

Pathophysiological aspects of the low anterior resection syndrome for treatment of rectal cancer

Aspectos fisiopatológicos da síndrome pós-ressecção anterior do reto para o tratamento de câncer retal

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A B S T R A C T

The number of patients with bowel dysfunction due to the treatment of rectal cancer has increased during the recent decades. Anatomical and functional disorders after the removal of the rectum are followed by increased stool frequency, urgency, multiple evacuations and flatus or stool incontinence characterizing the low anterior resection syndrome - LARS. The purpose of this article is to present a review of the literature on current concepts and pathophysiological aspects of bowel dysfunction after resection of rectal cancer. It is essential to understand these mechanisms for a better management of patients and recovery of their quality of life.

Keywords: Rectal Neoplasms. Postoperative Complications. Fecal Incontinence. Quality of Life. Organ Dysfunction Scores.

INTRODUCTION

Colo-rectal cancer is the third most common tumor in men, with 746,000 new patients in 2012, and second among women, with 614,000 new cases. In Brazil, in 2014, there was 15,070 new cases in men and 17,530 in women. These values correspond to an estimated risk of 15,44 new cases for every 100,000 men and 17,24 for every 100,000 women¹.

Even with the development of less invasive surgical techniques, radical resection of rectum via abdomen is still the best treatment with curative intent for rectal cancer. Surgery for median and inferior thirds tumors follow the principles of mesorectal total excision (MTE), standardized by Heald^{2,3} in 1982. This technique reduced local recurrence (formerly 15% to 40%) to 6% to 10%⁴. Tumors of the superior third of the rectum may be treated by mesorectal partial excision (MPE), with the same good oncological results as MTE⁵. These surgeries are known as anterior resection of rectum (ARR).

In spite of surgical technical evolution and attention to preservation of pelvic nerves, many patients develop severe urinary, sexual and intestinal disturbances following ARR⁶⁻⁹. The group of functional alterations of intestine following ARR is known as

low anterior resection syndrome – LARS^{10,11}. LARS is characterized by a combination of symptoms, that include increase of stool movements, evacuation urgency, multiple evacuations and incontinence of flatus and stool, that may negatively impact on quality of life, in special social aspects of patients submitted to ARR¹¹⁻¹⁴. In a study about this condition, Juul *et al.*¹⁵ evaluated 796 patients submitted to surgical treatment of rectal cancer and showed that quality of life following surgery is closely related to the severity of LARS symptoms. Patients with severe LARS presented the worse results of a questionnaire of the *European Organization for Research and Treatment of Cancer*, that evaluates quality of life of patients with cancer (EORTC QLQ-C30).

LARS symptoms may be identified right after the surgical procedure or after restauration of intestinal movement, when it was used temporary stoma deviation (colostomy or protective ileostomy). There may be progressive lowering of intensity of symptoms after some months, that stabilize (plateau) after 12 to 24 months of post-operative. After this follow-up, some patients may present normal or almost normal intestinal function, but most of them (60-80%) still present symptoms, with prejudice to daily activities and psycho-social aspects¹².

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Until the present moment, there is no specific treatment for LARS. Therapeutic approach is empirical, consisting of treatment of symptoms, with therapy for stool incontinence and other evacuation dysfunctions. Treatment must involve a multidisciplinary team and address several aspects, including nutritional and psychological evaluation of all patients. Behavioral therapy, dietetic restriction and use of clothe protectors are frequent in those patients¹⁶.

We used the rectal tumor descriptors, post-operative complications, stool incontinence, quality of life and organic dysfunction scores to search databases MEDLINE, LILACS and ScieLO, to obtain literature data.

LARS PHYSIOPATHOLOGY

Although correct physiopathology of LARS is still not well established, most studies agree with the hypothesis of multifactorial origin and some important aspects must be observed, about how ARR influences intestinal function (Figure 1). Rectum functions as a transient reservoir of stool and gas, and, consequently, partial or total resection results in diminished capacity to retain gas and stool. The restoration of intestinal transit after ARR and MTE with direct terminal-terminal colon-rectal anastomosis or colon-anus anastomosis are options that result in a reduced rectal reservoir and presumably cause flatus and stool incontinence.

