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PROCEEDINGS

RISK FACTORS FOR THE DEVELOPMENT OF LARS IN ANTERIOR RECTAL RESECTION FOR RECTAL CARCINOMA AND THE QUALITY OF LIFE OF PATIENTS WITH DEVELOPED LARS

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ABSTRACT

INTRODUCTION: Laparoscopic surgery has been established as a treatment method for patients with colorectal carcinoma. Thanks to the minimally invasive approach, patients with rectal carcinoma receive all the advantages of laparoscopic surgery without violating oncological principles.

Low anterior resection syndrome (LARS) is a symptom complex seen in patients operated on for rectal carcinoma. It includes the following symptoms: fecal incontinence, increased frequency of bowel movements or urgency of defecation, tenesmus. These symptoms can have a significant negative impact on the patient's quality of life.

AIM: The purpose of this study is to determine the risk factors for the development of LARS and the degree of manifestation of this syndrome in different groups of patients.

MATERIALS AND METHODS: As inclusion criteria in the present study, we defined patients with histologically verified adenocarcinoma of the rectum. A retrospective analysis was made of 44 patients for the period of 2019–2023 operated on in the Prof. Alexander Stanishev Clinic of Surgery. In all patients, individual characteristics were considered: gender, age, accompanying diseases, performed non-adjuvant treatment, distant carcinoma from LAR, stage of the disease, and type of anastomosis performed. Exclusion criteria of the study were: unresectable carcinoma, patients operated conventionally, laparoscopy with conversion to laparotomy, amputation a.m. Miles.

RESULTS: From the conducted research regarding risk factors, the following were related: gender (women have a higher risk of developing major LARS); age (between 50–69 years with a higher risk of developing LARS); the distance of the carcinoma from the LAR (at 0–6 cm from the LAR—a higher risk for the development of major LARS); radiotherapy (higher risk of developing major LARS); concomitant diseases (in all patients with diabetes—manifestation of major LARS); the advanced stage of the disease (at T3 ≥ according to TNM—the risk of developing LARS is higher).

CONCLUSION: According to our study, risk factors for the development of LARS are: female gender, low location of the rectal carcinoma, conducted radiotherapy, diabetes mellitus, and advanced stage of the disease.

Keywords: *rectal carcinoma, laparoscopic surgery, LARS*

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INTRODUCTION

Colorectal carcinoma (CRC) remains third most common cancer type (1) and the second leading cause of cancer-related deaths in both men and women combined according to the latest data from the World Health Organization (WHO). In fact, Asia contributes up to 49% of the total number of new cancer cases in the world, nearly half of which are found in China (2).

In Bulgaria, according to the latest statistics, CRC is the fifth most diagnosed cancer for both men and women and the sixth most common cause of cancer death (2). Therefore, surgery remains the main treatment for this disease. The main purpose of the surgery is to remove the tumor tissue by achieving negative surgical margins. The frequency of negative surgical margins ranges from 37% to 63% according to the location of the CRC.

Laparoscopic surgery (LS) is now being used for more cases requiring surgery than ever before, and it is extremely popular due to the advantages that offers over conventional open surgery (3). It has become widely used in treating colorectal cancer due to several advantages: less intraoperative bleeding/blood loss; less pain; less postoperative bleeding; faster recovery; fewer risk of complications, and, finally, a better cosmetic result (4,5,6,7).

As a result of all neoadjuvant therapies, operative and adjuvant treatments, we aim to achieve a high five-year survival rate as well as improve or maintain the quality of life among cancer patients (8).

There is no doubt that radical colorectal surgery improves the oncologial outcomes. However, the literature clearly documented that the social, physical, sexual, and psychological aspects of life are severely disturbed after a surgical treatment for CRC (9).

A significant portion of patients suffer from alterations in their quality of life (QoL), particularly after surgery on distal rectal tumors (10). Patients who require a stoma or who have low anterior resection syndrome (LARS) may face difficulty adapting to their new anatomy, managing the stoma, defecating, and continuing normal activities in their sociocultural environment. Patients pay an immense price following both sphincter-saving and sphincter-sacrificing surgery.

Low anterior resection syndrome is a symptom complex seen in patients operated on for rectal carcinoma. It includes the following symptoms: fecal incontinence, increased frequency of bowel movements or urgency of defecation, and tenesmus. These symptoms can have a significant negative impact on the patient's QoL.

The pathophysiological pathways leading to the manifestation of LARS are not yet fully understood and remain partially unclear (10,11,12,13). Due to the variety of symptoms associated with this condition, various etiological factors may be responsible for its development.

In this study, we examined several risk factors and their importance as prognostic markers for the development of LARS (Table 1).

