

LOW ANTERIOR RESECTION SYNDROME – PREVENTION, DETECTION, TREATMENT

Marina Vasile¹, O. Andronic^{1,2}, D.N. Păduraru^{1,2}, Alexandra Bolocan^{1,2}, D. Ion^{1,2}

¹The Emergency University Hospital Bucharest, Romania

²The University of Medicine and Pharmacy “Carol Davila”, Bucharest, Romania

Corresponding author: Octavian Andronic

Phone no.: 0040724024019

Email: andronicoctavian@gmail.com

ABSTRACT

Colorectal cancer is the third most common type of cancer, and the most common type of cancerous tumor that appears in the gastrointestinal sphere [2]. In recent years, the introduction of new imaging methods that produce higher resolution images of rectal tumors has made possible the emergence of targeted treatment for this type of cancer, the neoadjuvant therapies determining a tumor downstaging prior to potentially curative surgery and a higher survival rate. Surgical tumor excision with oncological safety limits is currently the only curative therapy in colorectal cancer, and can be associated with neoadjuvant or adjuvant radio and / or chemotherapy. Regarding treatment, there are not yet standard methods to compute or prevent this syndrome. The management of this condition is currently empirical, based on the treatment of symptoms, using the treatment already known for anal incontinence, urgent defecation, or difficulty initiating a bowel movement.

KEYWORDS: *rectal cancer, LARS, low anterior resection syndrome, QoL*

INTRODUCTION

One of the leading causes of death worldwide is cancer, of any nature. It causes millions of deaths annually worldwide. According to the World Health Organization and the International Agency for Research on Cancer, the incidence of the most common types of cancer differs between the two sexes. For men on the first place is lung cancer, followed by prostate cancer and then colorectal cancer. For the feminine is breast cancer followed by colorectal cancer [1]. Overall, colorectal cancer is the third most common type of cancer, and the most common type of cancerous tumor that appears in the gastrointestinal sphere [2]. In recent years, the introduction of new imaging methods that

produce higher resolution images of rectal tumors has made possible the emergence of targeted treatment for this type of cancer, the neoadjuvant therapies determining a tumor downstaging prior to potentially curative surgery and a higher survival rate.

Surgical tumor excision with oncological safety limits is currently the only curative therapy in colorectal cancer, and can be associated with neoadjuvant or adjuvant radio and / or chemotherapy. There are currently more types of surgeries in practice. Today, the most commonly used methods appear to be transabdominal, which are associated with techniques of preserving internal and external anal sphincters [3]. In patients where a distal margin can be obtained at the histopathological extemporaneous examination, methods of

preservation of anal sphincters are preferred because they prevent fecal incontinence and permanent colostomy. Approximately 80% of patients requiring surgical treatment for colorectal cancer can be treated by methods of preserving internal and external anal sphincters [3].

The concept of "total mesorectal excision" was introduced by the British surgeon Heald, about 30 years ago (1982), and revolutionized local disease control in rectal cancer, and preserving the sphincter apparatus in over 80% of cases.

For surgeons, the concept of "total mesorectal excision" combines five fundamental principles (16):

-definition of an avascular plan for dissection, which named by Heald as the sacred plane ("the Holy Plane"(17)); this plan ensures on one hand the radicalization of the resection (oncological result) and on the other hand the maintenance of the perirectal nervous structures (functional result)

-definition of a surgical objective: removal of the rectum and mesorectum as a whole, without any tearing, with circumferential margins intact

-definition of a parameter for assessing the radicality of the surgical act (the circumferential margin of resection); the radial edge is critical for recurrence, even more important than the proximal or distal edge

-recognition and preservation during the operation of the autonomic nerve plexus on which depend the erectile function and bladder-evacuation

-keeping intact the anal sphincter function and decreasing the number of colostomy

The removal of the rectal segment along with the various ways (surgery, radiotherapy, chemotherapy) that can damage the nervous or sphincter elements modifies in varying degrees the reservoir and the continence functions of the rectum, modifications brought together under the generic name of LARS(low anterior resection syndrome) .

The article aims to present the current data on prediction, prevention and correction of LARS in order to improve the quality of life in patients treated for rectal cancer.

