ORIGINAL ARTICLE

Predictive factors of major low anterior resection syndrome after surgery for rectal tumors

Facteurs prédictifs de syndrome de résection antérieure majeur après chirurgie pour tumeur rectale

Mehdi Trabelsi, Imen Samaali, Neirouz Kammoun, Amine Ben Safta, Anouer Oueslati, Wajih Dougaz, Mehdi Khalfallah , Hichem Jerraya, Ibtissem Bouasker, Ramzi Nouira, Chadli Dziri

Department B of Surgery, Charles Nicolle Hospital, University Tunis El Manar, Tunis, Tunisia

Abstract

Aim: To describe the epidemiological and clinical data of impaired functional outcome secondary to anterior resection of the rectum and to identify the predictive factors of major low anterior resection syndrome (LARS)

Methods: This retrospective study considered patients operated on for rectal tumors in surgical department in our hospital, between January 1st,2009 and December 31st, 2021. The primary outcome measure was the development of a major LARS immediately or after stoma closure. In order to identify independent predictors of major LARS, patients were divided into two groups: the "Major LARS" group and the "No Major LARS" group, and then we carried out a descriptive study, followed by an analytical study with logistic regression.

Results: We enrolled 42 patients operated for rectal tumor and had an anterior resection. Half of our patients developed LARS of which 14 developed major LARS. The median time to onset of LARS symptoms was 9 [2 -24] months.

At the end of this study, 2 factors were retained: age (OR=2.48; CI95% [1.2- 5.10], p=0.012) and pT3T4 stage (OR=5.95; CI95% [1.07- 33.33], p=0.041) as independent predictive factors of a major LARS. Neoadjuvant therapy was also a risk factor for major LARS in our study with a statistically significant difference (p=0.025) between the two groups "Major LARS" and "No major LARS".

Conclusion: LARS should be appropriately considered in the management of rectal cancer. Based on our results and data from the literature, age and mesorectal invasion were found to be independent predictors of major LARS.

Key words: Anterior rectal resection, Rectal tumor, Risk factors, Functional sequelae, Bowel function

Résumé

Objectif: De décrire les données épidémiologiques et cliniques de l'altération du résultat fonctionnel secondaire à une résection antérieure du rectum et d'identifier les facteurs prédictifs du syndrome de résection antérieure majeur (LARS majeur)

Méthodes: Cette étude rétrospective a porté sur les patients opérés de tumeurs rectales dans le service de chirurgie de notre hôpital, entre le 1er janvier 2009 et le 31 décembre 2021. Le critère de jugement principal était le développement d'un LARS majeur immédiatement ou après la fermeture de la stomie. Afin d'identifier les facteurs prédictifs indépendants d'un LARS majeur, les patients ont été divisés en deux groupes : le groupe "LARS majeur" et le groupe "Pas de LARS majeur", puis nous avons réalisé une étude descriptive, suivie d'une étude analytique avec régression logistique.

Résultats: Nous avons inclus 42 patients opérés d'une tumeur rectale et ayant subi une résection antérieure. La moitié de nos patients ont développé un LARS, dont 14 ont développé un LARS majeur. Le délai médian d'apparition des symptômes du LARS était de 9 [2 -24] mois.

Au terme de cette étude, 2 facteurs ont été retenus : l'âge (OR=2.48 ; CI95% [1.2- 5.10], p=0.012) et le stade pT3T4 (OR=5.95 ; CI95% [1.07- 33.33], p=0.041) comme facteurs prédictifs indépendants d'un LARS majeur. La radio chimiothérapie néoadjuvante était également un facteur de risque de LARS majeur dans notre étude avec une différence statistiquement significative (p=0.025) entre les deux groupes "LARS majeur" et "Pas de LARS majeur".

