RESIDENT'S CORNER

Low Anterior Resection Syndrome

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CASE SUMMARY

A 68-year-old woman presented to my clinic with a stage II rectal adenocarcinoma (tumor at 8 cm from the anal verge) and was interested in sphincter-preserving surgery. She underwent neoadjuvant chemoradiation and was planned to have a temporary diverting ileostomy. Using the Preoperative Low Anterior Resection Syndrome score (POLARS), she received 25 points and was predicted to develop minor low anterior resection syndrome (LARS) postoperatively. She still desired to have sphincter-preserving surgery, and her operation was performed without any complications. She then received adjuvant chemotherapy, and her ileostomy was reversed 6 months later. She now presents for follow-up 1 month after ileostomy reversal with complaints of being unable to control her flatus on an almost daily basis and having liquid stool leakage at least once a week. On further questioning, she states that she has 8 bowel movements per day, but they are not clustered. She endorses a need to rush to the toilet to avoid an accident a couple of times per month. From the patient's reported symptoms, her surgeon calculates that her LARS score is 25, equating to minor LARS. She is started on loperamide and returns 1 month later with an improvement in her symptoms.

CLINICAL QUESTIONS

- How can the postoperative probability of LARS be estimated using known preoperative and intraoperative risk factors?
- How can LARS be diagnosed and graded in the postoperative setting consistently across clinicians and hospitals/clinics?
- What are the treatment options available for minor and major LARS?

BACKGROUND

An estimated 43,030 patients were diagnosed with rectal cancer in the United States in 2018,[1] and many of these patients will undergo low anterior resection. After surgery, >70% of patients are affected by a collection of symptoms of neorectal dysfunction that have been noted since at least 1988.[2,3] This collection of symptoms is now collectively defined as LARS,[3] and it has a significant negative impact on these patients' quality of life, with more severe LARS having an increasingly detrimental impact.[4]

PRESENTATION AND DIAGNOSIS

LARS can manifest with a wide variety of symptoms of bowel dysfunction, and this is reflected in the difficulty of precisely defining LARS in the literature. Bryant et al provide the most widely accepted definition of LARS defining it as, "disordered bowel function after rectal resection, leading to a detriment in quality of life.[3]" The most common symptoms reported are incontinence to fecal matter and/or gas, increased frequency of bowel movements, and clustering of bowel movements.[5] These symptoms typically develop soon after restoration of intestinal continuity, and, although they may improve initially, bowel dysfunction has been shown to continue to be present >5 years after surgery.[2,6]

The recently developed POLARS score nomogram[7] can be used for preoperative counseling of patients about their expected postoperative bowel function. Because it consists of only 6 variables (age, sex, neoadjuvant radiotherapy, tumor height, total mesorectal or partial mesorectal excision, and use of a stoma or not), it is an efficient tool for counseling patients on long-term outcomes after low anterior resection. Of the 6 components, tumor height and neoadjuvant radiotherapy are the 2 individual factors that contribute the greatest to a higher expected LARS score.[7] The POLARS score may

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also aid in the diagnosis of LARS by providing a baseline rate of expected bowel function after low anterior resection. If a patient is at low risk of LARS (eg, a high tumor, no preoperative radiation) based on the POLARS score, alternative explanations of bowel dysfunction after rectal cancer surgery may be more likely, whereas patients with multiple risk factors for LARS and typical symptoms likely do indeed have LARS.