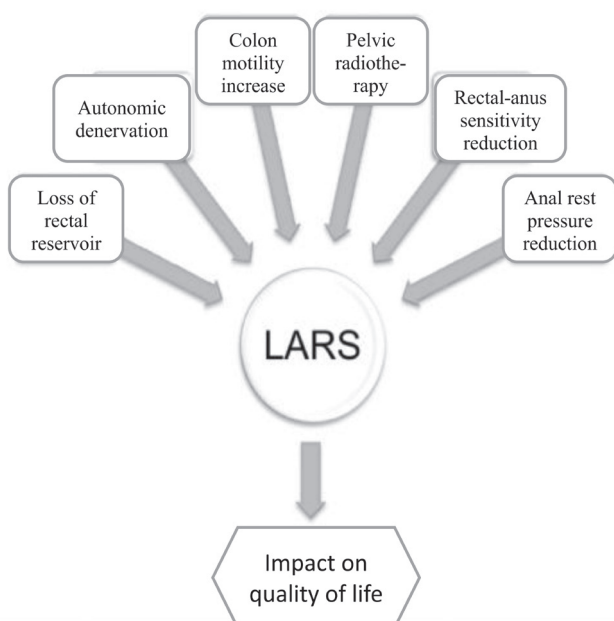


Figure 1. Physiopathology of LARS.

In spite of techniques to increase the volume of the “new rectum”, such as latero-terminal anastomosis and J pouch of distal colon, the functional advantages in relation to direct anastomosis are only transient in the first 24 months^{11,17,18}.

Some studies suggest that intestinal dysfunction would be more related to increased colonic motility than to the type of anastomosis. Lee *et al.*¹⁹, in a model animal, observed an increase of colonic motility of rats submitted to denervation of left colon, reinforcing that hypothesis. Most patients with LARS symptoms complain of increased gastro-colic reflex and increase of evacuation frequency. These alterations may result from autonomic denervation of distal colon and rectum, reducing inhibitory stimulation and increasing peristaltic movements of colon^{14,19}.

Patients submitted to pre-operative radio and chemotherapy, used routinely in more advanced rectal tumors and for those with suspicion of lymph node involvement at diagnosis, also present worse results related to frequency and intensity of LARS symptoms, when compared to patients treated only by surgery. The mechanism seems to be related to direct nerve lesion and pelvic fibrosis induced by pelvic irradiation. This treatment can also cause sexual and urinary dysfunctions due to nerve lesion^{20,21}.

Patients with LARS also present sensitivity diminishing of recto-anal transition, with prejudice to discriminate liquid and gas, affecting the recto-anal inhibitory reflex and the mechanisms of stool continence¹¹.

Change of rest anal pressure (internal anal sphincter – IAS) and maximum pressure of contraction (external anal sphincter – EAS) have been reported after ARR, causing soiling, and urgency and incontinence, respectively^{12,14}. Ho *et al.*²² demonstrated that alterations of IAS may be related to introduction of instruments via anus (staplers) and to denervation during dissection and pelvic irradiation. In that study, patients submitted to stapled anastomosis presented reduced anal rest pressure at anal-rectal manometry and higher incidence of fragmentation of internal anal sphincter at endo-anal ultrasonography after six months of surgery. Regarding EAS, it was not demonstrated until the present any structural

damage directly related to surgical technique, and its dysfunction probably is secondary to pudendal nerve lesion⁹.

EVALUATION OF INTESTINAL FUNCTION AT LARS

The clinical presentation of LARS symptoms, aside from being unspecific and observed in other defecation disturbances, are varied and difficult to be measured, since they are subjective and depend on the perception of patients. Several questionnaires (specific for intestinal function evaluation) are used to try to identify and measure how those functional alterations affect quality of life after ARR (9,23). As an example, the Wexner Fecal Incontinence Score (Wexner score, 1993)²⁴, The St. Mark's Incontinence Score (St. Mark's score, 1999)²⁵ and the Fecal Incontinence Severity Index (FISI, 1999)²⁶ evaluate stool incontinence without considering other frequent symptoms in LARS, such as urgency and re-evacuation. Other question forms, such as the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Colorectal Module (EORTC QLQ-CR29)²³ and the The Fecal Incontinence Quality of Life Scale (FIQL)²⁷ focus on quality of life and may complement questionnaires of evaluation of patients with LARS. The Memorial Sloan Kettering Cancer Center Bowel Function Instrument (MSKCC BFI, 2005)²⁸ was the first specifically proposed to evaluate intestinal function of patients submitted to sphincter preserving surgeries for the treatment of colon-rectal cancer. However, its use is restricted due to high number of items and lack of practicality.