Table 1. Risk factors for LARS.

Tumor distance from the anal verge (*low, mid, or high)*
Neoadjuvant therapy
Type of the anastomosis
Personal factors gender, age, comorbidity
TNM stage

AIM

The purpose of this study is to determine the risk factors for the development of LARS and the degree of manifestation of this syndrome in different groups of patients.

MATERIALS AND METHODS

The study included a cohort group of 44 patients with histologically verified adenocarcinoma of the rectum. Of these, 28 (63.6%) were male and 16 (36.7%) were female. The average age of all patients studied was 63 years, with the youngest patient being 33 years old and the oldest—84 years old. A retrospective analysis was performed.

All were hospitalized in the Department of Surgery at the Alexandrovska University Hospital in Sofia for the period between January 2019 and March 2023.

We excluded patients with unresectable cancer; conversion of laparoscopic to open surgery; abdominoperineal resection for rectal cancer and the need

for permanent stoma after low anterior resection of the rectum.

A scoring system for bowel dysfunction after low anterior resection (LAR) for rectal cancer based on symptoms and impact on quality of life has been developed and validated (14,15,16). Individual grade values are indicated by a LARS grade, which is divided into *No LARS*, *Minor LARS*, and *Major LARS*. Validity was tested by receiver operating characteristic curve (ROC curve) and Spearman's rank correlation, and discriminant validity was tested by Student's t-test.

The most important elements included in the score system are: 1) incontinence for flatus; 2) incontinence for liquid stool; 3) frequency; 4) clustering; and 5) urgency. The information obtained from the patients was through a questionnaire, with the questionnaire being sent to 124 patients and a response was received from 44.

The range (0–42 points) is divided into three groups: from 0 pts up to 20 pts (No LARS), from 21 pts to 29 pts (Minor LARS), and from 30 pts up to 42 pts (Major LARS). Results conducted in other clinics show good correlation and high sensitivity and specificity for Major LARS (17).

RESULTS

The average age of all patients with Major LARS was 62.6. We would like to note that when the score increased for the Major LARS, the average age decreased, which is in line with the results reported by other authors, with no convincing data showing a correlation between the age and the development of LARS (15, 16) (Fig. 1).

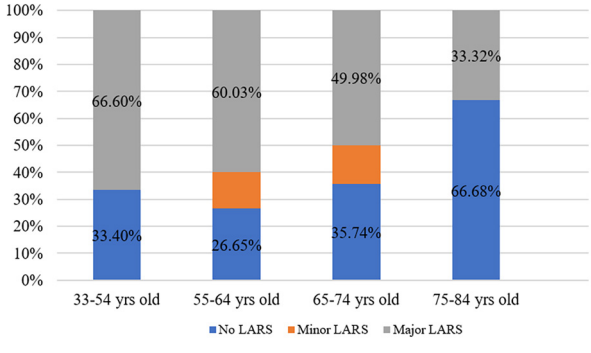

Fig. 1. Distribution of developed LARS by age.

As a result of our study, we could also draw the following conclusion—female patients are predisposed to the development of LARS with higher score compared to patients of the opposite sex.

Of the patients involved in the study, 63.6% were male and 36.4% were female (Fig. 2). By analyzing the degree of development of LARS, a higher rate of Major LARS was observed in women—62.5%, compared to 49.98% in men. It is interesting to note that in women there was either a total number of points corresponding to No LARS or a severely developed Major LARS (Fig. 3 and Fig. 4).

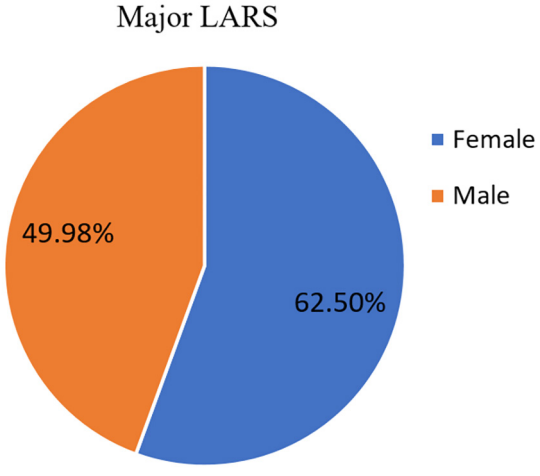

Fig. 2. Distribution for Major LARS.

