

Sexual dysfunctions following low anterior resection of the rectum in rectal cancer patients

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B – Data Collection
C – Statistical Analysis
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E – Manuscript Preparation
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ABSTRACT:

Introduction: Low anterior resection of the rectum (LAR) is a treatment of choice in patients with diagnosed low rectal cancer. Rectal cancer surgery has a close relationship with the urinary-sexual organs and also with related nerves and nerve plexus. Thus, the sympathetic and parasympathetic nerves of the pelvic area may be damaged. As a result of this, the important point is the sexual function loss following rectal surgeries. The aim of the study was to investigate the sexual disorders in patients with rectal cancer who underwent LAR.

Materials and methods: In this retrospective study the sexual activity, comfort of the experience, quality of sexual life (QoSL) during 3 periods were analyzed: before surgery, a month after and half a year after surgery. Analysis of demographic characteristics, comorbidities, previous surgeries, tumour characteristics and adjuvant therapy was performed.

Results: Most patients (64/100, 64%) expressed that LAR operation has strongly affected their QoSL, 32 patients reported a mild decrease in QoSL, while only 4 patients stated that did not experience any changes in QoSL. QoSL was assessed in 3 different periods of time: before the operation, 1 month after and 6 months after the operation (22,6±3.7 vs. 11.3±7.9 vs. 17.0±6.3; $P < 0.0001$ respectively). The decreased QoSL one and six months after surgery were significantly lower in patients with diagnosed hypertension and higher BMI ($P = 0.0283$).

Conclusions: Sexual disorders after LAR for rectal cancer are often underestimated and it is very important to be aware of them. In our study, it was determined that male sex, higher BMI and hypertension are related to impair of sexual dysfunction after LAR. We observed that the most severe complaints related to sexual activity occur one month after the procedure; after 6 months in most of the patients sexual disorders were decreased approaching the initial state.

KEYWORDS:

sexual dysfunction, rectal cancer, low anterior resection, surgical treatment outcomes

INTRODUCTION

Colorectal cancer (CRC) is the third leading cancer in the western world, accounting for about 500,000 deaths annually worldwide [1]. Nearly 40% of the CRC are located in the rectum [2, 3]. Rectal cancer (RC) has been considered and treated as an independent disease due to its primarily extraperitoneal location, a potential impairment of anorectal continence and the differences in metastatic behavior. Clinical symptoms of RC are often nonspecific, therefore it is diagnosed mainly in the advanced stage [2]. Delays in diagnosis lead to an increase of mortality and morbidity rates. Low anterior resection (LAR) including total mesorectal excision is the treatment of choice for mid or low rectal cancer [9, 10]. Recently the rectal cancer surgery has advanced significantly. The technical approaches to decrease local recurrence and urinary and sexual morbidity have been changed [4]. The surgical outcomes of LAR have changed according to the operation technique and complication rates.

Complication rates after rectal resection are described in 30% of patients and mortality after those operations varies from 2.4% to 4% [5, 6]. Complication rates may be decreased by careful dissections performed through the right tissues. Heald et al. observed that the prognoses of the patients who were followed up after total mesorectal excision in rectal cancer surgery were better and the local recurrence rates were lower [7]. Total mesorectal excision is defined as the resection of the whole mesorectum together with

its fascia via sharp dissections in addition to a complete dissection of the rectum. Autonomous nerve plexi are maintained as well. Maintenance of the pelvic nerves in total mesorectal excision has become the gold standard in the previous years [8]. Rectal cancer surgery has a close relationship with the urinary-sexual organs and also with related nerves and nerve plexi [9]. Thus, the sympathetic and parasympathetic nerves of the pelvic area may be damaged. As a result of this, an important point is the sexual function loss following rectal surgeries. Sexual dysfunction may arise via different symptoms in men and women and as a result of the damage in the autonomous nervous system of the pelvic area. Studies have revealed 20–46% impotence and 20–60% ejaculation problems among men [11, 13]. Among women, 30% libido loss, vaginal moisture loss, orgasm loss and dyspareunia have been reported. Thus, post-operational sexual problems are observed in one in three patients. These problems contain an important part of the factors that affect the life quality of the patients negatively following rectal surgery [14].

