \pm 1.96)$  compared to Mild group  $(7.0 \pm 3.21)$ ,

$P=0.001$ , as presented in 3. The present study reveals that there exists a statistically significant relationship between severe and mild LARS as assessed by two distinct methods. Specifically, the LARS score and MRI-RC score exhibit a significant negative correlation ( $P=0.000$ ) and are negatively correlated with defecation rate ( $P=0.028$ ). The evaluation method that aligns with the LARS score standard exhibits comparable efficacy, as demonstrated in Figures 4 and 5.

## **DISCUSSION**

In experimental model, the utilization of the globally recognized LARS scoring scale is preferred for modeling. The long-term follow-up evaluation of the study samples indicates that patients' perceptions of LARS-related symptoms evolve over time, with some patients experiencing gradual relief of their symptoms, while others continue to experience LARS symptoms for an extended period. By evaluating the anal function of 34 patients at different time points after operation, it was found that LARS was not a short-term intestinal adaptation process, but rather a potentially permanent pathogenic mechanism.<sup>8</sup> But the LARS assessment scale model presents subjective variances and immediacy among patients, rendering an accurate and objective evaluation of symptom severity unattainable. Consequently, we developed an imaging-based observation data model that facilitates the detection of the LARS score scale model in a more intuitive manner. To ascertain the efficacy of the model, we enlisted 26 individuals who were in good health, and subsequently compared them with all patients diagnosed with LARS. Based on the data outcomes, it is evident that there exist noteworthy variances in defecation rate and MRI-RC between LARS patients and the aforementioned healthy volunteers. The imaging model successfully identified both mild and severe LARS patients, revealing significant differences in defecation rate and MRI-RC score between the two groups. These findings suggest that the newly proposed evaluation model is comparable in effectiveness to the LARS scale. Therefore, MRI defecography can be used to study anterior resection syndrome more intuitively.

Defecation is a complex physiological process, which includes the synergistic action of anal inner and outer sphincter functional movement, colorectal functional movement, neurohormones, *etc.* Abnormalities in one of the links are highly likely to cause defecation dysfunction.<sup>9</sup> However, the pathophysiological mechanism of LARS remains unclear. Recent research indicates that the pathogenesis of the condition may have a strong correlation with the perirectal nerve, muscle injury, neorectal volume, and intestinal compliance, with the latter being potentially the most significant factor.<sup>10-13</sup> A considerable quantity of striplike scar images were detected in the postoperative CT images of the pre-rectal sacral soft tissues in the majority of patients. These scar tissues were observed to be firmly attached to the bowel during the surgical procedure, leading to a marked decrease in bowel compliance.<sup>14, 15</sup> Currently, the LARS score,<sup>7</sup> multiple quality of life score, fecal incontinence score, anorectal manometry, and other techniques are predominantly employed; however, these methods exhibit numerous drawbacks in their clinical application.<sup>16, 17</sup> There are cultural differences in the evaluation of the symptoms through the score.<sup>18</sup> Despite the widespread use of language and text processing in our country,<sup>19</sup> the subjective nature of this approach may result in clinical evaluations that do not align with the actual symptoms in certain cases. In clinical settings, the variability of successive measurements for a single patient and the inability of examination results to accurately reflect the long-term function of the intestinal tube pose significant challenges to the research and treatment of LARS.<sup>12, 20</sup> This study employed rectal MRI defecography to quantify relevant indices and analyze the pathophysiological characteristics of LARS, with the aim of proposing a novel evaluation criterion for assessing intestinal dysfunction following TME. By comparing with normal subjects, we found that rectal MRI defecography showed that the movement characteristics of neorectum after TME were quite different from those of normal subjects, in which there were more variations in the defecation process of neorectum in patients with severe LARS symptoms. In static images, the presacral structure of normal mesenteric tissue was in the shape of "funnel", and the neorectum

formed adhesion due to unclear presacral structure after TME. In the dynamic image, the new rectum has a low degree of activity because of adhesion, and the loss of intestinal pressure gradient conversion ability leads to insufficient defecation power. In order to better confirm the variation of defecation process in patients after TME, through imaging observation of intestinal activity and comparative study with defecation rate, it is found that the application of the new evaluation method on the basis of LARS score can directly evaluate the functional status of neorectum during defecation and complement LARS score.

