REVIEW ARTICLE

Low anterior resection syndrome (LARS)

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Key words: Neorectum; aetio-pathology; QOL; LARS; dyspareunia; ileostomy

Abstract

Patients develop a variety of bowel dysfunction following low or very low anterior resection for rectal cancer. These symptoms are known collectively as low anterior resection syndrome (LARS), and the extent to which it affects the quality of life of these patients can be assessed by the LARS score. Knowledge about anorectal functional anatomy is a prerequisite to understanding the aetio-pathology and clinical manifestation of LARS. Structural and functional impairment of the internal and external anal sphincter and the anal transition zone, loss of reservoir function of the rectum, increased colonic motility, proximal diversion, enteric nervous system remodelling and neuropathy of autonomic nerves in the pelvis are known to cause LARS.

Assessment of patients with LARS with MRI scan, endoanal ultrasound and anorectal manometry will help to identify the cause for LARS. Treatment of LARS will have to be tailored to the individual patient. The treatment protocol can start with conservative measures like pelvic floor rehabilitation, colonic irrigation and biofeedback therapy. Medication with Imodium and serotonin receptor antagonists may help some patients with LARS. Sacral nerve stimulation is a minimally invasive technique that has been used to treat patients with LARS for more than one year. Stoma creation will be considered in those with major LARS persisting for more than two years. Meticulous dissection with preservation of nerves and anal sphincters and anastomotic reconstruction techniques such as an end to side anal anastomosis or a colonic–J pouch anal anastomosis can minimize the occurrence of LARS.

Introduction and definition of the low anterior resection

Low anterior resection for cancer is defined as the operation which aims to completely remove the rectum with its tumour, including total mesorectal excision, followed by anastomosis of the proximal colon to the anal canal. Treatment for lower rectal cancer has improved over the last two decades. This is primarily because of the use of neoadjuvant chemotherapy and radiotherapy for effective local control and advances in surgical techniques with the invention of endo-anal circular stapling devices for anastomosis and sphincter preservation (1). As a result, many patients with a low rectal adenocarcinoma are now treated with low anterior resection with total mesorectal excision. Those in whom tumour-free margins are achieved with sphincter preserving surgery will be expected to have a better quality of life (QOL) compared with those who receive a permanent stoma. In reality, up to 90 percent of patients will experience symptoms of bowel dysfunction (2). The QOL of these patients did not differ from those who had received a permanent colostomy (3).

LARS is a collection of symptoms or ailments experienced by patients following low anterior resection. These symptoms include gas and faecal incontinence, faecal urgency, frequent bowel movements, bowel fragmentation and emptying difficulties (1). Neo-adjuvant chemoradiation for rectal cancer and total mesorectal excision (TME) have been associated with severe postoperative bowel dysfunction (4).

Apart from colonic dysfunction, patients can also experience genito-urinary dysfunction such as impotence, ejaculatory dysfunction and dyspareunia following low anterior resection. There is no general agreement, yet, about the inclusion of genito-urinary symptoms in the LARS scoring system (5), which is a validated scoring system to assess the extent to which QOL is affected (6).

Attempts have been made to reduce the incidence of LARS and to improve QOL but these are yet to achieve satisfaction. Thus, understanding the basic science behind LARS and its effect on QOL is essential to focus on future developments in the treatment of lower rectal cancer and in the prevention of LARS.

The aetio-pathology of LARS

Physiology of defaecation

The rectum is filled with faeces by colonic activity. Receptive relaxation of the upper rectum enables reservoir function (7).

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http://orcid.org/0000-0002-3303-603X
DOI: http://doi.org/10.4038/sljs.v37i1.8601

Distension of the lower rectum induces a recto-anal inhibitory reflex (RAIR), which causes relaxation of the internal anal sphincter (IAS), preparing the anal canal for defaecation. When socially inconvenient, it would be possible to recruit contraction of external anal sphincter (EAS) muscle and to halt defecation (8). The entry of rectal content into the upper anal canal allows sampling of content in the anal transition zone (ATZ), which is able to discriminate the nature of rectal content. The RAIR is effected by the myenteric plexus, controlled by the autonomic nervous system. The IAS receives sympathetic and parasympathetic innervation by the hypogastric and pelvic nerves respectively. The IAS is mainly responsible for the maintenance of continence at rest and during sleep (9).