Conclusion: Le LARS doit être pris en compte de manière appropriée dans la prise en charge du cancer du rectum. D'après nos résultats et les données de la littérature, l'âge et l'envahissement du mésorectum ont été retrouvés comme facteurs prédictifs indépendants d'un LARS majeur

Mots clés: Résection antérieure du rectum, Tumeur rectale, Facteurs de risque, Séquelles fonctionnelles, Fonction intestinale

Correspondance
Mehdi Trabelsi
Department B of Surgery, Charles Nicolle Hospital, University Tunis El Manar, Tunis, Tunisia
Email: mehdi.trabelsi1991@gmail.com

LA TUNISIE MEDICALE-2024; Vol 102 (10): 702-707 DOI: 10.62438/tunismed.v102i10.5177

Introduction

Colorectal cancer ranks third worldwide in terms of incidence and second in terms of mortality [1]. The treatment of rectal cancer is well codified, and is mainly based on surgical treatment consisting on anterior resection of the rectum with excision of the mesorectum [2]. However, it is still a major surgical procedure, which leads to changes in bowel movement over the medium and long term [3]. These changes consist in rectal evacuation or continence disorders, which put functional prognosis at risk [3].

The symptoms of these digestive functional sequelae are grouped under the term rectal anterior resection syndrome, or the "Low Anterior Resection Syndrome" known as LARS.

The first definition proposed of this syndrome was developed in 2012: it was described as disorders of bowel function after rectal resection, leading to a deterioration of the quality of life [3]. Then, in 2020, an international consensus definition of this syndrome was published [4]: It was the first definition of LARS developed from a large panel of patients, ultimately resulting in the identification of eight symptoms: variable, unpredictable bowel function, altered stool consistency, increased stool frequency, repeated painful stools, emptying difficulties, urgency, incontinence and soiling; and eight consequences, which reflect the essential aspects of the syndrome and its impact on quality of life [4]. Many scores have been described and used in the literature to define this syndrome like the Cleveland Clinic Florida Fecal Incontinence Score (CCFIS) or Wexner score [5], but as its name suggests, it assessed only symptoms associated with incontinence after rectal surgery. As a result, since its validation [6], the LARS score, which assessed the severity of these functional disorders and reflected their impact on quality of life, has become the standard [7,8].

It was designed as a simple tool for the clinical assessment of anterior resection syndrome, and was used to classify disorders into three categories: no LARS, minor LARS and major LARS [7,8]. Today, up to 50% of long-term cancer survivors suffer from these disorders, which affect their quality of life [9].

To date, data concerning risk factors of major LARS are still limited [10,11].

The purpose of our study was to identify digestive functional disorders following rectal surgery for rectal tumors, and the predictive factors of major LARS.

Methods

This retrospective study considered patients operated on for rectal tumors in surgical department in our hospital, between January 1st,2009 and December 31st, 2021. All parts of the study and access to the medical records were approved by the local Ethics Committee. All the participants consented to a structured interview wherein they completed a questionnaire to assess their defecation function. All patients operated for rectal tumors who had rectal anterior resection with colorectal anastomosis, with temporary protective stoma, were included. The type of stoma (ileostomy vs colostomy) depended on the surgeon's choice. Patients operated on for rectal tumors who underwent another procedure as an abdominoperineal amputation or a derivative stoma (tumors invading the sphincter and/or unresectable metastatic tumors) were not included in this study. Patients operated on for rectal tumors who had undergone an anterior resection and died, lost during the follow-up period or unreachable were excluded from the study. We have excluded also patients who could not be able to have their stoma closed or had local recurrence. Primary outcome was the occurrence of major LARS after restoring digestive continuity.

This assessment was based on the "LARS score": This is a validated 5-item questionnaire created in 2012 by Emmertsen et al [6]. The 5 items are: Incontinence for flatus, Incontinence for liquid stools, frequency of bowel movements per day, clustering of stools and urgency. A score was assigned to each item, and the total was calculated. The range of the score is 0 to 42 with the limits of 0 to 20 (no LARS), 21 to 29 (minor LARS), and 30 to 42 (major LARS) [6].

At the end of this evaluation, our patients were divided into two groups: the first group, "Major LARS", corresponded to patients whose LARS score was equal or greater than 30.

