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Translation of the article

# Rehabilitation of patients with low anterior resection syndrome

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**ABSTRACT** *AIM: to develop a conservative rehabilitation program for patients with severe symptoms of LARS.*
*PATIENTS AND METHODS: since January 2019, 50 patients after low anterior resection were included in the study. The main group included 25 patients who underwent biofeedback therapy and tibial neuromodulation in 3–6 months after surgery. Functional results before and after treatment were evaluated by anorectal manometry. The control group included 25 patients, according to the Propensity score matching.*
*RESULTS: the median score on the LARS scale, in the main group was 41.0 ± 2.8 points, in the control — 38 ± 4. With sphincterometry, the median pressure at rest before treatment was 30.0 ± 7.8, with a voluntary contraction of 140.6 ± 56.0 mm Hg. After the conservative treatment, patients in the main group had significantly better results: the median score on the LARS scale decreased from 41 ± 2.8 to 17 ± 8 points ($p < 0.0001$), the median pressure after treatment increased from 30.0 ± 7.8 to 36.0 ± 8.0 ($p = 0.004$), with a voluntary contraction from 140.6 ± 56.0 to 157.5 ± 53.2 mmHg ($p = 0.008$). Comparing the results of the questionnaire of the main group with the control group after the stoma closure and after 12 months, it turned out that in the main group there was a significant decrease in the severity of LARS: 17.0 ± 8.0 scores vs. 35.0 ± 4.5 ($p = 0.0003$), which shows an improvement in the tone and contractility of the sphincter after conservative treatment.*
*CONCLUSION: comprehensive biofeedback therapy and tibial neuromodulation improves the functional results of patients with severe LARS.*

**KEYWORDS:** *rectal cancer, low anterior resection syndrome, LARS, incontinence, BOS therapy, tibial neuromodulation*

**CONFLICT OF INTEREST:** *The authors declare no conflict of interest.*

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## INTRODUCTION

Low anterior resection syndrome (LARS) occurs in 25–90% of the patients who have undergone surgery, including transanal mesorectumectomy (TME) for rectal cancer [1].

LARS is a disease characterized by frequent stools (up to 65 times a day or more), prolonged and incomplete bowel emptying, sudden urge to defecation and incontinence, resulting from a violation of the reservoir and evacuation function after removal of most of the rectum [2].

The severity of symptoms directly depends on the severity of the LARS. This problem leads to a decrease in the quality of life and hinders the social adaptation of patients [3]. The search for new options to reduce the severity of LARS is one of the most pressing problems of colorectal surgery at the moment all over the world.

According to the published data, a lot of conservative options for LARS have been proposed,

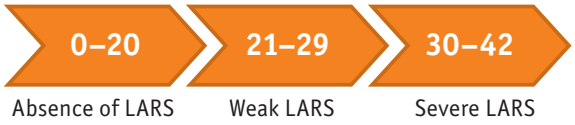


**Figure 1.** *Severity LARS*

such as the use of various pharmacological agents (probiotics VSL#3, serotonin 5-HT3 receptor antagonists) and physiotherapeutic methods (sacral and tibial neuromodulation, biofeedback therapy). Sacral and tibial neuromodulation, as well as biofeedback therapy have shown the greatest effectiveness in reducing the severity of LARS [4–6]. However, recently, there is no clear position in the treatment of patients with LARS. The aim of the study was to workout a treatment program for LARS.

## PATIENTS AND METHODS

Fifty patients who underwent low anterior resection since January 2019, have been included in the study. It was prospective, comparative, and single-center. The protocol of the study was reviewed and approved at the meeting of the local ethics committee on 23.10.2018.

All the patients were surveyed 3–6 months after the closure of the preventive stoma using the international LARS Score, which was also translated and validated in Russia [7,8]. The scale is a questionnaire consisting of 5 questions: episodes of anal incontinence, frequency of stool, the need for repeated defecation within an hour after stool. The answer to each question is assessed from 0 to 16; the sum of the points allows to assign the patient to one of the three degrees (Fig. 1). The absence of LARS — 0–20 points, weak LARS — 21–29 points, severe LARS — 30–42 points [8].

