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REVIEW ARTICLE

Etiology and management of low anterior resection syndrome based on the normal defecation mechanism

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Abstract
Low anterior resection syndrome (LARS) commonly develops after an anal sphincter-preserving operation (SPO). The etiology of LARS is not well understood, as the anatomical components and physiological function of normal defecation, which may be damaged during the SPO, are not well established. SPOs may damage components of the anal canal (such as the internal anal sphincter, longitudinal conjoint muscle, or hiatal ligament), either mechanically or via injury to the nerves that supply these organs. The function of the rectum is substantially impaired by resection of the rectum, division of the rectococcygeus muscle, and/or injury of the nervous supply. When the remnant rectum is small and does not function properly, an important functional role may be played by the neorectum, which is usually constructed from the left side of the colon. Hypermotility of the remnant colon may affect the manifestation of urge fecal incontinence. To develop an SPO that minimizes the risk of LARS, the anatomy and physiology of the structures involved in normal defecation need to be understood better. LARS is managed similarly to fecal incontinence. In particular, management should focus on reducing colonic motility when urge fecal incontinence is the dominant symptom.

Keywords Low anterior resection syndrome · LARS · Physiology of defecation

Introduction

Low anterior resection syndrome (LARS) is an altered defecation status that can occur after an anal sphincter-preserving operation (SPO) for rectal cancer. Approximately 80% of patients who undergo SPOs experience varying degrees of LARS [1]. The typical symptoms of LARS that decrease quality of life (QOL) are fecal urgency, fecal incontinence, frequent bowel movements, and bowel-emptying difficulties [1]. The development of severe LARS is reportedly associated with low anastomotic height, preoperative radiation therapy, and anastomotic leakage [2–4]; probably caused by their damaging effects on the factors related to the mechanism of defecation. However, it is still unclear which of the operative maneuvers in the SPO is most strongly linked to disruption of the normal mechanism of defecation to induce LARS. To identify the factors that are essential for defecation, but are potentially being damaged during the SPO, we searched the literature for studies describing the anatomy and physiology related to normal defecation. We also reviewed the possible etiology and ways to prevent LARS during the SPO procedure.

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Damage to the anal canal during the SPO procedure

The integrity of the anal sphincter is considered one of the most important factors for the maintenance of fecal continence. The internal anal sphincter (IAS) is responsible for approximately 55–75% of the resting anal tone [5, 6]. The anal canal can be completely closed with the aid of the anal vascular cushion [7]. Postoperative fecal soiling or incontinence may result from structural damage to the IAS induced by the operative maneuver of intersphincteric resection (ISR), or from secondary trauma to the IAS induced by the insertion of an anastomotic device via the anus during low anterior resection (LAR) [8–10]. Functional degradation of the IAS may also be caused by damage to the nerve supply to this muscle, especially when the surgical approach

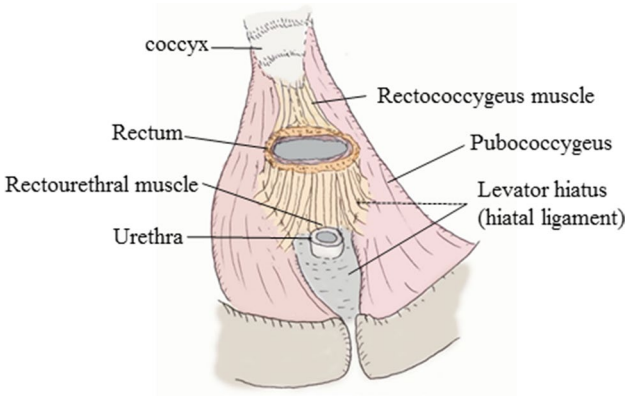

Fig. 1 Anatomical structure around the levator hiatus, which is reportedly involved in defecation. Modified from [12, 13, 15, 16]