The second group, "No major LARS", corresponded to patients with a LARS score below 30, and included patients with minor LARS or no LARS. We collected variables from medical records, operative and pathological reports, and LARS questionnaire data. Each patient was interviewed at the outpatient unit or called by phone by the investigator, who explained the purpose of the questionnaire and asked the questions in Arabic. The questionnaire was filled in by the investigator after assessment of the patient's complaint. The variables collected were divided into preoperative, intraoperative and postoperative variables.

Statistical analysis

The analysis of the data was performed with statistical software (Statistical Package for the Social Science version 26.0). Categorical variables were expressed by their percentages, continuous variables by the mean and standard deviation when the distribution was Gaussian, otherwise by median value with extremes. Categorical variables were compared using Pearson's Chi2 test or Fisher's exact test for groups when appropriate. The comparison of two means on independent series was carried out using the student's t-test or Mann-Whitney U test when appropriate. For all statistical tests, a value of $p<0.05$ was considered the threshold of significance. For each pre-, intra- and postoperative variable, we performed a bivariate analysis, then variables associated with a $p\leq0.10\%$ were entered into a logistic regression model to identify independent predictive variables of major LARS. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. The Hosmer-Lemeshow test was applied to assess the goodness of fit of the

model.
Statistical significance was set at a level of $p \leq 0.05$.

Results

A total of 135 patients were found to be eligible for this study. Of these, 30 patients had abdominoperineal amputation, 35 were not suitable to close the stoma and 28 patients were dead, lost during the follow-up period or were unreachable. Finally, the remaining 42 patients were evaluated (Figure 1).

