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Postoperative Bowel Function After Anal Sphincter-Preserving Rectal Cancer Surgery: Risks Factors, Diagnostic Modalities, and Management

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Low anterior resection syndrome (LARS) refers to a disturbance of bowel function that commonly manifests within 1 month after rectal cancer surgery. A low level of anastomosis and chemoradiotherapy have been consistently found to be risk factors for developing LARS. Thorough history taking and physical examination with adjunctive procedures are essential when evaluating patients with LARS. Anorectal manometry, fecoflowmetry, and validated questionnaires are important tools for assessing the quality of life of patients with LARS. Conservative management (medical, physiotherapy, transanal irrigation), invasive procedures (neuromodulation), and multimodal therapy are the mainstay of treatment for patients with LARS. A stoma could be considered when other treatment modalities have failed. An initial meticulous surgical procedure for rectal cancer, creation of a neorectal reservoir during anastomosis, and proper exercise of the anal sphincter muscle (Kegel's maneuver) are essential to combat LARS. Pretreatment counseling is a crucial step for patients who have risk factors for developing LARS.

Keywords: *Rectal neoplasm; Surgical procedures; Bowel function; Diagnosis; Therapy*

INTRODUCTION

Surgery is the main treatment option for patients with rectal cancer. The primary goal of surgery is to achieve the best oncologic outcome. Recently, sphincter-preserving surgery (SPS), including a low anterior resection (LAR) and an intersphincteric resection, has been more frequently used than an abdominoperineal resection (APR) in the treatment of such patients. Although SPS has shown oncologic outcomes as favorable as those of an APR [1], those excellent oncologic outcomes at present do not coincide with excellent functional outcomes for patients [2, 3].

Studies have indicated that following a traditional restorative resection, a large proportion of surviving patients experience major bowel, urinary, and sexual dysfunctions on a daily basis that result in low quality of life (QoL) [3]. These postoperative complaints after SPS are known as low anterior resection syndrome (LARS), which has been reported in 30%–80% of patients undergoing SPS. In a systematic review published by Keane et al. [4], the most frequently reported symptoms were incontinence (97%), stool frequency (80%), urgency (67%), evacuatory dysfunction (47%), and gas-stool discrimination (34%). To date, many studies have addressed the symptoms of LARS. However, significant variability exists in reported outcomes. A systematic review of 48 studies of long-term functional outcomes after SPS reported that 65% of the studies did not use a validated assessment tool [5]. The purpose of this paper is to present the results of a review of current evidence

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on postoperative bowel function after SPS in patients with rectal cancer. To identify risk factors for LARS we reviewed diagnostic modalities for evaluating postoperative bowel function after SPS, and proper treatments for patients with LARS.

RISK FACTORS FOR LARS

Anal continence is caused by several continence factors, including anatomical and physiological substrates, the rectum with its reservoir function, the anal sphincter muscle, the anoderm, and neurological functions at local spinal and cerebral levels [6]. Surgical treatment can change the structure and the physiology of the anorectum, leading to functional problems. Risk factors for LARS include a rectal tumor, the location of the tumor, surgery-related damage, and preoperative chemoradiation therapy (CRT). Huge tumors with the capacity to invade neural structures can result in nerve damage [6]. A low level of tumor location, i.e., a low level of anastomosis, has been identified as a major risk factor for developing LARS [7]. In a study by Battersby et al. [7], low tumor location within 6 cm from the anal verge was a high-risk factor for having major LARS. Low-lying tumors are also mostly subjected to preoperative CRT, thus intensifying the risk for developing severe LARS. After an operation, the fecal capacity of the neo-rectum is decreased, which can lead to increased bowel movements and urgency [8]. The anal sphincter may be damaged directly due to anal stretching when the circular stapler is introduced into the anal canal. In a study by Gross [6], intraoperative measurement of the resting anal pressure at each step of the surgery during a LAR showed that resting anal pressure levels were significantly decreased only after stapling.

Autonomic nerve damage and myenteric plexus denervation can occur during a LAR with a total mesorectal excision (TME) [9]. Sphincter function in patients whose autonomic nerves are completely preserved is significantly better than that in patients whose autonomic nerves have suffered some damage. In a study by Emmertsen et al. [10], patients who underwent a TME had a significantly higher risk of major LARS than those who underwent a partial mesorectal excision. However, because the oncologic outcome is the primary goal of treatment, a TME should be done for patients having low rectal cancer.