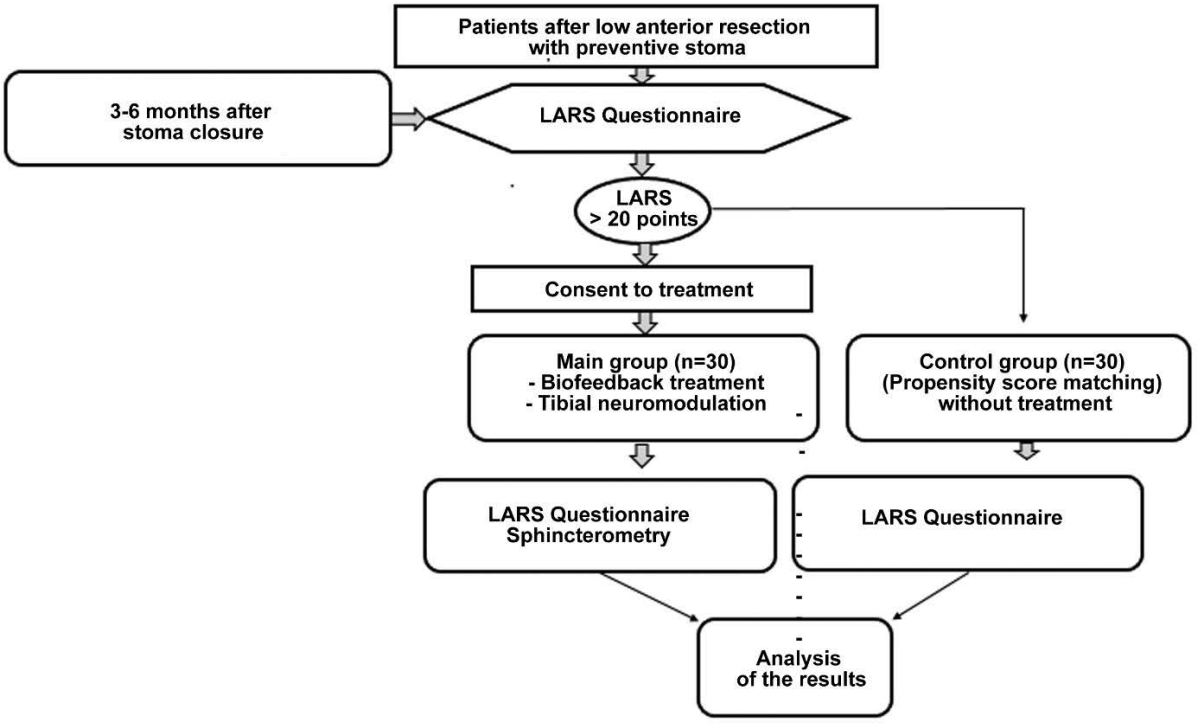


**Figure 2.** *Study design*

**Table 1.** *Characteristics of patients with LARS*

| Indicators | Main group, *n* = 25 | Control group, *n* = 25 | *p* |
|---|---|---|---|
| Gender<br>Male<br>Female | <br>15 (60.0%)<br>10 (40.0%) | <br>10 (40.0%)<br>15 (60.0%) | 0.1 |
| Age (M ± SD), years | 60 ± 14 | 64 ± 10 | 0.4 |
| Body mass index (M ± SD), kg / m$^2$ | 25 ± 3 | 25 ± 5 | 0.1 |
| Neo adjuvant chemoradiotherapy | 6 (24.0%) | 5 (20.0%) | 0.7 |
| Surgery:<br>Low anterior resection | <br>25 (100.0%) | <br>25 (100.0%) | <br>1 |
| Splenic flexure mobilization | 10 (40.0%) | 8 (32.0%) | 0.5 |
| Distance of the tumor from the anal verge Me (quartile), cm | 6 (5; 9) | 9.4 (9; 9.7) | 0.3 |
| Cancer stage:<br>I<br>II<br>III<br>IV | <br>10 (40.0%)<br>8 (32.0%)<br>5 (20.0%)<br>2 (8.0%) | <br>8 (32.0%)<br>5 (20.0%)<br>11 (44.0%)<br>1 (4.0%) | 0.9 |
| Adjuvant hemoradiotherapy | 13 (52.0%) | 15 (60.0%) | 0.5 |
| Anastomosis type:<br>“End to end”<br>“Side to end” | <br>24 (96.0%)<br>1 (4.0%) | <br>22 (88.0%)<br>3 (12.0%) | 0.1 |
| Anastomotic leakage | 3 (12.0%) | – | 0.07 |
| Preventive stoma | 25 (100.0%) | 25 (100.0%) | 1 |
| Median time of stoma closure<br>Me (quartiles), months | 8 (7.04; 8.9) | 8.4 (7.4; 9.3) | 0.4 |

The main group included 25 patients who underwent biofeedback and tibial neuromodulation after a questionnaire survey and determination of the LARS severity (Figure 2). The control group included 25 patients without treatment, using the “pseudo randomization” method (Propensity score matching).

The second survey was done in the main group after the treatment, and in the control group a year after the ileostomy closure by telephone call. In the main group, the functional

**Table 2.** *Sphincterometry results in patients of the main group*

| Anorectal manometry: | Before treatment | After treatment | *p* |
|---|---|---|---|
| Mean resting pressure in the anal canal mmHg (M ± SD) | 30.0 ± 7.8 | 36.0 ± 8.0 | 0.004 |
| Maximum pressure during voluntary contraction in the anal canal mmHg (M ± SD) | 140.6 ± 56.0 | 157.5 ± 53.2 | 0.008 |

**Table 3.** *The degree of LARS in patients of the main and control groups*

| Indicators | Main group | Control group | *p* |