MATERIAL AND METHODS

We have researched the medical literature on the causes of LARS, methods of quantification and prevention of this syndrome, and treatment methods.

Patients receiving treatment using anal sphincter preservation methods may also experience multiple symptoms that substantially affect their quality of life, symptoms other than those present in patients with stoma. There is no consensus on the quality of life in patients with abdominal perineal resection of the rectum (Hartmann) [4]. There are a number of symptoms that appear after a low anterior resection of the rectum, LARS (low anterior resection syndrome), including anal incontinence or urgency in defecation, frequent stools, difficulty in starting defecation, increased intestinal gas [3] . These symptoms have a major impact on the quality of life of patients who underwent colorectal cancer surgery, and between 25 and 80% of these patients develop LARS [4].

Results obtained from surgical resection of rectal cancer or improved over the last 20 years, especially the survival rate and the rate of local recurrence [5].

Rectal dysfunction (LARS syndrome) that occurs in patients who survive rectal cancer is a major problem. LARS syndrome is multifactorial. Several pathophysiological mechanisms have been identified for this syndrome, including: inner sphincter dysfunction or decrease in anal canal sensitivity, disappearance of anorectal reflexes and reduction of rectal reservoir capacity and compliance [5].

This syndrome presents a number of risk factors that may cause it to occur [3]:

- neoadjuvant and adjuvant radiotherapy
- postoperative chemotherapy
- low anastomosis location
- temporary protection colostomy
- obstructive symptoms
- post-anastomosis complications

The normal functioning of the remaining anatomical structures after rectal surgery depends on the use of neoadjuvant chemotherapy or postoperative radiotherapy. Most regimens assume the association of these aggressive therapies for a period of 4 and 6 weeks after surgery [2]. In many patients, an increase in the frequency of the stools after

postoperative radiotherapy was reported, as well as a marked decrease in the anal continence and rectal reservoir compliance, together with the change in bowel movements capacity and pattern [2].

To better quantify LARS, that occurs following the low anterior resection of rectal tumors (LARS), a scoring system was developed (by Emmertsen KJ, Laurberg S) for the bowel dysfunction after low anterior resection (LAR) for rectal cancer, on the basis of symptoms and impact on quality of life. This score is the only one that can diagnose LARS(18).

LARS-score - Scoring Instructions

Add the scores from each 5 answers to one final score.

Do you ever have occasions when you cannot control your flatus (wind)?	
<input type="checkbox"/> No, never	0
<input type="checkbox"/> Yes, less than once per week	4
<input type="checkbox"/> Yes, at least once per week	7
Do you ever have any accidental leakage of liquid stool?	
<input type="checkbox"/> No, never	0
<input type="checkbox"/> Yes, less than once per week	3
<input type="checkbox"/> Yes, at least once per week	3
How often do you open your bowels?	
<input type="checkbox"/> More than 7 times per day (24 hours)	4
<input type="checkbox"/> 4-7 times per day (24 hours)	2
<input type="checkbox"/> 1-3 times per day (24 hours)	0
<input type="checkbox"/> 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?	
<input type="checkbox"/> No, never	0
<input type="checkbox"/> Yes, less than once per week	9
<input type="checkbox"/> 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?	
<input type="checkbox"/> No, never	0
<input type="checkbox"/> Yes, less than once per week	11
<input type="checkbox"/> Yes, at least once per week	16
Total Score:	<hr style="width: 100px; border: 1px solid black;"/>
Interpretation:	
0-20:	No LARS
21-29:	Minor LARS
30-42:	Major LARS

Figure 1 - LARS score

A study that took place in Denmark between 2001 and 2007 quantifies fecal incontinence after anterior resection of rectal cancer with or without neoadjuvant therapy using a score that associates symptoms with the quality of life of these patients [8]. All patients who received rectal cancer curative surgery in Denmark between 2001 and 2007 were contacted and it was developed a questionnaire that quantifies normal defecation and quality of life, including LARS syndrome, which was applied to the patients who did not suffer from a local recurrence of the tumor in 2009 [8].