Prior research has solely relied on the LARS score scale, which is primarily influenced by patients' subjective perceptions, to assess defecation dysfunction.<sup>21</sup> The LARS score gradually tended to a stable value half a year after operation, and the LARS score tended to change from severe to moderate,<sup>22-24</sup> but it was found that the two groups of data could not reflect significant physiological changes in anorectal function in the new experimental model. The lower MRI-RC score reflects that decreased intestinal compliance is the main factor leading to defecation disorders and high LRAS scores. The intestinal motility and compliance were quantitatively analyzed by analyzing the range of motion of the intestinal wall in the dynamic image by MRI defecography combined with weighing the contrast medium for defecation. The defecation disorder mainly comes from three aspects: (1) The formation of a novel perirectal adhesion scar results in rectal stiffness, which impairs the normal physiological processes of contraction and dilatation. The severity of the symptoms associated with LARS is directly proportional to the length of the scar; (2) Anastomotic stricture; (3) The capacity to defecate voluntarily is solely dependent on the abdominal pressure generated by the contraction of the abdominal muscles, resulting in a highly disorganized defecation process owing to the absence of bowel motility. This is because the rectum of normal people is generally empty and collapsed in a quiet state. The movement of feces in the colon is generally the reverse pressure gradient transformation of peristaltic waves and the movement mode dominated by cyclic motor pattern of the distal colon.<sup>25</sup> In order to

prevent the defecation reflex caused by the rapid filling of the rectum in a short period of time, the above two control modes help to control normal defecation and abstinence.<sup>26, 27</sup> The primary point of origin for CMP is located at the junction of the rectum and sigmoid.<sup>26</sup> Through the observation of patients with intestinal dysfunction after TME, it is found that due to the consideration of the safety of the surgical margin, the upper incisional margin is usually removed at the position away from the tumor 10cm, so the starting area of CMP is inevitably removed. The lower digestive tract of all patients in this study was reconstructed solely through the utilization of partial sigmoid colon and distal residual rectal anastomosis. From the images of defecography, it can be seen that the movement pattern was not observed during defecation, and the transformation process of the pressure gradient of the neorectum was out of balance. For the neorectum that loses mesenteric tissue and adheres to the anterior sacrum, the transport capacity of intestinal contents is reduced, and the next intestinal canal cannot be dilated effectively in the process of propulsion. As a result, a large amount of dynamic energy produced by abdominal pressure can not be transferred continuously, resulting in the phenomenon of "squeezing toothpaste". The decrease of the degree of dilatation and the range of movement can lead to a significant decrease in the maximum tolerance capacity of the intestine compared with the original rectum (the neorectal volume is fixed in a short time and the later stage will increase the intestinal dilatation due to compensation), which reflects the decrease of intestinal compliance. For patients with low rectal cancer, the vast majority of neorectal compliance decreased after operation.<sup>14</sup> However, some scholars believe that the colonic transport capacity of patients with severe LARS is enhanced.<sup>28</sup> This is due to a significant increase in systolic pressure in the neorectum of severe LARS patients due to increased adhesion tension.<sup>29</sup> In the late recovery of the neorectum, the intestinal canal forms a new pressure gradient, but the intestinal compliance is still not recovered from the image, each defecation can only discharge a small amount of feces, so that the intestinal pressure is temporarily reduced. The defecation reflex disappears, and when the intestines push forward a small amount of feces, there will be a new defecation reflex

that leads to an increase in the number of defecation, so this phenomenon does not mean that the patient's transport capacity is enhanced, but a sign of reduced intestinal compliance. However, it is worth noting that the loss of anterograde and retrograde CMP may also lead to different symptoms of LARS heterogeneous phenotypes, such as stool retention and incontinence.