Once the clinician believes the diagnosis of LARS is correct, numerous questionnaires exist to assess the patient's bowel function. Two questionnaires specifically designed to assess bowel dysfunction after low anterior resection are the Memorial Sloan Kettering Cancer Center Bowel Function Instrument (MSKCC BFI)[5] and the LARS score.[4] Both the MSKCC BFI and the LARS score have been validated in multiple languages and have been demonstrated to correlate with various quality-of-life surveys.[8] The MSKCC BFI is longer and provides a more comprehensive assessment of LARS symptoms and their impact on a patient's daily life. The LARS score is shorter and allows rapid stratification of patients into a no LARS, minor LARS, or major LARS group. Depending on the intent of the user, one questionnaire may be more appropriate than the other is, although they can also be used in combination. One advantage of the LARS score is that there is the accompanying POLARS nomogram to predict a patient's postoperative LARS score and the corresponding LARS group (none, minor, or major). The POLARS nomogram consists of only 6 variables (age, sex, neoadjuvant radiotherapy, tumor height, total mesorectal or partial mesorectal excision, and use of a stoma or not), enabling it to be used efficiently in the clinic for patient counseling on long-term outcomes after low anterior resection. Tumor height and neoadjuvant radiotherapy are the 2 individual factors that contribute the greatest to a higher expected LARS score.[7]