The conclusion of the study was that this syndrome is a frequent manifestation that occurs in these patients and is maintained in the long run. Also, the use of neoadjuvant therapy, whether administered on a long or short term, and complete resection of the mesorectum, are independent risk factors for LARS [8].

In order to highlight this syndrome, anorectal manometry has proven to be a useful method, which determines the correct functioning of the anal sphincter. This highlights the pressures that occur during the contraction of the anal sphincter and also the length that contracts [9]. Adjuvant techniques using an anorectal balloon may point out the presence of rectal inhibitors, rectal sensitivity, its ability to contract and its compliance. Although anorectal manometry is used as a standard diagnostic method for Hirschprung disease, it is increasingly used to diagnose idiopathic constipation (in patients with less than 3 stools per week) and anal incontinence (especially after rectal resection for colo-rectal cancer) [9].

Anorectal manometry has also been proposed as a preoperative assessment method to determine the patients to whom the anal incontinence may occur following the various types of surgery that they will suffer.

Regarding treatment, there are not yet standard methods to compute or prevent this syndrome. The management of this condition is currently empirical, based on the treatment of symptoms, using the treatment already known for anal incontinence, urgent defecation, or difficulty initiating a bowel movement (4). In addition, it seems that rectal cancer specialists do not yet have a full understanding of this syndrome or the symptoms that most disturb the patient after anal sphincters preservation techniques. These symptoms may also affect the quality of life differently in different patients. Physicians generally tend to overestimate the impact of anal incontinence on frequent bowel movements and underestimate the impact of urgency on defecation and constipation in these patients [4].

A meta-analysis attempted to determine the efficiency of anal function rehabilitation as a method of treatment for the symptoms that occur after anterior resection of the rectum, they observed several functional and clinical

parameters, and especially the quality of life of patients. The investigated treatment methods consisted of biofeedback and nerve stimulation of sacral nerves [10].

There are several methods of treatment for LARS syndrome, of which we mention, in order of use [11]:

1. Changes in diet, fiber
2. Enema (transanal irrigation)
3. Sacral nerve stimulation
4. Anterograde irrigation
5. Advanced surgery
6. Making a stoma

Conservative methods

Conservative methods are dedicated to the relief and control of symptoms and are the first line of treatment for anal incontinence in the LARS syndrome. Patients suffering from this syndrome should be instructed to avoid food that can lead to soft stools or increased stool frequency. Natural fibers or bulking agents (substances that contribute to increasing the volume of the food without significantly contributing to its energy value) such as psyllium seeds, methylcellulose can increase the consistency of the stools and increase the amount of faeces eliminated at a bowel movement. Also, therapeutic agents that cause constipation, such as loperamide, can be useful and are often used. Also tricyclic antidepressants (eg Amitriptyline) can be used because they decrease the motility of the colon. The efficiency of these methods of treatment is not well documented in the literature [11].

Biofeedback and multimodal rehabilitation are other first-line methods in the treatment of anal incontinence that occurs in these patients. Biofeedback uses visual signals and teaches the patient how to train the contractility of the external anal sphincter and how to use the pelvic muscles [11]. Medical literature also states that multimodal rehabilitation improves functional outcome in LARS syndrome [10].

Enemas

These are used to clean the colon and relieve the symptoms of anal incontinence. Patients irrigate and remove colon content every day this way. The administration procedure is simple and well tolerated by long-term patients [11]. The results of this type of treatment were

good to reduce anal incontinence in post resection patients (for rectal cancer) [11].

Electric stimulation of sacral nerves

The anal incontinence that occurs following the intraoperative injury of the anal sphincter nervous complex can be treated by surgical repair of nerve continuity, with satisfactory results. However, in most cases surgical repair of functional impairments without apparent anatomical lesions has rather poor results. Thus, the use of sacral nerve stimulation as an anal incontinence treatment that appears on an intact anatomical sphincter but with a functional deficiency, or for other sphincter lesions, seems an attractive alternative [10].

Modulation of nerve function is an area of medicine that has seen a rapid increase in recent years and will become over time a procedure that will bring many benefits in various medical areas. The concept of nerve stimulation of the pelvic floor appeared in the early 19th century when the first neuromuscular stimulation methods were developed (Hopkinson, 1966).