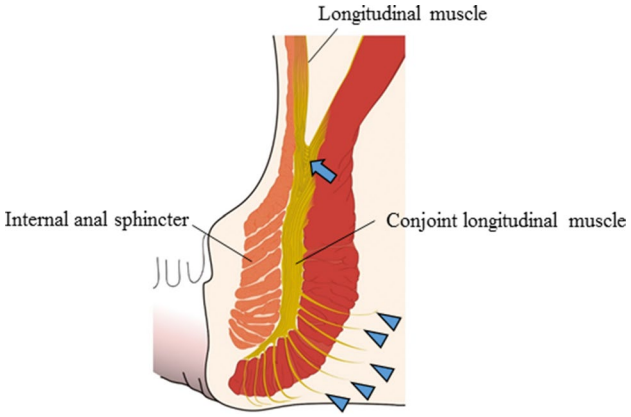

Fig. 2 Structure of the conjoint longitudinal muscle (LM) on the lateral side of the anal canal. The attachment of the rectal wall to the levator ani muscle is mediated by the circumferentially spreading LM [20, 21] (arrow). The extension of the rectal LM penetrates into the external sphincter muscle at its distal part and fixes the anorectum to the pelvis [17–19] (arrow head)

reaches the posterolateral side of the prostate where both the sympathetic and parasympathetic nerve fibers enter the rectal wall and are then distributed to the IAS, or when the intermuscular nerve fibers to the IAS are divided [11].

The most cranial side of the anal canal has been called the "levator hiatus", and this is the region through which the anal canal, urethra, and vagina pass [12]. These intrahiatal organs are connected circumferentially with the fascia on the pelvic surface of the levator muscle by the "hiatal ligament" [12] (Fig. 1). During defecation, the hiatal ligament functions as connecting tissue for the opening of the anal canal, which is mediated by the contraction of both the pubococcygeus muscle and the iliococcygeus muscle [13, 14].

The conjoint longitudinal muscle (LM) in the anal canal is an extension of the rectal LM. This conjoint LM penetrates into the external sphincter muscle at its distal part [17, 18] and fixes the anorectum to the pelvis [19] (Fig. 2). During bowel evacuation, the LM contracts to shorten the anal canal [19]. Part of the mechanism for normal evacuation induced by the LM and the hiatal ligament may be damaged during the operative procedures of either LAR or ISR, when surgical dissection reaches the intersphincteric space.

Perirectal structures associated with normal defecation

During bowel evacuation, the rectal longitudinal muscle (LM) and the conjoint LM contract to shorten the anal canal [19]. In addition, a pair of strong smooth muscles are located on the dorsal side of the rectum and attached to the coccyx. This is generally called the "rectococcygeus (-al) muscle" (Fig. 1), and contraction of this muscle is believed to shorten the rectum to assist in the evacuation of feces [22]. The rectococcygeus muscle has been defined as the two bands of smooth muscle tissue arising from the 2nd and 3rd coccygeal vertebra and blending with the rectal longitudinal smooth muscle fibers on the posterior wall of the anal canal [23]. It was recently reported that the LM of the rectum is thick on the posterior side and lies on the levator ani muscle [20], suggesting that the "rectococcygeus muscle" is actually part of the LM that is thickened in the posterior wall of the rectum. It has also been found that the attachment of the rectal wall to the levator ani muscle is mediated by the circumferentially spreading LM [20, 21], suggesting that the LM in this region may be equivalent to the "hiatal ligament" surrounding the rectum. During LAR for rectal cancer, both the rectococcygeus muscle and the hiatal ligament are often divided to obtain a sufficient horizontal margin anally. The division of these structures is a typical part of the ISR procedure. Thus, the SPO maneuver impairs the functional roles originally performed by these structures.