|---|---|---|---|
| The mean point on the LARS scale before treatment (M ± SD) | 41.0 ± 2.8 | 38.0 ± 4.0 | 0.1 |
| The mean point on the LARS scale after treatment (M ± SD) | 17.0 ± 8 | 35.0 ± 4.5 | 0.0003 |

parameters of the anal sphincter were assessed by anorectal manometry before and after treatment (sphincterometry and the rectal compliance test).

**Treatment Program**

The patients of the main group got a ten-day conservative rehabilitation by the method of complex biofeedback therapy and tibial neuromodulation (TNM).The complex biofeedback therapy was performed with the Urostim device (Canada), including the program to improve the function of retaining intestinal contents under the control of two-channel recording — manometric and electromyographic (EMG) to train the correct doing the sphincter muscle contraction exercises, without involving the muscle structures of the anterior abdominal wall; the program to improve the reservoir function and increase the threshold of sensitivity of the bowel to filling.

Tibial neuromodulation was performed with a Bio-Bravo device (Germany) by electric stimulation of the tibial nerve of both lower limbs in order to cause neuromodulating impact on the pudental nerve (and through it on the pelvic floor muscles and external anal sphincter) through signal transmission with *n.tibialis* during antidromic pulse propagation. The impact occurs with a pulsed electric current of 20–25 mA with a frequency of 20 Hz in an intermittent mode (the stimulation period is 5 sec.; the rest period is 10 sec.). The course consisted of 10 sessions, with the duration of 20 minutes each [15,16].

Subsequently, to assess the treatment effectiveness, a repeated questionnaire survey and a study of the anal sphincter function with anorectal manometry were performed. Complex sphincterometry was performed using a nonperfusion water filling sensor and skin electrodes with a WPMS Solar device (the Netherlands). Parallel recording of the signal amplitude of bioelectric activity and values of intra-channel pressure at rest, with voluntary contraction of the sphincter, coughing, and tension of the muscles of the anterior abdominal wall was performed.