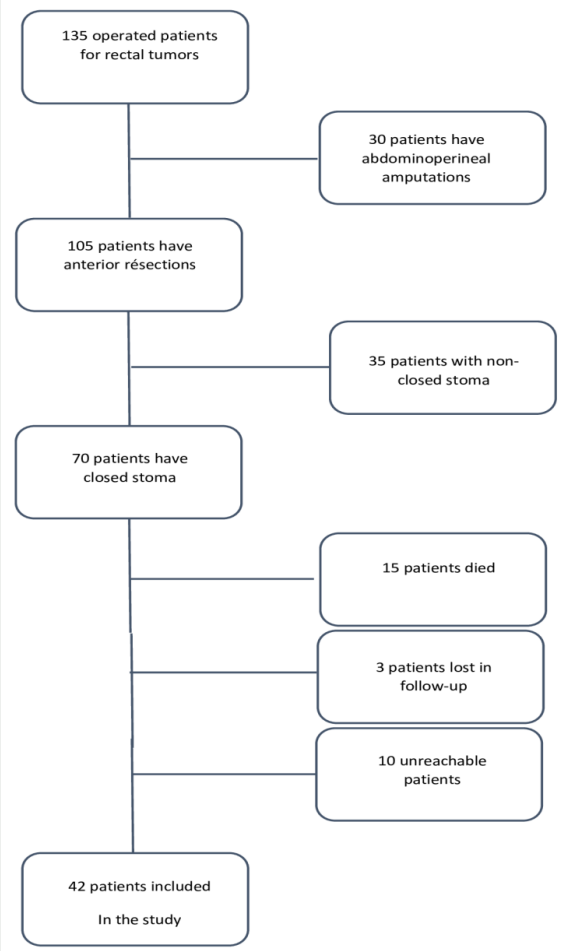

Figure 1. flow chart of the study

Twenty-three patients were female and 19 were males. The mean age was 59.12 ± 12.4 years, with extremes of 29 and 92 years. 21 patients developed LARS in our series (50%). They were distributed as follows: 7 patients with minor LARS (17%) and 14 patients with major LARS (33%). The median time to onset of LARS symptoms was 9 months, with extremes of 2 and 24 months. The most frequent sign was the “Incontinence for flatus” reported by 40 patients (95%), followed by the increase in the “frequency of bowel movements per day” reported by 38 patients (92%), then the “urgency” of bowel movements observed in 28 patients (66%). We retained 14 patients who had a major LARS (33%) and 28 patients did not (67%). We divided patients into two groups: the "Major LARS" group and the "No Major LARS" group in order to conduct a comparison for epidemiological, pre-operative, intra-operative and postoperative data.
There was no significant difference between the two groups in terms of gender, medical and surgical history and various functional signs. The difference in mean age between the groups was statistically significant (p=0.013), with a younger age in the "major LARS" group (62 ± 11 years vs. 52 ± 12.7years). Epidemiological and semiological data features were summarized in Table 1.

Table 1. Epidemiological data features of the patients

Epidemiologic Variables	No major LARS (28)	Major LARS (14)	P
Age (mean ± standard deviation)	62 ± 11	52 ± 12,7	0,013
Gender			
Male	13 (46%)	6 (43%)	0,826
Female	15 (54%)	8 (57%)	
Diabetes			
No	22 (79%)	12 (86%)	0,697
yes	6 (21%)	2 (14%)	
Cardiovascular disorders			
No	18 (64%)	8 (57%)	0,653
Yes	10 (36%)	6 (43%)	
Respiratory disorders			
No	27 (96%)	14 (100%)	1
Yes	1 (4%)	0 (0%)	
Obesity			
No	27 (97%)	14 (100%)	1
Yes	1 (3%)	0 (0%)	
ASA score			
1	18 (64%)	7 (50%)	
2	10 (36%)	5 (36%)	
3	0 (0%)	2 (14%)	
Semiological Variables			
Hematochezia			
No	13 (46%)	4 (29%)	0,266
Yes	15 (54%)	10 (71%)	
Diarrhea			
No	27 (96%)	11 (79%)	1
Yes	1 (4%)	3 (21%)	
Constipation			
No	17 (61%)	12 (86%)	0,159
Yes	11 (39%)	2 (14%)	
Abdominal pain			
No	15 (54%)	9 (64%)	0,508
Yes	13 (46%)	5 (36%)	
Weight loss			
No	17 (61%)	11 (79%)	
Yes	11 (39%)	3 (21%)	0,313
Anemia			
No	24 (86%)	10 (71%)	0,406
Yes	4 (14%)	4 (29%)	

In the "major LARS" group, we had more palpable tumors in the rectal examination (71%) than in the "No major LARS" group (50%), but there was no significant difference between the two groups. On the pathological exam, there were more moderately-differentiated adenocarcinomas and fewer well-differentiated adenocarcinomas in the "major LARS" group versus the "No major LARS" group but also with no significant difference. Mesorectal invasion assessed on imaging data (cT3T4) was predominantly

observed in the "major LARS " group (93%) versus the "No major LARS " group (61%), with a significant difference (p=0.036). clinical and paraclinical data features were summarized in Table 2.

Table 2. Clinical and paraclinical data features of the patients

Variables	No major LARS (28)	Major LARS (14)	P
Palpated tumor on rectal examination			
No	14 (50%)	4 (29%)	
Yes	14 (50%)	10 (71%)	0,186
Distance from anal margin in centimetres on rectal examination (moyenne ± SD)	10 ± 3,7	8 ± 3,25	0,075
Endoscopy			
Circumferential tumor			
No	15 (54%)	10 (71%)	0,266
Yes	13 (46%)	4 (29%)	
Distance from anal margin			
in centimeters in endoscopy (mean **±SD)**	8,64 ± 2,75	7,5 ± 2,44	0,181
Histology			
Well-differenciated adenocarcinoma	21 (75%)	6 (43%)	
Moderately-differenciated adenocarcinoma	2 (7%)	8 (57%)	
Villous tumor	5 (18%)	0 (0%)	
Imaging data			
Mesorectal invasion			
No	11 (39%)	1 (7%)	**0,036**
Yes	17 (61%)	13 (93%)	
Biology			
haemoglobin in g/dl (mean **±SD)**	12 ± 1,69	11,9 ± 2.69	0,879
Albumin in g/l (mean **±SD)**	37,23 ± 3,99	38,14 ± 4,45	0,528
Creatinine in umol/l median (extremes)	70,57 (38-115)	64 (46 - 106)	0,258