The function of the rectum

During the SPO procedure, curative resection of the cancer necessitates removal of most of the rectum. Therefore, it is essential to understand how the rectum works in normal defecation when discussing the etiology of LARS. During the basal phase, the rectum remains mostly empty or may contain a small amount of feces without conscious awareness [24]. The initiation of defecation is believed to be triggered by a propagated burst of contraction in the sigmoid colon, which may deliver fecal material into the rectum [25]. The accumulation of feces in the rectum results in the urge to defecate at varying intervals: the majority of people feel this urge once or twice a day [15]. When the intrarectal pressure increases with the occurrence of high-amplitude propagated contraction in the sigmoid colon, the IAS subsequently relaxes. This is usually called the recto-anal inhibitory reflex

(RAIR) in manometric studies. If it is not a suitable place or time for defecation, the external anal sphincter and pelvic floor muscles are contracted voluntarily to delay defecation [15, 25]. Furthermore, the normal rectum shows periodic motor activity that propagates in a retrograde direction, which may decrease the intrarectal pressure and suppress the defecation urge [26].

It has been reported that the recto-anal inhibitory reflex is mediated by the enteric nervous system [27]; however, several studies support the theory that the reflex is regulated by extrinsic nerves from the spinal cord [28, 29]. The IAS has a sampling reflex that enables detection of the rectal contents via the intermittent relaxation of the muscle [30]. This sampling mechanism is believed to play an important role in maintaining fecal continence [31]. These fundamental mechanisms for fecal continence may be damaged during the SPO procedure by the removal of a substantial amount of the rectal wall or by the division of either the extrinsic or intrinsic nervous supplies to the rectum and some components of the anal canal.

Innervation of the rectum and anal canal

The efferent visceral nerve supply to the rectum and the IAS is from the inferior hypogastric plexus, also called the pelvic plexus. The inferior hypogastric plexus is a mixture of both sympathetic nerve fibers from the superior hypogastric plexus via the hypogastric nerves, and parasympathetic nerve fibers from the pelvic splanchnic nerves [32]. The inferior hypogastric plexus also contains afferent nerve fibers from the rectum and the IAS [16], which follow the parasympathetic fibers in a retrograde fashion to the S2–S4 spinal sensory ganglia [33]. The inferior hypogastric plexus gives rise to several peripheral plexuses, including the rectal plexus, the vesical plexus, the prostatic plexus, and the uterovaginal plexus. The rectal plexus provides the nervous supply to the rectum and the IAS. A nerve branch goes into the rectal wall just below the peritoneal reflection [34] and a branch to the IAS runs inferiorly along the fascia of the levator ani muscle and enters the IAS at the height of the dentate line from the 2–3 and 9–10 O'clock directions [11]. The anatomical features of the nervous systems that supply the lower rectal wall and the IAS make it likely that these nervous systems will be damaged during TME. TME is reportedly one of the major causes of LARS [3]. Further analysis to identify the precise location of these nerves is necessary to help preserve these nerves intraoperatively. In the typical LAR procedure, which is total mesorectal excision (TME), the pudendal nerve and its branching inferior anal nerve are preserved without being damaged. Therefore, as the pudendal nerve mediates contraction of the levator ani and relaxation of the external sphincter muscle during defecation [15], there should be no impairment of these functions postoperatively; however, there is a possibility of nerve injury in patients who require lateral pelvic lymph node dissection and a surgical maneuver near Alcock's canal.

Motility of the neorectum and low anterior resection syndrome

The mechanism of postoperative LARS has not been clarified but is likely to be multifactorial. One of the causes of urge fecal incontinence in patients who have not undergone any abdominal operations is higher motility of the left descending and sigmoid colon, together with hypersensation of the rectum [35]. Similarly, in patients who have undergone a SPO, spastic hypermotility of the neorectum is correlated with the severity of defecatory urgency [36]. This hypermotility may be associated with the extrinsic denervation of the neorectum during the operative procedure [37, 38]. Severe LARS is also reported to be associated with an increased postprandial response with a significant increase in pressure in the neorectum, further suggesting that LARS may be caused by physiological changes resulting from neural damage [39]. Efforts to reduce LARS symptoms by creating a colonic J-pouch or performing side-to-end anastomosis have not yielded substantial benefits [40], indicating that the physical form of the neorectum is not strongly associated with the manifestation of LARS.