Initially, an assessment of the functionality of each sacral nerve is performed, which controls the external sphincter (striated). This assessment can be performed using anorectal manometer, observing the increase of local pressure or following perineal movements (the most commonly used method) [12]. More specifically, the stimulation of the sacral nerve S2 causes spasms in the perineal muscles and internal heel rotation or lateral rotation of the entire leg along with the contraction of the toe and foot [12]. Stimulation of S3 nervous branch causes a movement of constriction of the levator ani and plantar flexion of the first toe. S4 stimulation determines contraction of the levator ani with a visible bellows-like perineal movement and does not cause any activity in the lower limb. If these moves can be demonstrated, the preferred place to achieve stimulation is sacral foramen S3, S4 can be used when S3 can not be located. With the patient in prone position and under general anesthesia without muscle relaxants, needle electrodes are inserted into the sacral holes S2, S3 and S4 bilaterally. The electricity is applied with the gradual increase of the intensity and the characteristic

movements of the pelvic floor are monitored. The needle is then replaced with a flexible electrode that is exteriorized to the skin and connected to an electrical stimulator. Then the nerve is continually stimulated for a week with pulse duration of 210 seconds, a frequency of 15 Hz and an amplitude varying between 1 V and 10 V, depending on the patient's perception of muscle contraction [12].

Electrical stimulation of sacral nerves as a treatment method for anal incontinence has shown good results both in the short and long term. This method is especially indicated for patients with an integral sphincter device, whose incontinence comes from a functional and less morphological change [12].

Antegrade irrigation

Antegrade colonic enemas involve the construction of a catheterisable conduit in the proximal colon through which enemas or irrigation fluid can be given to evacuate the colon and rectum. Although this procedure is most commonly used for chronic constipation, it can be utilized in incontinent individuals[12]. The procedure is performed by isolating the appendix and its blood supply, amputating the distal end of the appendix and reimplanting it in the cecum. The proximal end of the appendix is exteriorized. A skin flap is used to bury the appendix, minimizing mucous drainage[13]. In adults this procedure has been modified by using the colon instead of the appendix.

Advanced surgery

Gluteoplasty or the surgical transposition of gluteal muscles, is one of the oldest surgical treatments for fecal incontinence. The gluteal muscles are well vascularized, supplied by the inferior gluteal artery. It is larger and stronger than the gracilis muscle and provides more bulk to help buttress the anal canal. It is activated during walking, which allows it to function as a significant adjunct to the external sphincter. Finally, mobilization of the gluteus muscle does not impair gait or pelvic stability[14]. A variety of techniques have been used, but the most studied method involves division of both gluteus muscles from the sacrum, splitting one muscle, subcutaneously tunneling, and wrapping one strip anterior and one strip posterior to the rectum. These muscle

strips are then sutured together and to the ipsilateral mobilized muscle[14].

Artificial Muscle Devices or implants can be used nowadays to treat fecal incontinence. They are described as devices that can “replace” the anal sphincter or that can strengthen it. There are many Available Artificial Sphincter Prostheses at the moment.

1. AMS 800™ from American Medical Systems- There is a fluid-filled cuff around the anal canal allows for continence. In order to release stool, one manually pumps the liquid from the cuff to the reservoir[15].

2. Acticon™ Neosphincter – it's a modified version of the first one. This device also contains a septum port to easily adjust the fluid quantity after implantation. The implantation includes three to four incisions to place the cuff around the anal canal, the reservoir to the abdomen and the 12 mm-wide and 36 mm-long pump into the scrotum or labium in a subcutaneous pouch[15].

3. A.M.I.® Soft Anal Band- it is a fluid-based system for continence treatments. Pressing the valve placed in a subcutaneous abdominal pouch opens the cuff. Its closing requires manual activation by squeezing the fluid reservoir. Therefore, the patient can manually control the cuff pressure. At rest, for example, a significantly reduced pressure improves tissue perfusion and regeneration. In addition, the pressure-regulation port allows the amount of fluid to regulate the maximum exerting pressure[15].