In the "Major LARS" group, there were more patients for whom neoadjuvant radiochemotherapy was indicated (86%) versus 50% in the "No Major LARS" group, with a significant difference (p=0.025). There was no significant difference between the two groups in terms of delay between surgery and the end of neoadjuvant treatment. Neoadjuvant treatment and preparation for surgery data features were summarized in Table 3.

Table 3. Neoadjuvant treatment and preparation for surgery data features of the patients.

Variables	No major LARS (28)	Major LARS (14)	p
Neoadjuvant treatment			
No	14 (50%)	2 (14%)	**0,025**
Yes	14 (50%)	12 (86%)	
Radiochemotherapy			
No	14 (50%)	2 (14%)	**0,025**
Yes	14 (50%)	12 (86%)	
Treatment period in days (mean **±SD)**	29.4 ± 8.7	33.9 ± 5.07	0,120
Response to neoadjuvant treatment			
Partial	14 (100%)	11 (92%)	0,480
No response	0 (0%)	1 (8%)	
Delay between surgery and the end of neoadjuvant treatment in days median (extremes)	79,07 ±26,36	77,58 ±24,73	0,883

There was no significant difference between the two groups in terms of tumor location, extent of mesorectal excision, location and type of anastomosis. No significant difference was found between the two groups in terms of post-operative follow-up. There was more anastomotic leakage in the "major LARS" group, but no significant difference (p=0.406). Adjuvant chemotherapy was indicated more in the "Major LARS" group (64%) with no significant difference (p=0.508). Post-operative follow-up data features were summarized in Table 4.

Table 4. Post-operative follow-up data features of the patients.

Variables	No major LARS (28)	Major LARS(14)	p
Uneventful follow-up			
No	5 (18%)	4 (29%)	0,451
Yes	23 (82%)	10 (71%)	
Medical complications			
No	27 (96%)	13 (93%)	1
Yes	1 (4%)	1 (7%)	
Anastomotic leakage			
No	24 (86%)	10 (71%)	0,406
Yes	4 (14%)	4 (29%)	
Abdominal wall abscess			
No	28 (100%)	14 (100%)	-
Yes	0 (0%)	0 (0%)	
Evisceration			
No	28 (100%)	14 (100%)	-
Yes	0 (0%)	0 (0%)	
Post operative intestinal obstruction			
No	27 (96%)	14 (100%)	1
Yes	1 (4%)	0 (100%)	
Reoperation			
No	27 (96%)	14 (100%)	1
Yes	1 (4%)	0 (0%)	
Post-operative chemotherapy			
No	13 (46%)	5 (36%)	0,508
Yes	15 (54%)	9 (64%)	

There were no differences in histological type, TNM stage, number of lymph nodes harvested or metastatic ones, or circumferential resection margin between the two groups. There was no significant difference between the two groups in terms of delay between the restoration of intestinal continuity and surgery or adjuvant therapy (p=0.898 and p=0.455 respectively). There were also no differences in terms of time to onset of LARS symptoms (p=0.908).

The variables retained in the bivariate analysis were introduced in a logistic regression analysis. Two factors were retained: age and pT3T4 stage as independent predictors of major LARS

In other words, younger patients and patients who had greater invasion of the mesorectum, were more likely to develop a major LARS (OR = 2.48 and OR= 5.95 respectively) (Table 5).