Continued distension of the lower rectum stimulates the mechanoreceptors in the rectum and pelvic floor, which will result in stimulation of myenteric nerves in the sigmoid colon and rectum, resulting in increased local peristalsis. The afferent impulses from stretch receptors travel to spinal segments; the parasympathetic nerves via the pelvic splanchnic nerves (Nervi erigentes) to sacral segments and sympathetic nerves via the hypogastric nerves. Stimulation of parasympathetic motor neurons in the sacral spinal cord will increase peristalsis throughout the large intestine resulting in sets of high amplitude propagated sequences (HAPS) that will generate the "call to stool". Sympathetic nerves inhibit HAPS (8).

When defaecation is not convenient, contraction of the external sphincter and pelvic floor is modulated by the somatic motor neurons at the sacral segments of the spinal cord via the pudendal nerve (S2, 3, 4). Continuation of defaecation is facilitated by contraction of anal canal longitudinal muscle leading to shortening of the anal canal and relaxation of pelvic floor muscles. Usually, the descent of the pelvic floor is confined to 2 cms. Involuntary colorectal motor activity and voluntary straining increase rectal pressure resulting in a net expulsive force that is directed postero-inferiorly. Simultaneously, the anorectal angle, which is acute in a position of rest, becomes obtuse, resulting in straightening of the anal canal. The net rise in intra-rectal pressure over anal canal pressure results in the expulsion of faeces. At the end of defaecation the pelvic floor will raise and resting anal sphincter tone will return to establish a state of continence (8).

The aetiological factors affecting the process of defaecation after low anterior resection

Alteration in functional anatomy of the ano-rectum in low anterior resection

- IAS

Structural damage to the IAS can occur by stretch during anastomotic reconstruction with circular staplers. This can also result from excision of the upper part of IAS in very low anterior resection (10). Scarring after radiotherapy can also affect the functional integrity of IAS (9). Injury to autonomic nerves supplying the IAS either during surgery or during radiotherapy, will affect RAIR and anal sampling. This functional derangement can result in a reduction in anal resting pressure and faecal soiling (10).

-Anal transition zone (ATZ)

Excision of the ATZ during intersphincteric dissection and mucosal proctectomy in extended low anterior resection has the potential to impair anal sampling resulting in flatus incontinence and soiling (9, 10).

-The external anal sphincter (EAS)

The external anal sphincter is at risk of direct injury during low and extended low anterior resection of the rectum (11) and as a result of pudendal neuropathy, which may occur following neo-adjuvant radiotherapy and in anastomotic sepsis. Urgency and faecal incontinence are sequelae of pudendal neuropathy (2).

-Rectal reservoir

Reservoir function of the rectum is lost in TME with colo-rectal or colo-anal anastomosis. Further, damage to autonomic nerves in TME and following neoadjuvant radiotherapy can lead to denervation of the rectal stump. This will have an impact on the reservoir function of the rectum (7). When the neorectum is filled with faeces it will contract due to its intrinsic colonic property. Radiation-induced fibrosis will further reduce the capacity and compliance of the neorectum. The outcome of these functional derangements would be frequent bowel movements and bowel fragmentation.

-Colonic motility

High ligation of the inferior mesenteric artery and mobilization of the left colon can cause autonomic denervation. Reduction in sympathetic inhibitory action can, in turn, produce high amplitude propagated sequences (HAPS) leading to increased peristalsis of the colon (2,12,13). This can manifest as the increased gastrocolic reflex, urge to defaecate and loose stools (14).