Irradiation can cause damage to the myenteric plexus and inhibit impulse conduction. It may also directly damage anal sphincter muscles and cause fibrosis. Canda et al. [11] showed that preoperative CRT could significantly decrease resting and squeezing anal canal pressures and adversely affect the Wexner continence score and the answers on the fecal incontinence QoL questionnaire. In a study by Ekkarat et al. [12], when both low rectal anastomosis and preoperative CRT were present, almost all patients (93%) were likely to have bowel-related quality-of-life (BQOL) impairment, and almost two-thirds experienced major BQOL impairment.

DIAGNOSTIC MODALITIES

Evaluation of LARS begins with history taking and physical examination. Patient questionnaires, such as the LARS score (2007) and the Memorial Sloan Kettering Cancer Center Bowel Function Instrument (MSKCC-BFI; 2005), can be used to stratify patients based on the severities of their symptoms to guide therapy [13]. Objective test methods, such as anorectal manometry and fecoflowmetry (FFM), can also be used. The physician can evaluate postoperative anorectal function based on these tests and suggest an appropriate treatment (Table 1).

Questionnaires

Assessing dysfunctional bowel syndrome from a patient's perspective is one of the important methods for evaluating the severity of LARS. According to research by Chen et al. [14], a significant gap exists between the expert's perspective and the patient's experience with LARS. They showed that even experts might not have a complete understanding of which symptom was the most uncomfortable for their patients. However, how to systematically ask questions and to evaluate and interpret the answers to those questions to provide proper management depends on the physician. To date, numerous types of questionnaires have been used to assess bowel function after colorectal surgery. Among them, 2 scoring systems, the LARS score and the MSKCC-BFI score, were designed specifically to evaluate LARS. Both are meticulously formulated and have been validated in different countries with the ability to reflect the impact of bowel dysfunction on QoL.

The LARS score is based on the answers to 5 questions: incontinence for flatus, incontinence for liquid stool, fecal frequency (number of bowel movements per day), clustering of (less than an hour between) bowel movements, and urgency. The total score based on the answers to these 5 questions ranges from 0 to 42 points. Depending on the total score, patients are classified into 3 groups: no LARS (0–20), minor LARS (21–29), and major LARS (30–42). Major LARS is associated with seriously compromised QoL. Therefore, it requires treatment. Minor LARS may or may not need to be treated medically. The LARS score has been shown to correlate with self-reported QoL in a study involving in 4 participating countries (Sweden, Spain, Germany, and Denmark). Moreover, the LARS score's being a simple scoring method and having clinically meaningful severity categories are its strengths in clinical practice [15]. The MSKCC-BFI is the first questionnaire designed to specifically evaluate functional outcome after SPS for patients with rectal cancer. It consists of 18 questions about the frequency of different aspects of LARS with 5 answers ranging from never to always for each question. It allows a more comprehensive and thorough evaluation of LARS. However, the lengths of questions and the tedious nature of the scoring system may influence its practicality [16]. In summary, the MSKCC-BFI is ideal for more delicate assessment while the LARS score is simple, intuitive, and practical. In addition, the LARS score has been validated

Table 1. Selected literature on functional outcomes after a low anterior resection

Study	Surgical procedure	Bowel function evaluation	Functional outcomes
Kakodkar et al. [35]	LAR with TME (CAA)	Anorectal manometry Wexner continence questionnaire	Frequency: 3.3 ± 0.17 MBP (cmH_2O): 37.7 ± 0.41 MSP (cmH_2O): 76.6 ± 0.54 MTV (mL): 146.3 ± 4.06 Compliance (mL/cmH_2O): 3.83 ± 0.27 RAIR – absent in half Wexner score: 4.37 ± 0.2
Akagi et al. [36]	ISR	Anorectal manometry Wexner continence questionnaire	Frequency: 5.1 (1–20) MBP (cmH_2O): 41 (4–84) MSP (cmH_2O): 178 (20–346) Wexner score: 7.2 (1–20) Patient satisfaction (%) -Very low 8.8 -Medium 19.3 -Perfect 71.9
Dulskas and Samalavicius [37]	LAR with TME	Anorectal manometry Wexner continence questionnaire	Frequency: 3.3 ± 0.17 MBP (cmH_2O): 43 ± 5.7 MSP (cmH_2O): 100 ± 8.9 MTV (mL): 140 ± 8.2 Wexner score: 6.3 (mean score)
Shibata et al. [38]	LAR with TME (CAA and intraoperative radiation) -EORTC QLQ-C30	MSKCC Sphincter Function Scale	More than one-half of the patients treated by sphincter preservation, EBRT, IORT, and chemotherapy had an unfavorable functional outcome.
Emmertsen et al. [10]	LAR -TME vs. PME -Neoadjuvant vs. no Neoadjuvant	LARS score European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30	Higher risk of major LARS with neoadjuvant therapy after TME and with temporary diverting stoma LARS score has high sensitivity and specificity for identifying patients with major bowel dysfunction causing impairment of QoL
Juul et al. [39]	LAR (no stoma)	LARS score EORTC QLQ-C30	Patients with major LARS fare substantially worse in 7 of the 8 EORTC QLQ-C30 compared with patients with no/minor LARS.
Qin et al. [40]	LAR -nCRT vs nCT	LARS score Postoperative pelvic MRI	nCRT had a higher risk of developing major LARS than nCT alone