Table 5. Independent factors of major LARS on the multinomial logistic regression analysis

Variables	OR	CI95%	P
Age	2,48	[1,2- 5,10]	p=0,012
Stade pT3T4	5,95	[1,07- 33,33]	p=0,041

OR: odds ratio - **CI95%**: Confidence Interval à 95%; Hosmer–Lemeshow test: **p** = 0,357

Discussion

This study showed that “Age” and “mesorectal invasion” were independent predictive factors of major LARS. Twenty-one of our patients developed LARS. Fourteen of these patients (33%) developed major LARS, these results are in line with the literature data, which ranges from 50% to 90% [3,11,12], with a prevalence of major LARS of 17% to 56% [13–20]. With regard to age, data concerning the risk of developing major LARS are contradictory. In our series, the difference in mean age between the two groups was significant (p=0.013), with a younger age in the "major LARS" group. In the multivariate study, age was an independent factor of major LARS, this may be explained by the fact that younger patients become aware of the functional symptoms of LARS earlier and more rapidly, and their impact on quality of life is felt more acutely than older patients. This result was also described in the study by Pieniowski et al, which looked at the prevalence of LARS in 481 patients. In fact, the prevalence of LARS, and especially major LARS, was higher in the “50-79 age” group, with a significant difference (p<0.001) compared to the age group over 79 [13,21]. The Japanese study by Paku et al and the European study by Juul et al also identified young age as a risk factor for major LARS [7,22]. On the other hand, Sturiale et al considered that an age > 70 years increased significantly the probability of functional disorders after anterior resection [17]. Other studies found no association between age and the risk of major LARS [23,24]. In our study, mesorectal invasion assessed on imaging data (cT3T4) was predominantly observed in the "Major LARS" group (93%) versus the "No Major LARS" group (61%), with a significant difference p=0.036. This result was in accordance with the study published by Pieniowski et al, where 70% of patients with major LARS had a cT3T4 stage on preoperative data [13]. The effect of neoadjuvant treatment is no longer, considered as a topic for debate. The majority of studies on LARS have retained the negative effect of neoadjuvant radiotherapy on bowel function after anterior resection, with a major impact on quality of life [10,13,14,19,25–27].

In our study, no significant difference was found between the two groups in term of gender. A similar result was described in a Chinese meta-analysis of 5102 patients included in 21 studies [10]. The impact of tumor location, extent of mesorectal excision and location or type of anastomosis performed (mechanical or manual) on bowel function after anterior resection has not been demonstrated in our serie. The low level of anastomosis has been shown to be a major risk factor for LARS in several studies [10,19,21]. In the cohort study by Hain et al, inter-sphincter rectal resection and manual colo-anal anastomosis indicated for tumors located less than 4 cm from the anal margin were two independent predictors of major LARS [24]. In our study, there was no significant difference between the two groups in terms of post-operative outcomes. There were more colorectal or coloanal anastomotic leakage in the "major LARS" group, but no statistically significant difference (p=0.406 respectively). It’s important to note that anastomotic leakage was shown to be an independent predictor of major LARS in the study by Hain et al [24], as well as in the study by Kim et al [27]. There was no significant difference in terms of delay between the restoration of digestive continuity and the resection or the adjuvant chemotherapy (p= 0.898 and p=0.455 respectively). Several studies have focused on the presence of a protective ileostomy and the duration for restoring digestive continuity: three studies found an increased risk of major LARS for patients who had a protective stoma [10,20,25], three others found that the delay for restoring digestive continuity represents a significant risk factor for major LARS [14,17,28]. Recently, two meta-analyses found that patients with protective ileostomy were twice as likely to develop LARS [29]; and confirmed that the presence of an ileostomy and stoma closure delay are both risk factors for LARS [30]. An optimal cut-off value for stoma closure time of 128 days was proposed by Xia et al. beyond which the probability of developing major LARS becomes significant [28]. In our study, we were able to identify three risk factors for LARS in the bi-variate analysis: age, mesorectal invasion (cT3T4) and neoadjuvant treatment; and in the multivariate analysis, we retained two factors as independent predictors of major LARS: age and pT3T4 stage. This result is in accordance with the literature data. Our study is the first one, done in a sample of Tunisian patients operated for rectal tumors, to focus on the definition of functional digestive disorders after sphincter-preservation rectal surgery. However, our study has limitations that can be summed up in the retrospective nature of the work and the limited size of the sample.