The reservoir rectal function was studied using a pressure probe with the MMS Solar GI device (the Netherlands), with a gradual filling of the latex rectal balloon with air in increments of 20 ml and an interval of 20 seconds, the gauge pressure curve was recorded. When filling the balloon, the following indicators were reflected: the first

threshold of sensitivity, the threshold of constant sensitivity, the feeling of the first urge to defecate and the threshold of the constant urge to defecate.

**Statistical Analysis**

The statistical analysis was performed using the Statistica 13 program (TIBCO, the USA). The data with continuous and parametric values were described by the mean and standard deviation.

Values with a nonparametric distribution were described by the median and quartiles.

Cross-group comparisons of continuous values were performed using the t-test; the binary and parametric values — by using the Fisher exact test. The differences in the continuous values before and after the rehabilitation program were revealed using the paired t-test. When compared, the differences were considered significant at $p < 0.05$.

## RESULTS

According to the protocol, since January 2019, fifty patients who underwent low anterior rectal resection for cancer have been included in the study. The presence of low anterior resection syndrome was confirmed on the basis of the LARS questionnaire 3 months after the preventive stoma closure.

When comparing the groups as per gender, age, body mass index, treatment, as well as the time of stoma closure, no significant differences were revealed between the groups (Table 1).

The main group included 15 (60.0%) men and 10 (40.0%) women, the control group included 10 (40.0%) men and 15 (60.0%) women ($p = 0.1$). The average age was 60 ± 14 years in the main group, 64 ± 10 years in the control group ($p = 0.4$). The body mass index was 25 ± 3 kg/m$^2$ in the main group and 25 ± 5 kg/m$^2$ in the control group ($p = 0.1$). The neoadjuvant chemoradiotherapy was used in 6 (24.0%) patients of the main group and 5 (20.0%) patients of the control group ($p = 0.7$). All the patients underwent low anterior resection with a preventive stoma for cancer.

The splenic flexure mobilization was performed in 10 (40.0%) patients in the main group and in 8 (32.0%) in the control group ($p = 0.5$). The adjuvant chemotherapy was performed in 13 (52.0%) patients of the main group and 15 (60.0%) of the control group ($p = 0.5$). The median (Me, quartiles) of preventive stoma closure periods in the groups was 8 (7.04; 8.9) and 8.4 (7.4; 9.3) months ($p = 0.5$).

It should be noted that 3/25 (12%) patients of the main group had anastomotic leakage (grade B). The control group showed no signs of anastomotic leakage.

The survey of the patients before treatment showed that the mean score (M ± SD) in the patients of the main group was 41.0 ± 2.8 on the LARS scale, and in the control group — 38.0 ± 4.0 ($p = 0.1$). In the main group, according to sphincterometry, the mean resting pressure before treatment was 30.0 ± 7.8, with a voluntary contraction of 140.6 ± 56.0 mm Hg (Table 2).

After a conservative physiotherapy in the main group, a questionnaire survey and sphincterometry were repeated. It turned out that subjective indicators improved: the mean score on the LARS scale decreased from 41.0 ± 2.8 to 17.0 ± 8.0 points ($p = 0.000001$), and the mean pressure after treatment increased from 30.0 ± 7.8 to 36.0 ± 8.0 ($p = 0.004$), with a voluntary contraction from 140.6 ± 56.0 to 157.5 ± 53.2 mm Hg ($p = 0.008$).

Comparing the results of the survey of the patients in the main group with the controls after the closure of the stoma and after 12 months, it turned out that in the main group there was a significant decrease in the LARS severity: 17.0 ± 8.0 points versus 35.0 ± 4.5 ($p = 0.0003$), which indicates an improvement in the tone and contractility of the anal sphincter against the background of conservative treatment (Table 3).

## DISCUSSION

Low anterior resection syndrome is a socially significant problem that leads to disability and decrease of the quality of life

[3,14]. In addition, the treatment of LARS is a rather complex problem due to the lack of a standardized algorithm for conservative treatment.