LAR with TME, low anterior resection with total mesorectal excision; CAA, coloanal anastomosis; ISR, intersphincteric resection; MSKCC, Memorial Sloan-Kettering Cancer Center bowel function instrument; (EORTC) QLQ-C30, European organization for research and treatment of cancer; LARS score, low anterior resection syndrome score; MRI, magnetic resonance imaging; MBP, mean basal pressure; MSP, mean squeezing pressure; MTV, maximum total volume; RAIR, rectoanal inhibitory reflex; EBRT, external beam radiation therapy; IORT, intraoperative radiation therapy; QoL, quality of life; nCRT, neoadjuvant chemoradiotherapy; nCT, neo-adjuvant chemotherapy.

Manometry parameter	Normal value	Wexner score
MBP	40–70 mmHg	0 = perfect continence
MSP	80–160 mmHg	20 = complete incontinence
MTV	>160 mL	

in several languages while the MSKCC-BFI has only been validated in English and Italian.

Other questionnaires for assessing bowel function after colorectal surgery are St. Mark's Incontinence Score (St. Mark's score), the Fecal Incontinence Severity Index, and the Wexner score. Many studies have used these questionnaires to assess functional outcomes after SPS on patients with rectal cancer. However, these tools are primarily focused on fecal incontinence without reflecting the overall risk of LARS or the impact on QoL. Because LARS is more than just a fecal incontinence problem, such questionnaires may not capture all symptoms of the patient [14].

Anorectal manometry

Anorectal manometry is an objective test to evaluate anal sphincter function and rectal capacity. It is commonly employed in patients with anorectal dysfunctions, such as dyssynergic defecation, LARS, constipation, and fecal incontinence. It is not required to diagnose LARS, but it can be used to monitor the patient's response to treatment. Using a balloon catheter and a pressure sensor, it records the following parameters: resting pressure, maximum squeezing pressure, rectoanal inhibitory reflex (RAIR), maximum tolerated volume (rectal capacity), and compliance.

Efthimiadis et al. [17] showed that the anal resting pressure was lower after a LAR, with the RAIR being absent in 80% of the patients. Moreover, the rectal capacity and the compliance were lower in all patients, but no change in maximal squeezing pressure was reported. These results correlated with clinical symptoms. After 6 months, the severities of the clinical symptoms tended to be reduced, which coincided with the manometric results. In a study by Ihnát et al. [18], resting anal pressure, rectal sensitivity, and rectal compliance were significantly lower in patients who had major LARS than they were in patients with minor or no LARS. These results indicate that manometry parameters are related to the severities of the symptoms, i.e., to the LARS score.

Fecoflometry

FFM has been reported to be an accurate and useful tool for assessing postoperative anorectal motor function [19]. It was introduced by Shafik and Abdel-Moneim [20] as a dynamic method for examining the anorectal motor activity that could simulate the natural act of defecation. It uses a scale-redesigned uroflowmeter that can record maximal fecal flow. The FFM system consists of a weight transducer, an amplifier, and a chart recorder (Takei Medical & Optical Co, Tokyo, Japan). As the anorectal pressure was being monitored, 1,000 mL of normal saline enema was introduced at 37°C under gravity through a 6F catheter while the patient was in the left lateral position. When the patient could no longer tolerate the addition of more saline without the need to defecate, the saline introduction was stopped. At that time, the patient was asked to hold the enema as long as possible. The patient was then placed on the commode of the fecoflowmeter in a sitting position with hips flexed at 90° and asked to defecate as naturally as possible. The tolerance volume (TV), evacuative volume (EV), and maximal fecal stream flow rate were measured. The evacuative rate was then calculated [ER = (EV/TV) × 100(%)]. Ryu et al. [19] reported that compared to the Wexner score and manometry, FFM was relatively useful for providing a quantitative and comprehensive postoperative evaluation of the anorectal motor function in patients who had undergone a SPS.