Conclusion

The incidence of LARS was found to be 50% in our study, with 33% of major LARS, that’s why it should be appropriately considered in the management of rectal cancer even if oncological considerations must take priority. Based on our results and data from the literature, age and mesorectal invasion were found to be independent predictors of major LARS.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA A Cancer J Clin. 2021;71:209–49.
2. Phelip JM, Tougeron D, Léonard D, Benhaim L, Desolneux G, Dupré A, et al. Metastatic colorectal cancer (mCRC): French intergroup clinical practice guidelines for diagnosis, treatments and follow-up (SNFGE, FFCD, GERCOR, UNICANCER, SFCD, SFED, SFRO, SFR). Digestive and Liver Disease. 2019;51:1357–63.
3. Bryant CL, Lunniss PJ, Knowles CH, Thaha MA, Chan CL. Anterior resection syndrome. The Lancet Oncology. 2012;13:e403–8.
4. Keane C, Fearnhead NS, Bordeianou LG, Christensen P, Basany EE, Laurberg S, et al. International Consensus Definition of Low Anterior Resection Syndrome. Diseases of the Colon & Rectum. 2020;63:274–84.
5. Jorge MJN, Wexner SD. Etiology and management of fecal incontinence. Diseases of the Colon & Rectum. 1993;36:77–97.