Quality of life of patients with low anterior resection syndrome

The major factor that impairs QOL following SPO is bowel dysfunction [41]. The primary defecatory symptoms that impair QOL are "incontinence of flatus or liquid stool", "bowel frequency", "clustering", and "urgency". Among these symptoms, the most important determinant in the LARS score is "urgency", followed by "clustering" [42]. The global QOL after LAR is reportedly identical to that after abdominoperineal resection [43–45]. However, compared with patients who have undergone abdominoperineal resection, those who have undergone LAR score higher in physical functioning [44, 46, 47] and body image [45].

Treatment strategy for low anterior resection syndrome

The term "LARS" is well known by specialized colorectal surgeons in the USA and Spain, and recognized by more than 80% of all colorectal surgeons [48]. However, a method to assess the severity of LARS has not been established. Moreover, the majority of treatments used to ease symptoms are lifestyle and dietary measures, with or without drug treatment [48], which implies that individual, detailed

treatments for LARS in accordance with the symptoms might not be widely provided. As the etiology of LARS is still unclear, the management is empirical and symptom-based, using therapies for fecal incontinence [49].

Regarding dietary measures for the management of fecal incontinence, it is suggested that patients should avoid substances that cause stool softening (such as caffeine, citrus fiber, spicy food, and alcohol), whereas dietary fiber (such as methylcellulose) is recommended [50, 51]. Although dietary management is strongly recommended for fecal incontinence, there is no strong evidence to support the effectiveness of dietary measures in the treatment of LARS [1, 52]. Medications used for LARS mostly comprise those that prevent excessive motility of the colon. Antidiarrheal agents such as loperamide and atropine reduce colonic motility and may increase the IAS tone. In male patients with LARS, the 5-HT3 antagonist, ramosetron, is reportedly effective in reducing the number of toilet visits and urge fecal incontinence [53]. A 5-HT3 antagonist is recommended for patients with LARS who have strong postprandial contraction of the neorectum [1].

Pelvic floor rehabilitation, including Kegel's exercise and biofeedback training, is reportedly effective for improving the fecal incontinence score, stool frequency, and health-related QOL [54, 55]. Transanal irrigation has also been found to improve the LARS score [56], fecal continence [57], defecatory urgency [58], and some components of the SF-36 [59], and reduce the number of toilet visits [56, 59].

The treatment of choice for fecal incontinence is sacral nerve modulation (SNM) [60], the mechanism of action of which is suggested to be through the afferent nerves from the anorectum [61] and central levels [62]. SNM reportedly decreases antegrade colonic motility, increases retrograde activity [63], and impairs postprandial changes in rectal tone [64], which may be the mechanism of urge fecal incontinence. It is unknown whether SNM is still effective after afferent nerve injury during LAR; however, the success rate of SNM for fecal incontinence in LARS is reportedly comparable to that for other forms of fecal incontinence [65, 66]. The final therapy for severe LARS is stoma creation [1].

Conclusions

The etiology of LARS lies in the surgical maneuvers performed during the SPO. The factors contributing to the manifestation of LARS include not only resection of most of the rectum, which is one of the key organs for defecation, but also damage to the extrinsic innervation of the IAS and/or rectal wall, and disruption of the structures around the levator hiatus. Further investigation of the precise anatomy of the nerve supplies, and of the development of surgical techniques that avoid injury of these structures during SPO, is warranted. Furthermore, it is anticipated that possible treatment options for severe LARS in the future will comprise medications based on the physiology of LARS, well-organized physical rehabilitation protocols, and more widespread application of retrograde irrigation using good apparatus.

Compliance with ethical standards

Conflict of interest We have no conflicts of interest directly relevant to the content of this manuscript.

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