In 2012, Emmertsen *et al.*²⁹ published the development and validation of the Low Anterior Resection Syndrome Score (LARS score). This is an objective and efficient tool for evaluation of intestinal function following ARR, easy to be used in clinical practice and with scores based on the impact of every LARS symptoms in quality of life of patients. The evaluated items of the LARS score include flatus incontinence, liquid stool incontinence, increase of evacuation frequency, multiple evacuations and evacuation urgency (Table 1). Score for each item is not linear and is based on the frequency and impact at quality of life, and may vary from 0 to 42 points. This is the first question form that evaluate intestinal function

in patients after ARR that considered the frequency of symptoms and the impact on quality of life³⁰⁻³².

DISCUSSION

While the number of patients that survived rectal cancer surgery with definitive stoma decreases, the number of patients submitted to sphincter preserving surgeries increase, with severe functional disturbances of intestine⁹. Colo-rectal anastomosis performed to avoid definitive colostomy is the preferred choice of most surgeons, but is not always the best option for the patient⁹. Some studies have shown that patients submitted to abdominal-perineal amputation and definitive colostomy have better quality of life than patients submitted to ARR, due to the symptoms caused by colon-anal anastomosis^{9,33}.

Although most studies of LARS focus on structural changes of rectum and anus, evidences point to the important role in this condition on colon motility alteration and inhibitory reflex and anal sensitivity disturbances that must be more studied in the future.

Mortality and local recurrence were the main areas of rectal cancer studies in the last decades, but, at the moment, the evaluation of functional results and quality of life of patients submitted to ARR is gaining importance due to the increase of patients that survived rectal cancer and that resumed their daily activities¹⁴.

Also, intestinal function evaluation by scores may contribute to the identification of therapeutic

Table 1. "LARS score" evaluated symptoms.

LARS score items	Punctuation
Flatus incontinence	0-7
Liquid stool incontinence	0-3
Evacuation frequency	0-5
Re-evacuation (fragmented evacuation)	0-11
Evacuation urgency	0-16
LARS score classification:	
0-20 no LARS	
21-29 light LARS	
30-42 intense LARS	

interventions that would have lower functional impact on the treatment of rectal cancer, and to objectively and practically evaluate the symptoms at follow-up³⁴⁻³⁶. The use of these question forms, such as the "LARS score", is being internationally discussed by translation, validation and cultural adaptation, to objectively evaluate organic functions such as the intestinal^{30, 37,38}. Standardization of evaluation of patients with LARS may also contribute to multicentric studies and meta-analysis of culturally different populations, and the proposal of algorithms for their treatment.

The high incidence of LARS symptoms, even in specialized centers of rectal cancer treatment, demonstrates that functional and structural alteration caused by rectum removal may be minimized, but not avoided. And, possibly, future studies must focus on the development of non-surgical techniques of minimally invasive surgeries for the treatment of rectal cancer. In the meantime, it must be adopted treatment to lower the symptoms as soon as they are diagnosed. The treatment at the present includes dietary adequacy, ingestion of fibers that contribute to the fecal bolus, use of drugs such as loperamide

in patients with diarrhea, anorectal biofeedback, trans-anal irrigation, neuro-sacral stimulation or even definitive stoma surgery in patients with severe symptoms and that considered that previous life was better than after reconstruction of intestinal transit.

The mechanism by which those functional intestinal alterations occur after rectal removal must be understood to minimize those effects on quality of life of patients.

CONCLUSIONS

Although many studies of LARS and its functional alterations of intestine exist, etiology and physiopathology are still not well explained. However, most evidences point out to the multifactor origin, influenced by physiological disturbances of intestinal motility and anal sensitivity, and to structural and anatomic modifications of pelvis after the surgical procedure. Intestinal function evaluation and early identification of patients with severe symptoms must be systematic at surgical follow-up, and the multidisciplinary treatment must be immediately proposed, to minimize impact on quality of life of patients.

R E S U M O

O número de pacientes com distúrbios funcionais intestinais em decorrência das operações para o tratamento do câncer retal tem aumentado durante as últimas décadas. Alterações anatômicas e funcionais após a retirada do reto provocam aumento da frequência evacuatória, urgência evacuatória, evacuações múltiplas e incontinência para fezes e flatos, caracterizando a síndrome da ressecção anterior baixa ou LARS - "low anterior resection syndrome". Este artigo apresenta uma revisão geral do tema, com ênfase para conceitos atuais e aspectos fisiopatológicos de distúrbios funcionais do intestino após o tratamento cirúrgico do câncer retal. É fundamental que o cirurgião compreenda esses mecanismos, para melhor abordagem dos pacientes e restabelecimento da sua qualidade de vida.

Descritores: Neoplasias Retais. Complicações Pós-Operatórias. Incontinência Fecal. Qualidade de Vida. Escores de Disfunção Orgânica.

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