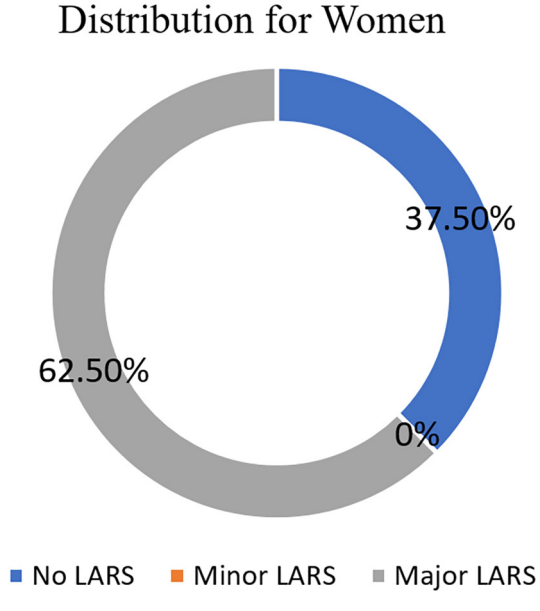

Fig. 3. Distribution for women with LARS.

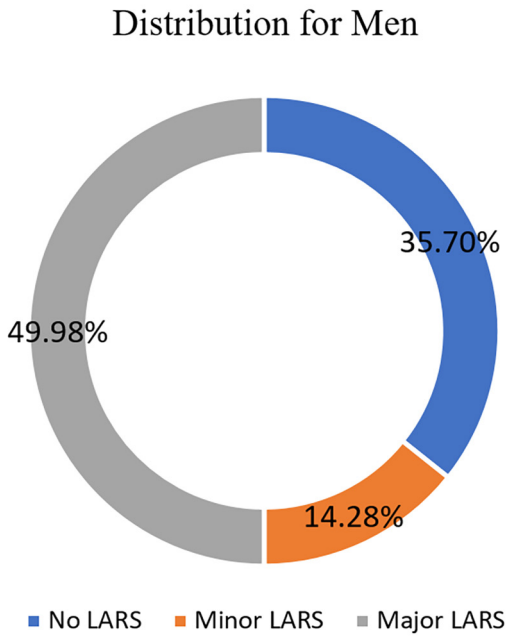

Fig. 4. Distribution for men with LARS.

The patients were divided into three groups according to the location of the tumor from the anal verge: those with a tumor between 0 and 6 cm (low rectum); between 7 and 11 cm (mid rectum) and between 12 and 15 cm (high rectum).

The first group included 20 patients out of a total of 44 who had a tumor located from 0 cm to 6 cm from the anal verge. Fifteen of these 20 patients had a severe form of developed LARS (Major LARS); 2 had Minor LARS, and 3 had unmanifested LARS, making the impression that of those patients with less developed or No LARS, the majority did not undergo non-adjuvant radiotherapy (Fig. 5).

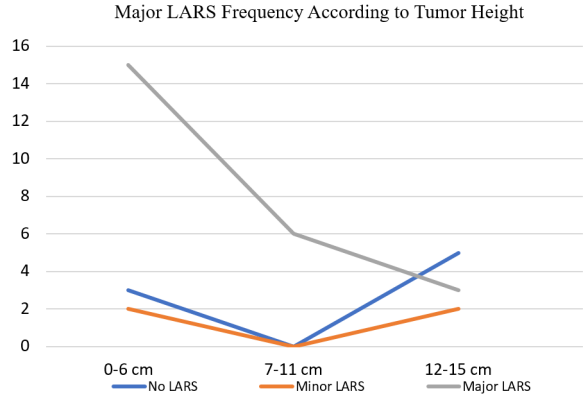

Fig. 5. Tumor height.

There were a total of 14 patients with rectal carcinoma located between 7 and 11 cm from the anal verge. Of these, 6 had a Major LARS score, and the rest, according to the retrospective analysis, did not develop LARS. Again, the number of patients who did not undergo nonadjuvant therapy among the patients with No LARS in midrectal cancer prevailed.

Of the patients grouped in the third group, high rectal cancer (12–15 cm), 50% had no passage disturbances or those mentioned in the definition of LARS, 20% had Minor LARS, and 30% had complaints falling in the Major LARS group.

Of the patients participating in the study, 17 (38, 64%) did not undergo neoadjuvant radiotherapy. A total of 64.7% of these patients were with or without slight passage disturbances postoperatively; 11.8% were with Minor LARS, the remaining 23.5% were with developed Major LARS.

The patients who had undergone neoadjuvant radiotherapy were 27. Approximately 75% of them had a high degree of developed LARS, 7% had Minor LARS, and approximately 18% did not develop LARS (Fig. 6).