So, one of the options for LARS is the method of biofeedback therapy. For the first time it was tested in 1974 by Engel B. [11]. It is a non-drug treatment option aimed at activating internal reserves, during which the patient receives information about the state of various physiological processes and learns to regulate them. This method has proven itself in the treatment of LARS.

Kim K.H. et al. showed a significant decrease in the LARS symptoms after treatment, but the study was retrospective and included 70 patients with severe LARS symptoms who underwent the biofeedback therapy. The results were assessed using the Wexner's scale after 10 weeks. At the same time, against the background of conservative treatment, the indicators improved from 13.0 to 8.4 points, and there was an improvement in the anal continence, a decrease in the frequency of stools and discontinuation of antidiarrheal drugs use ($p < 0.001$) [12]. However, it is worth emphasizing that the use of the Wexner's Score questionnaire does not cover all the LARS symptoms. In addition, this scale is not validated for this disease.

Another treatment option for LARS is tibial neuromodulation. This is one of the most accessible and effective options. Its main advantage over sacral neuromodulation is a simpler and non-invasive method of treatment. Thus, when the posterior tibial nerve is irritated, the anus is stimulated through the L4-S3 [13, 14]. Altomare D.F. et al. assessed the effectiveness of tibial neuromodulation in LARS. The study included 21 patients with a low anterior resection syndrome, who underwent 12 sessions of tibial neuromodulation. The results were assessed using the LARS scale. There was an improvement in the indicators from 32 to 27 points ($p = 0.009$) [14]. The presented circumstances illustrate that the use of any of the treatment methods may lead to a positive trend, i.e. a decrease in the LARS severity.

At the same time, the search for alternative options is aimed at improving the results of rehabilitation.

In another similar work, presented by Vigorita et al. [14], the effectiveness of the tibial nerve stimulation in the LARS treatment was assessed. The study included 10 patients with severe LARS symptoms, who underwent the test tibial stimulation. Three patients were excluded due to poor functional response at the first stage. Seven patients underwent the second stage of stimulation for 6 weeks. The results were assessed 3 weeks after the end of the stimulation using the Wexner scale, the indicators improved from 14 to 10 points ($p = 0.034$) [13].

The presented studies are few and reflect the use of only one of the existing treatment options or the comparison of several methods in the treatment of LARS. However, it is not always correct to use scales to assess only the function of the sphincter in these patients.

In this regard, this study is interesting, as we have developed a treatment program that includes complex biofeedback and tibial neuromodulation. It turned out that after the treatment, there was a improvement in the contractility of the sphincter, as evidenced by the sphincterometry before and after the treatment: 30.0 ± 7.8 and 36.0 ± 8.0 mm Hg (at rest, $p = 0.004$), 140.6 ± 56.0 and 157.5 ± 53.2 mm Hg (with voluntary contraction, $p = 0.008$), respectively.

The LARS scale after the treatment decreased from 41.0 ± 2.8 to 17.0 ± 8.0 points, showing a significant difference in the effectiveness of the treatment ($p < 0.0001$). When compared with the control group, where conservative treatment was not performed, the patients showed significantly better functional results. In the control group the average point on the LARS scale decreased over time — after a year by only 3 points from 38.0 ± 4.0 to 35.0 ± 4.5.

Thus, the use of a comprehensive conservative approach, including biofeedback therapy and tibial neuromodulation in patients with severe LARS, significantly improves the functional parameters of the anal sphincter, and

there is also a decrease in the severity of LARS, which leads to an improvement in the quality of life and better social adaptation of patients.

**AUTHORS CONTRIBUTION**

*Concept and design of the study: Islam O. Nafedzov, Stanislav V. Chernyshov, Mikhail V. Alekseev, Oksana Yu. Fomenko,*
*Collection and processing of the material: Islam O. Nafedzov, Svetlana V. Belousova*
*Statistical processing: Islam O. Nafedzov, Alexey A. Ponomarenko*
*Writing of the text: Islam O. Nafedzov, StanislavzV. Chernyshov, Evgeniy A. Khomyakov*
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