6. Emmertsen KJ, Laurberg S. Low Anterior Resection Syndrome Score: Development and Validation of a Symptom-Based Scoring System for Bowel Dysfunction After Low Anterior Resection for Rectal Cancer. Annals of Surgery. 2012;255:922–8.
7. Juul T, Ahlberg M, Biondo S, Emmertsen KJ, Espin E, Jimenez LM, et al. International Validation of the Low Anterior Resection Syndrome Score. Annals of Surgery. 2014;259:728–34.
8. Juul T, Battersby NJ, Christensen P, Janjua AZ, Branagan G, Laurberg S, et al. Validation of the English translation of the low anterior resection syndrome score. Colorectal Dis. 2015;17:908–16.
9. Scheele J, Lemke J, Wittau M, Sander S, Henne-Bruns D, Kornmann M. Quality of Life after Rectal Cancer Resection Comparing Anterior Resection, Abdominoperineal Resection, and Complicated Cases. Visc Med. 2022;38:138–49.
10. Ye L, Huang M, Huang Y, Yu K, Wang X. Risk factors of postoperative low anterior resection syndrome for colorectal cancer: A meta-analysis. Asian Journal of Surgery. 2022;45:39–50.
11. Sun R, Dai Z, Zhang Y, Lu J, Zhang Y, Xiao Y. The incidence and risk factors of low anterior resection syndrome (LARS) after sphincter-preserving surgery of rectal cancer: a systematic review and meta-analysis. Support Care Cancer. 2021;29:7249–58.
12. Emmertsen KJ, Laurberg S. Bowel dysfunction after treatment for rectal cancer. Acta Oncologica. 2008;47:994–1003.
13. Pieniowski EHA, Nordenvall C, Palmer G, Johar A, Tumlin Ekelund S, Lagergren P, et al. Prevalence of low anterior resection syndrome and impact on quality of life after rectal cancer surgery: population-based study. BJS Open. 2020;4:935–42.
14. On behalf of the LARRIS Trial Management Group, Hughes DL, Cornish J, Morris C. Functional outcome following rectal surgery—predisposing factors for low anterior resection syndrome. Int J Colorectal Dis. 2017;32:691–7.
15. Dilke SM, Hadjittofi C, Than M, Tozer PJ, Stearns AT. Anterior Resection Syndrome and Quality of Life With Long-term Follow-up After Rectal Cancer Resection. Diseases of the Colon & Rectum. 2022;65:1251–63.
16. Croese AD, Lonie JM, Trollope AF, Vangaveti VN, Ho Y-H. A meta-analysis of the prevalence of Low Anterior Resection Syndrome and systematic review of risk factors. International Journal of Surgery. 2018;56:234–41.
17. Sturiale A, Martellucci J, Zurli L, Vaccaro C, Brusciano L, Limongelli P, et al. Long-term functional follow-up after anterior rectal resection for cancer. Int J Colorectal Dis. 2017;32:83–8.
18. Croese AD, Zubair ON, Lonie J, Trollope AF, Vangaveti VN, Mushaya C, et al. Prevalence of low anterior resection syndrome at a regional Australian centre: Anterior resection syndrome prevalence. ANZ Journal of Surgery. 2018;88:E813–7.
19. Benli S, Çolak T, Türkmenoğlu MÖ. Factors influencing anterior/low anterior resection syndrome after rectal or sigmoid resections. Turk J Med Sci.
20. Carrillo A, Enríquez-Navascués JM, Rodríguez A, Placer C, Múgica JA, Saralegui Y, et al. Incidencia y caracterización del síndrome de resección anterior de recto mediante la utilización de la escala LARS (low anterior resection score). Cirugía Española. 2016;94:137–43.
21. Pieniowski EHA, Palmer GJ, Juul T, Lagergren P, Johar A, Emmertsen KJ, et al. Low Anterior Resection Syndrome and Quality of Life After Sphincter-Sparing Rectal Cancer Surgery: A Long-term Longitudinal Follow-up. Diseases of the Colon & Rectum. 2019;62:14–20.
22. Paku M, Miyoshi N, Fujino S, Hata T, Ogino T, Takahashi H, et al. Development and evaluation of a Japanese prediction model for low anterior resection syndrome after rectal cancer surgery. BMC Gastroenterol. 2022;22:239.
23. Bondeven P, Emmertsen KJ, Laurberg S, Pedersen BG. Neoadjuvant therapy abolishes the functional benefits of a larger rectal remnant, as measured by magnetic resonance imaging after restorative rectal cancer surgery. European Journal of Surgical Oncology (EJSO). 2015;41:1493–9.
24. Hain E, Manceau G, Maggiori L, Mongin C, Prost à la Denise J, Panis Y. Bowel dysfunction after anastomotic leakage in laparoscopic sphincter-saving operative intervention for rectal cancer: A case-matched study in 46 patients using the Low Anterior Resection Score. Surgery. 2017;161:1028–39.
25. Ekkarat P, Boonpipattanapong T, Tantiphlachiva K, Sangkhathat S. Factors determining low anterior resection syndrome after rectal cancer resection: A study in Thai patients. Asian Journal of Surgery. 2016;39:225–31.
26. Qin Q, Huang B, Cao W, Zhou J, Ma T, Zhou Z, et al. Bowel Dysfunction After Low Anterior Resection With Neoadjuvant Chemoradiotherapy or Chemotherapy Alone for Rectal Cancer: A Cross-Sectional Study from China. Diseases of the Colon & Rectum. 2017;60:697–705.
27. Kim S, Kang SI, Kim SH, Kim J-H. The Effect of Anastomotic Leakage on the Incidence and Severity of Low Anterior Resection Syndrome in Patients Undergoing Proctectomy: A Propensity Score Matching Analysis. Ann Coloproctol. 2021;37:281–90.
28. Xia F, Zou Y, Zhang Q, Wu J, Sun Z. A novel nomogram to predict low anterior resection syndrome (LARS) after ileostomy reversal for rectal cancer patients. European Journal of Surgical Oncology. 2023;49:452–60.
29. Keane C, Sharma P, Yuan L, Bissett I, O'Grady G. Impact of temporary ileostomy on long-term quality of life and bowel function: a systematic review and meta-analysis. ANZ Journal of Surgery. 2020;90:687–92.
30. Vogel I, Reeves N, Tanis PJ, Bemelman WA, Torkington J, Hompes R, et al. Impact of a defunctioning ileostomy and time to stoma closure on bowel function after low anterior resection for rectal cancer: a systematic review and meta-analysis. Tech Coloproctol. 2021;25:751–60.