TREATMENT OF LARS

Because of the multifactorial etiologies and the different pathophysiologic findings of LARS, reaching a consensus on the treatment of patients suffering from it is difficult. To date, management options have been empirical and symptom-based and have used existing therapies for fecal incontinence. Because many management options are available, the proper treatment should be chosen based on the severities of the symptoms.

Neorectal reservoir formation

Neorectal reservoir dysfunction and small neorectal capacity have been postulated as causes of urgency and fecal incontinence. They were also found to correlate with decreased maximum tolerated volume in several anorectal manometry studies and with a small neo-rectum in defecography. Construction of a neorectal reservoir, such as the colonic J-pouch (a), Baker-style side-to-end anastomosis, and transverse coloplasty, has been added to achieve a better bowel function. However, a systematic review of randomized trials could not demonstrate that reservoir construction improved the symptoms of patients with LARS over the long term [21]. Similarly, data assessing the ability of neorectal reservoirs to mimic rectal continence mechanisms are unavailable [22]. Liang et al. [23] investigated the functional and surgical outcomes of a laparoscopic-assisted colonic J-pouch versus straight reconstruction after a TME. Patients in the J-pouch group were found to have less disability, as shown by their quick return to partial activity, full activity, and work. However, both groups experienced increased stool frequency, incomplete defecation, and fragmentation postoperatively. A Cochrane review demonstrated that the colonic J-pouch was superior to a straight end-to-end anastomosis, although long-term data did not show any superiority according to the type of reconstruction [24].

Medication

Dietary regimens, bulking agents, antidiarrheal medications, probiotics, and even steroids have been used to control the symptoms of LARS. When fecal incontinence is the dominant symptom of LARS, bulking agents with a high fiber diet and antidiarrheal drugs are preferred choices because they can increase anal sphincter tone, leading to improved fecal continence [22]. However, medications are only effective in selected patients. In addition, they can only control a single symptom. Currently, their impacts

on patient satisfaction and QoL are doubtful and supporting evidence is lacking. Thus, further evaluation is needed [13].

Itagaki et al. [25] investigated whether serotonin (5-HT3) receptor antagonists, which are known to be effective in treating patients with irritable bowel syndrome, might be effective in treating patients with LARS. Based on all parameters, including incontinence score, urgency grade, and the number of toilet visits per day, they demonstrated that 5-HT3 antagonists were effective in treating patients with LARS.

Physiotherapy

Physiotherapy treatment includes biofeedback, pelvic floor muscle training (PFMT), and rectal balloon training (RBT) and aims to restore muscular strength, coordination, and the timing of contractions. Biofeedback therapy (BFT) is the first-line treatment for patients with fecal incontinence. With BFT, patients can obtain information about the activities of their pelvic floor muscles via a visual display. Liang et al. [26] demonstrated that BFT for patients with LARS after rectal cancer surgery could significantly improve incontinence scores and stool frequency, although they could not show that it significantly alleviated urgent evacuation. They also found that increasing the number of cycles of therapy had a better effect.

PFMT consists of selective voluntary contractions and relaxations of the pelvic floor muscles and the anal sphincter. This training aims to maximize the strengths of the pelvic floor muscles and the anal sphincter [27]. In 2014, a systematic review [28] was performed to evaluate the effectiveness of pelvic floor rehabilitation in improving functional outcome after SPS for rectal cancer. Four of the 5 studies included in this systematic review showed that functional outcome was improved in terms of continence, stool frequency, and QoL. However, the studies included in this systematic review, mostly focused on fecal incontinence and stool frequency without covering the whole spectrum of symptoms experienced by patients with LARS. The available data were extracted from studies of limited quality, and pooling of data was not possible due to the heterogeneities of the pelvic floor rehabilitation protocols and the fecal incontinence scoring systems that had been used. RBT is rectal sensitivity training by stepwise reductions in rectal balloon distension. Bols et al. [27] investigated the efficacy of RBT combined with PFMT. They showed that RBT had beneficial effects on the control of urgency, the external anal sphincter function, the subjective rating of improvement, and lifestyle adaptations.