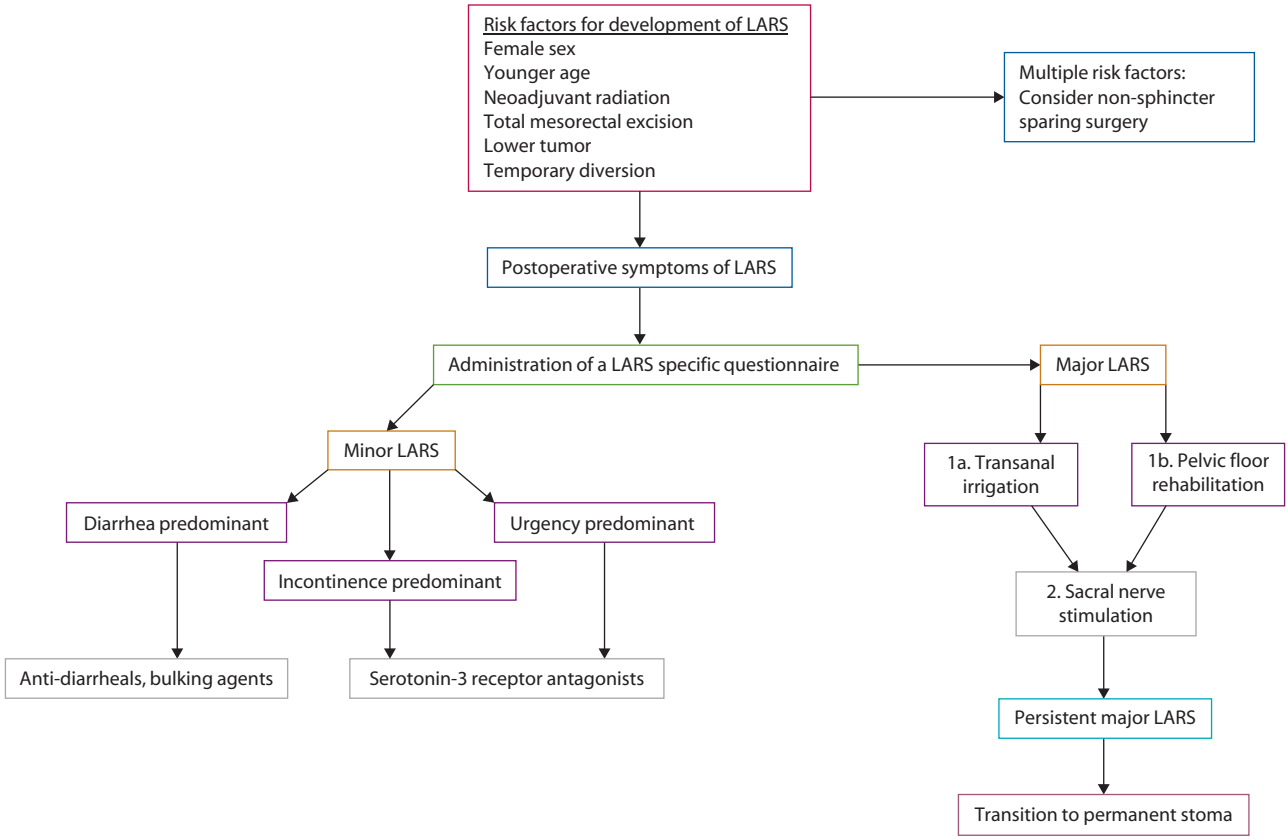
MANAGEMENT

Treatment of LARS depends on severity of symptoms and whether it is classified as minor or major. Minor LARS can largely be treated medically, and the treatment principles are based on the predominant symptom (diarrhea, incontinence, or urgency) of an individual patient's LARS. For diarrhea-predominant LARS, loperamide or bulking agents such as psyllium are typically used given the former's efficacy in treating diarrhea-predominant irritable bowel syndrome. It is important to note that neither of these therapies has been evaluated in the treatment of LARS specifically. In contrast, serotonin-3 receptor antagonists (eg, ramosetron) have been studied for urgency and diarrhea-predominant LARS, with patients reporting improved symptom control. Importantly, patients treated within 6 months of low anterior resection reported less urgency after treatment than those treated >6 months after surgery.[9]

Treatment options for major LARS have been studied more thoroughly than the pharmacologic therapies of minor LARS have. First-line treatment typically consists of transanal irrigation,[10] which can be accompanied or followed by pelvic floor rehabilitation.[11] Transanal irrigation can begin once major LARS is diagnosed. Irrigation volume can range from 250 mL to 1 L of tepid tap water and should be performed every 24 to 48 hours. Patients should work with their surgeon and the stoma nurses to develop a regimen that is optimal for their level of bowel dysfunction. Both have been demonstrated to improve quality of life in patients experiencing LARS, but length of treatment and follow-up time has varied widely. Therefore, it is difficult to definitively conclude how long transanal irrigation should be trialed before re-evaluation, but 1 year has been suggested previously.[6] If, when the LARS score is reassessed, the patient has minor LARS, any remaining symptoms can be treated medically as described above. If the patient is still experiencing major LARS after transanal irrigation therapy and pelvic floor rehabilitation, neurostimulation should be considered. The use of sacral nerve stimulation has shown promising results for patients with major LARS who are refractory to other treatments. A systematic review from 2015 identified 43 patients treated with sacral nerve stimulation in a progressive fashion from either an acute testing phase or peripheral nerve evaluation to eventual permanent implantation. Different studies have reported varying thresholds to advance to permanent placement, ranging from a subjective improvement in symptoms to an improvement in symptoms of >50% to 70%. Of patients who proceeded to permanent implantation, the success rate was 94%, and the overall intention-to-treat success rate was 74%. Despite the success of sacral nerve stimulation, the authors expressed the need for caution in interpreting the results, and they stressed that sacral nerve stimulation should be reserved for patients who failed the other more conservative therapies discussed above.[12] The role of percutaneous tibial nerve stimulation as an alternative to sacral nerve stimulation is yet to be determined. Lastly, what remains unknown and needs to be evaluated is how quality of life is changed in patients who choose to undergo permanent stoma creation because of refractory LARS.

Common to all of the discussed treatment methods are a small number of patients included in the published studies and, most importantly, the lack of a uniform scoring system to grade the degree of LARS and its improvement with treatment. Now that the LARS score has been validated in multiple languages and is being used with increased frequency, future studies may be more amendable for meta-analysis, because long-term outcomes would be consistently measured on a common scale. With improved survival after surgery for rectal cancer, there will be an increasing population of patients who experience LARS, and treatment algorithms will need to be better defined. In addition, with increasing use of local excision for rectal cancer, the incidence and severity of LARS in these patients need to be defined. In the interim, stepwise treatment from the least invasive intervention to more invasive therapies should be advocated, and treatment choice should be dictated by the predominant symptom of LARS present. See

EVALUATION AND TREATMENT ALGORITHM



evaluation and treatment algorithm for risk factors for the development of low anterior resection syndrome (LARS) and treatment options depending on the severity. See e-valuation and treatment algorithm for risk factors for the development of low anterior resection syndrome (LARS) and treatment options depending on the severity.

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