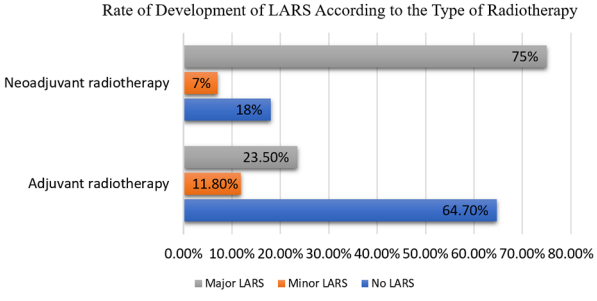

Fig. 6. Rate of development of LARS according to the type of radiotherapy.

Regarding the accompanying diseases in our study, it seems that all patients with diagnosed non-insulin-dependent diabetes mellitus and those with glucose intolerance had severe LARS.

All patients with an advanced form of Major LARS were in T2-T3 stage according to the TNM classification, which could be associated with the need for higher destruction of the surrounding tissue in larger tumors.

DISCUSSION

In this study, as a result, we reached a percentage of patients with developed LARS (Minor and Major) after an anterior rectum resection of approximately 63.6%, which is approximately the same percentage as in other studies of other authors worldwide (18).

Abdominoperineal resection (APR) was the optimal surgical approach for mid and low rectal adenocarcinomas. In recent years, with the introduction of a guidelines for diagnosis and treatment of colorectal cancer (neoadjuvant radiotherapy in mid and low rectal carcinoma) and because of better understanding of perirectal lymphatic drainage and advances in surgical techniques, the safe distal surgical resection margins have been reduced from 5 to 2 cm. These advancements allow the shift from APR to sphincter-sparing surgery (19). Unfortunately, by agreeing to go through this treatment method, most patients are not aware of the QoL changes that can occur after this type of surgery (low anterior resection of the rectum).

After an anterior resection of the rectum, in 50% to 90% of patients, LARS is thought to last from 6 to 12–18 months after surgery, in rare cases—up to 5 years. The anterior resection syndrome not only changes the QoL, but also has a negative effect on the normopsychic condition of both the patients and their relatives (20, 21).

With this study, conducted among patients operated in Department of Surgery of Alexandrovska University Hospital in Sofia, we wanted to do a comparative analysis to help us in assessing the risk of developing LARS in operated patients. A total of 62.5% of the patients included in the study were female, which could be explained by the wider pelvis in women, as well as the changes that occur due to the childbearing function of the woman (22).

The average age of the patients with developed LARS was 62.6 years, which was again a result close to those of foreign authors, but no significant analysis can be made in regard to the different age groups due to the smaller number of patients in the studied cohort.

In addition to the structural disorder and affecting of the sphincter apparatus during surgery, the study has found that all patients with a concomitant disease—diabetes mellitus, had a developed Major LARS, but not all patients with Major LARS were diabetics. No significant difference between the development of LARS and the presence of diabetes mellitus as an accompanying disease has been established.

Preoperative radiation in rectal cancer is part of the complex treatment of CRC to reduce tumor mass, reduce the stage, and modify the surgical treatment to accomplish sphincter-preserving surgery or eliminate the need for surgical treatment at all (10, 23). Radiation is known to impair the conductivity of the intramuscular nerve plexus and increase muscle fibrosis and thus leads to increased incontinence and decreased sensitivity (20). Changes after radiotherapy are a prerequisite for the vulnerability of bowels, anastomotic leakage, or presence of some of the symptoms of LARS. In the patients examined, about 75% of them had undergone a neoadjuvant therapy, which shows a significant correlation between patients who are undergoing neoadjuvant and those with a developed major form of LARS after surgery (10,14).

As in many other studies (14, 24), after our analyses, we found a link to the height of the tumor from the anal verge. A total of 75 percent of the patients with a tumor formation located between 0–6 cm of anal edge had severe anterior resection syndrome (24).

All patients with developed LARS (Minor or Major) were with T3-stage tumors; different N; different M. As a result of our study, we could point out that patients with T3 are high-risk in terms of developing LARS, which has not been confirmed in another survey. Most noted that TNM was not a statistically significant factor in the development of LARS (25).

Patients who participated in our study were also divided into two groups by the anastomosis type. In the first group were those in whom a mechanical stapler was used and T-T anastomosis was made and in the second group are those in which a coloanal anastomosis was performed. The data on postoperative complication or symptoms of LARS showed that the type of anastomosis did not have a significant effect, which was confirmed statistically in the analysis of several other authors (26).

CONCLUSION

The results of this retrospective study show individual risk factors (gender, age, and accompanying diseases) and independent risk factors (radiation, tumor height, TNM stage) related to the frequency and extent of LARS manifestation.

In conclusion, we could point out that the female sex, the younger age, neoadjuvant radiotherapy, advanced stage of the disease, and the location of the tumor from the anal verge are high-risk factors for the development of a major form of LARS.

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