-Proximal diversion

Temporary ileostomy performed with TME causes mucosal and muscular architecture of colon. With atrophic changes muscular and villous architecture of colon, there will be impaired absorption and secretion. The diversion can also lead to neuronal changes. There will be remodelling of submucosal and myenteric plexus of the enteric nervous system. After reversal of ileostomy, the patients may experi-

Table 1. LARS Score questioner (with points allocated to respective answers)

Do you ever have occasions when you cannot control your flatus (wind)?	□ No, never	0
	□ Yes, less than once per week	4
	□ Yes, at least once per week	7
Do you ever have any accidental leakage of liquid stool?	□ No, never	0
	□ Yes, less than once per week 3	3
	□ Yes, at least once per week	3
How often do you open your bowels?	□ More than 7 times per day (24 hours)	4
	□ 4-7 times per day (24 hours)	2
	□ 1-3 times per day (24 hours)	0
	□ Less than once per day (24 hours)	5
Do you ever have to open your bowels again within one hour of the last bowel opening?	□ No, never	0
	□ Yes, less than once per week	9
	□ Yes, at least once per week	11
Do you ever have such a strong urge to open your bowels that you have to rush to the toilet?	□ No, never	0
	□ Yes, less than once per week	11
	□ Yes, at least once per week	16

LARS Score and impact on QoL

0-20 = No LARS , 21-29 = Minor LARS , 30-42 = Major LARS

LAR score has a sensitivity of 72.54 % and specificity of 82.52% for major LARS.

It also shows a very good correlation with severity of LARS (6).

ence diarrhoea and frequent stools affecting the QOL (15).

-Enteric nervous system remodelling

Remodelling of enteric nerve function and fibrosis with stricture formation at the site of coloanal anastomosis could result in obstructive symptoms such as constipation and difficulty emptying (15).

-Neuropathy of autonomic nerves in the pelvis

Urinary and sexual dysfunction such as dypareunia and impotence would be due to damage to autonomic nerves during pelvic dissection during TME (16, 17, and 18).

The LARS score in the evaluation of the severity

Many assessment tools have been devised to objectively quantify impaired anal continence; the St Marks Faecal Incontinence Grading Score, the Wexner Incontinence Score and the Rockwood Faecal Incontinence Severity Index, the latter specifically designed to assess the quality of life in patients with faecal incontinence. The LARS scoring system, which concerns those who have had low anterior resection of the rectum, has been designed taking into consideration the diversity of symptoms affecting QOL in patients with sphincter sparing surgery (11 – Table 1).

LARS scoring system assesses the degree to which low anterior resection affects the QOL in patients treated with sphincter sparing surgery for rectal cancer. Five clinical manifestations of LARS are considered in this scoring system; incontinence to flatus, leakage of liquid stool, frequency of bowel movement, clustering of defaecation and faecal urgency. A scale is used to quantify the impact of each symptom of bowel dysfunction on the QOL of patients. The score thus obtained ranges from 0 to 42. Patients having a score ranging from 0 to 20 will be considered those who don't have LARS.

Those with a score 21 to 29 are classified as minor and 30 to 42 as major LARS respectively. The score is useful to assess the prevalence of LARS and the impact of sphincter sparing rectal excision on patients' QOL. It can also evaluate the effectiveness of various treatment modalities on the QoL of patients with rectal cancer. Further, this would be a useful tool to assess the impact of preventive interventions taken during surgery to prevent LARS postoperatively (6).

Diagnostic investigations

Once the clinical diagnosis of LARS is made on subjective symptom analysis the following investigations could aid to arrive at an objective assessment for bowel dysfunction;

Defaecography / MR Defaecography

Defaecography can demonstrate the characteristic features of anorectal functional disorders in LARS. It enables visualization of contrast in the anal canal at rest, a widened anorectal angle, reduced evacuation fraction and a low volume neorectum (9). The patient could be assessed in a horizontal or vertical position by magnetic resonance (MR) defaecography depending on whether the MR magnet is closed or open respectively. Assessment of bowel dysfunction in LARS by MR defaecography could reveal detailed information about the anorectal angle, the pelvic floor descent and anal canal opening (19).