Changes in the anatomical structure of the rectum and presacral fascia after operation and the establishment of the neorectum are bound to form LARS, which exists for a long time and can not be cured by any intervention.<sup>30</sup> The research on this symptom mainly comes from the feelings of the patients. In the process of long-term patience and adaptation, the intestinal canal compensates to increase the storage capacity of feces, that is, some patients feedback that the symptoms have improved, but this part of patients must match the size of the anastomosis with the transport capacity of the neorectum in order to have such an effect. One year after TME, the LARS score of the patients often returned to moderate state, and the patients could also return to normal work and life. However, in the images of defecography, it was found that most of the patients were still in a difficult defecation process, so the evaluation of LARS symptoms could not accurately and objectively reflect the real state. The long-term observation of LARS symptoms is not necessarily in the gradual recovery, but the adaptation of patients to form new defecation habits.

The limitation of this study lies in the sample size. There are many heterogeneity in the defecation process of severe LARS patients, indicating that a considerable sample size is needed for in-depth comparison in the future. All studies were conducted after intestinal preparation in advance, which is standard practice for defecography, but this may cause spontaneous contraction of the colon, especially high-amplitude transmitted contractions that may be associated with symptoms such as defecation urgency and incontinence.<sup>25</sup> In the future, it will be valuable to conduct a comprehensive assessment of anorectal function in conjunction with rectal defecography to determine other

physiological features that may lead to LARS symptoms and subgroups, such as neorectal mobility and anal sphincter dysfunction.

With the high degree of human evolution, every tissue of the human body plays an irreplaceable role. The emergence of TME operation improves the survival rate of patients with rectal cancer, but the sharp separation of presacral tissue destroys the nerve tissue and aseptic inflammation of the wound leading to intestinal adhesion may be an important factor leading to anterior resection syndrome. Although the disease is cured, it brings long-term trouble to the patients. At present, as a globally recognized evaluation method, the LARS score has many drawbacks and its subjectivity is too strong, which hinders the research and treatment of anterior resection syndrome. In order to observe the intestinal compliance more intuitively and quantify it, we creatively use the five-line zoning score method to be more accurate than the rectal manometry method, and more in line with the true movement state of the intestine, but the self-feeling of patients with this symptom is the gold standard. Through our team's innovative application of MRI defecography to judge and quantify the compliance of neorectum after low rectal cancer surgery, we establish the objective diagnosis and severity evaluation criteria of LARS MRI defecography after rectal cancer operation, so that quantify the severity of LARS by objective clinical evaluation index, it is more helpful to scientifically evaluate the value of all kinds of scientific research on prevention and treatment of LARS.

## **CONCLUSION**

As a new evaluation standard, MRI defecography has good application value in the diagnosis and evaluation of LARS, it can supplement the defect of subjective influence of LARS score, and promote the exploration of the pathogenesis of LARS.

## **ARTICLE HIGHLIGHTS**

*Research background*

Over 90% of rectal cancer patients suffered low anterior resection syndrome (LARS) after sphincter preserving resection (SPR) surgery. Currently, the LARS score, 7 multiple quality of life score, fecal incontinence score, anorectal manometry, and other techniques are predominantly employed to assess LARS.

#### *Research motivation*

The LARS score has many drawbacks and its subjectivity is too strong, which hinders the research and treatment of anterior resection syndrome.

#### *Research objectives*

We want to establish a model that comparable in effectiveness with the LARS scale by MRI defecography, quantify the severity of LARS, and can be more helpful to scientifically evaluate the value of all kinds of scientific research on prevention and treatment of LARS.

#### *Research methods*

The experimental model of 34 patients with anterior resection syndrome was established by LARS score, and a new LARS evaluation index was established by using the dynamic image of MRI defecography to verify the experimental model.

#### *Research results*

Both severe LARS and mild LARS had significant statistical significance in two different evaluation methods. There was a significant negative correlation between LARS score and MRI-RC score, and also has a negative correlation with the defecation rate.

#### *Research conclusions*

MRI defecography and standard LARS scoring method may have the same evaluation effect and can be used as an evaluation index to study the pathogenesis of LARS.

*Research perspectives*

The mechanism leading to LARS symptoms needs a very comprehensive physiological study to accurately answer this important question.

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