Transanal irrigation

Transanal irrigation (TAI) has been reported as a simple and effective treatment for patients with disordered defecation. In a systematic review by Christensen and Krogh [29], TAI showed a positive effect in 79%–100% of patients with LARS following surgery for rectal cancer. Rosen et al. [30] evaluated the efficacy of TAI in patients suffering from LARS. In their prospective study, significant improvements in the functional outcomes in terms of the number of times defecating and the incontinence scores were reported. TAI is an effective treatment, is technically easy to learn, and can be self-administered. However, according to a study by Christensen and Krogh [29], a risk of enema-induced perforation (0.002%) exists.

Neuromodulation

Neuromodulation can be tried in patients who have not been treated with conservative therapy. Sacral nerve stimulation (SNS) can lead to alleviate the symptoms in patients with fecal incontinence who are not responsive to medical therapy [31]. SNS is a 2-stage procedure with an initial percutaneous 3-week test period to assess the patient's response, followed by definitive implantation of a pulse generator if a reduction of more than 50% of episodes of fecal incontinence per week is achieved [32]. In a systematic review by Ramage et al. [31], the effectiveness of SNS on patients with LARS was analyzed based on patient-reported symptoms, fecal incontinence scores, QoL scores, and anorectal physiology. The results showed an overall reduction in the number of fecal incontinence episodes, with an overall intention-to-treat success rate of 74%. However, that review was limited by the heterogeneity of data due to the different scoring systems that had been used. In a French multicentric study by Mege et al. [32], SNS significantly reduced the median Wexner and LARS scores in 86% of the patients, although no significant difference in detailed minor (i.e., not wearing pads) or major (i.e., wearing pads) episodes was reported.

Percutaneous tibial nerve stimulation is one of the applicable treatment methods that can improve fecal incontinence and urinary incontinence [33]. It modulates the function of the sacral nerve with indirect low-voltage stimulation of the tibial nerve at the ankle through a fine needle electrode connected to an external pulse generator. This procedure consists of inserting a small electrode over the medial malleolus adjacent to the posterior tibial nerve. The adhesive superficial electrode is placed under the arch of the foot. These 2 electrodes are connected to a neurostimulator that generates electricity. This procedure takes about 30 minutes [34] and is known to be less invasive, less adverse, and cheaper than SNS. Altomare et al. [33] found that 9 of 21 patients who underwent this procedure showed significant reductions in the numbers of fecal incontinence episodes.

Martellucci [13] suggested that the long-term symptoms of LARS seem to be caused by physiological changes due to neural damage more than by structural changes in the neo-rectum and proposed an algorithm for the treatment of patients with LARS. He suggested that a multimodal approach could significantly alleviate symptoms over individual techniques alone. After 2 years, when functional alterations tended to become permanent, a definitive stoma could be proposed for selected patients.

SUMMARY AND CONCLUSION

In summary, a low level of anastomosis, a history of preoperative radiotherapy, and nerve damage during a surgical procedure are risk factors for LARS. Colorectal experts can use scoring systems, such as the LARS score and the score on the MSKCC-BFI questionnaire, along with objective testing tools, to assess a patient's functional status. Patients with minor LARS can be managed with medication and physiotherapy, such as biofeedback and pelvic floor rehabilitation. However, patients with severe symptoms should be treated with more aggressive rehabilitation and neuromodulation. Despite these treatments, if the severities of the symptoms persist for more than 2 years, permanent stoma formation should be considered very carefully with patients' and caregiver's consents.

Pretreatment counseling is a crucial step for patients who have risk factors for developing LARS. Selective choice of preoperative chemoradiotherapy, a meticulous initial surgical procedure for rectal cancer, the creation of a neorectal reservoir during surgery, and proper anal sphincter muscle exercise (Kegel's maneuver) are essential if the occurrence of LARS is to be minimized. Multimodal treatment and a team approach are also essential. In the future, experts should systemically approach and manage patients who suffer from LARS based on a thorough understanding of the importance of functional problems after SPS. For that, more data need to be collected in a standardized manner, and, based on those data, more research should be initiated.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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