Endo-anal USS (EUS)

LARS resulting from structural damage to the anal sphincter complex is assessed by EUS. Both the internal and external anal sphincter can be visualized and defects in the sphincters predicted with an accuracy of over 98percent in experienced hands (20).

Anorectal manometry

An anorectal manometry is a standard tool for evaluation of anorectal dysfunction in LARS. Patients with LARS have decreased resting anal sphincter pressure, at times, reduced squeeze pressures and reduced rectal volume tolerability and low rectal compliance. Also, squeeze pressure may be normal in patients with LARS (21).

Clinical management

Non-operative

-Pelvic floor rehabilitation

Pelvic floor rehabilitation is a standard method for the rehabilitation of patients with LARS. This consists of pelvic floor muscle training, biofeedback training and rectal balloon volume training. It has been shown that pelvic floor training significantly improves the frequency of stool and incontinence of faeces (22). Pelvic floor muscle training must be instructed to all the patients who had sphincter sparing surgery for rectal cancer irrespective of presence or absence of diverting stoma. Patients will experience improvement in symptoms of LARS when a tailored approach, using more than a single rehabilitative technique, is used (2).

-Colonic irrigation

Retrograde neo-rectal irrigation is efficacious in treating patients with LARS especially those with faecal incontinence and increased bowel frequency. In cases of delayed (more than 4-8 weeks) closure of a diverting stoma and in those with severe LARS persisting one month after low anterior resection retrograde enema irrigation of 250 ml of lukewarm tap water could be performed either daily once in 2 to 3 days. It is best that pelvic floor rehabilitation is performed along with neorectal irrigation with an enema. For patients with a diverting stoma ante-grade, trans-stomal enema irrigation or balloon volumetric training could be advocated. Patients should be periodically assessed with LARS score to evaluate improvement in LARS (2).

-Biofeedback therapy (BFT)

It is a process by which patients are trained to contract and relax the pelvic floor and anal sphincters with the help of balloons, myometry and manometry. BFT has been shown to increase rectal capacity and to reduce faecal incontinence and stool frequency (7).

-Sacral nerve stimulation (SNS)

SNS should be considered for those with major LARS score persisting even after one year (2). In brief, low voltage electrical stimulation of sacral nerve roots by trans-cutaneous implantation of an electrode at the third sacral foramen and a pulse generator placed subcutaneously in the buttock completes the assembly (23). SNS is thought to result in improvement in anorectal function via pelvic afferent and central mechanisms (24). It has been reported that SNS improves the quality of life in patients with LARS by improving the ability to hold stool and to defer defaecation. It also reduces postprandial urgency (25).

-Pharmacotherapy

Those patients with LARS with post postprandial frequency

may benefit from serotonin induced 5-HT3 receptor antagonists. Those patients with LARS with predominant diarrhoea have been shown to benefit from loperamide. Protective pads may be useful in those troubled by faecal soiling (1). Probiotics, steroids and nonsteroidal anti-inflammatory drugs have no benefits in LARS (22).

-Stoma

In those patients with major LARS even after 2 years, a stoma should be considered for better QOL. Also, in selected patients with severe LARS, neo-sphincter reconstruction might be considered (2).

Minimizing LARS and improving functional outcome in LAR

Surgical techniques

In general, sharp dissection with minimal use of diathermy will prevent possible injury to pelvic nerves. Avoiding injury to hypogastric nerves during high ligation of an inferior mesenteric artery is an essential initial step during entry into the pelvis. TME that is performed for cancer distal to the upper rectum when compared with partial mesorectal excision (PME), which is performed for proximal rectal cancer, will have a short or no rectal stump with a low anastomosis. As such, patients undergoing TME are at greater risk of developing LARS compared with those having PME (15).

A straight colo-anal anastomosis has less compliance and capacity when compared to other techniques such as colonic –J pouch anal anastomosis or an end to side anal anastomosis, and is more likely to be associated with LARS, though the difference in function is likely to last no more than a year (7, 26).

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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