CONCLUSIONS

LARS is an increasingly common clinical entity in relation to the frequency of rectal cancer and the management of the sphincter preservation treatment.

Assessing the etiological and pathogenic complexity of LARS is the first step in improving the quality of life in patients that will undergo the rectal cancer therapeutic complex.

We believe that the correct surgical technique, that aims to preserve the function of the rectum and anal sphincter, remains the central benchmark in major LARS prevention.

Other methods and interventions can improve the quality of life to the extent that the

main intervention preserved as much as possible from the initial functional reserve.

REFERENCES

- [1]World Health Organisation Website
- [2]Y. Ziv , A. Zbar , Y. Bar-Shavit , I. Igov. Low anterior resection syndrome (LARS): cause and effect and reconstructive considerations. *Tech Coloproctol* (2013) 17:151–162
- [3]Jacopo Martellucci, Low anterior resection syndrome (LARS). [www. Up to date. com](http://www.Up to date. com)
- [4]Jacopo Martellucci. Low Anterior Resection Syndrome: A Treatment Algorithm. *DISEASES OF THE COLON & RECTUM VOLUME 59: 1* (2016)
- [5]timothy J R, Nicholas B, Kirk A L. Low Anterior Resection Syndrome: Current Management and Future Directions. *Clin Colon Rectal Surg.* 2016 Sep; 29(3): 239–245
- [6]Worley G, Chand M. The Functional Consequences of Rectal Cancer Surgery. *Worley and Chand, Intern Med* 2014, S1:007.
- [7]Katrine J E, Søren L. 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 Volume 255, Number 5, May 2012.*
- [8]Bregendahl S, Emmertsen KJ, Lous J, Laurberg S. Bowel dysfunction after low anterior resection with and without neoadjuvant therapy for rectal cancer: a population-based cross-sectional study. *Colorectal Disease 2013 The Association of Coloproctology of Great Britain and Ireland.* 15, 1130–1139
- [9]Tae Hee Lee, Adil E Bharucha. How to Perform and Interpret a High-resolution Anorectal Manometry Test. *J Neurogastroenterol Motil* 2016; 22(1): 46-59
- [10]Visser WS, Te Riele W, Boerma D: Pelvic Floor Rehabilitation to Improve Functional Outcome After a Low Anterior Resection: A Systematic Review. *ann coloproctol* 2014; 30(3): 109-14.
- [11]Lundby L, Duelund- Jakobsen J. Management of fecal incontinence after treatment for rectal cancer. *Current Opinion in Supportive and Palliative Care* 2011, 5:60–64
- [12]Scott A. B, David A. Margolin. Sacral Nerve Stimulation for the Treatment of Fecal Incontinence. *CLINICS IN COLON AND RECTAL SURGERY/VOLUME 18, NUMBER 1 2005*
- [13]Margolin DA. New Options for the Treatment of Fecal Incontinence. *Ochsner J.* 2008 Spring; 8(1): 18–24.
- [14]Keetley C. B. Appendicostomy. *Br Med J.* 1905. pp. 863–865
- [15]Elisa Fattorini, Tobia Brusa, Christian Gingert, Simone E. Hieber, Vanessa Leung, Bekim Osmani, Marco D. Dominietto, Philippe Büchler, Franc Hetzer, and Bert Müller. Artificial Muscle Devices: Innovations and Prospects for Fecal Incontinence Treatment. *Ann Biomed Eng.* 2016; 44: 1355–1369.
- [16]Heald RJ, Daniels I - Rectal cancer management: Europe is ahead, in Büchler MW, Heald RJ, Ulrich B, Weitz J- Rectal Cancer Treatment, Springer-Verlag, Berlin-Heidelberg, 2005 (Recent results in cancer research 2005), 165: 75-81
- [17]Heald RJ – The ‘Holy Plane’ of rectal surgery, *J R Soc Med* 1988, 81: 503-508
- [18]Ann Surg. 2012 May;255(5):922-8. doi: 10.1097/SLA.0b013e31824f1c21. Low anterior resection syndrome score: development and validation of a symptom-based scoring system for bowel dysfunction after low anterior resection for rectal cancer. Emmertsen KJ1, Laurberg S.