Sexuality and intimacy are considered crucial to a human's well-being and are, as such, important aspects of quality of life [21]. Poor quality of sexual functioning and a lower sexual satisfaction are important risk factors for a worse quality of life [17].

The aim of our study was to investigate the sexual disorders in patients with rectal cancer who underwent LAR. The sexual activity,

comfort of the experience, and QoSL during 3 periods were analyzed: before surgery, a month after and half a year after surgery. An analysis of demographic characteristics, comorbidities, previous surgeries, tumour characteristics and adjuvant therapy was performed.

MATERIAL AND METHODS

This retrospective study was conducted on the patients with rectal cancer who underwent LAR in the Department of General and Colorectal Surgery at Medical University of Lodz between January 2003 and June 2016. The patients who underwent surgical procedure in this period were informed about the study and were included in the study after their consents were obtained. A total of 121 patients who were followed up with a diagnosis of rectal cancer and met the inclusion criteria were included in the study.

Inclusion criteria and surgical treatment

The treatment of the patients was decided in a multidisciplinary manner (according to the consensus of the General Surgery, Pathology, Radiation Oncology, Medical Oncology, Gastroenterology and Radiology Departments) following the discussion sessions performed in the Radiology and Pathology committees of the hospital. The surgical treatment was decided by evaluating age, tumour grade and presence of concomitant diseases of the patients. Patients were qualified for LAR when the location of the tumour was defined as inferior rectum (0–6th cm from the anal entry). The treatment was started based on the diagnosis via the pathology report. Whole blood analyses, routine blood tests chest X-ray and electrocardiographic examinations were performed in all the patients. The patients were asked about the presence of any additional diseases, and the general situations of the patients were evaluated. For the pre-operative grading, thoraco-abdominal computed tomography and transrectal ultrasonography examinations were performed. The grading was performed according to the 7th edition of the American Joint Committee on Cancer (AJCC). Intestinal clearance was performed via oral sodium phosphate (90 mL/dose) 1 day before the surgical operation. Cefazolin sodium and metronidazole (500 mg) were started in all the patients on the day of anaesthesia. This period was extended for the patients who developed infections (such as post-operative wound infection or pneumonia). Low-molecular-weight heparin was applied via intramuscular route to the patients for thromboembolic prophylaxis and continued until the patients were mobilized actively.

Total mesorectal excision (TME) operation was performed for all the tumours. The inferior mesenteric artery was tied and cut close to the place where it branches from the aorta, and the inferior mesenteric vein was tied and cut at the inferior level of the pancreas in all the patients.

All the surgical interventions were performed by experienced surgeons and teams by using open surgery methods. The pelvic nerves were intended to be protected in all the patients, particularly the hypogastric nerves.

Exclusion criteria

Patients who were unwilling to participate in the study, those receiving neo-adjuvant chemoradiotherapy, those developing ma-

ior complications such as anastomosis leakage or pelvic abscess or those with metastatic rectal cancer were excluded from the study.

Patient data collection

The patients were asked to complete an anonymous questionnaire, which was particularly constructed in cooperation with a professional psychologist for this study. The survey was concerning their sexual activity before and after surgical procedure. The questionnaire comprised of 37 closed-ended questions. Question concerning QoSL were evaluated from 0 to 5 points and the maximal available score was 35. Higher score was correlated with better QoSL. Only fulfilled questionnaires were included in further statistical analysis. The interviews were performed face-to-face during control follow-up visits in the Surgical Outpatient Clinic or via telephone calls.

STATISTICAL ANALYSIS

The data collected in the study were analyzed using a statistical software STATISTICA 13.1 (StatSoft Inc., USA). The analyzed results were expressed as means \pm standard deviations for continuous variables and numbers and percentages for categorical variables. Normality of distribution of the tested quantitative parameters was verified using the Shapiro-Wilk test. The tested groups were compared using the Student's t-test (or non-parametric Mann-Whitney's tests, depending on variable distribution) and χ^2 test (or Fisher's exact test).

When more than two variables with normal distribution and different variations were compared, the analysis of variances ANOVA was used; otherwise and with categorical variables, the Kruskal-Wallis test was used. Levene's test was used to test homogeneity of variances. Logistic regression was used to analyze relations between selected dependent variables and preference of independent variables that were significantly associated in the univariate analysis ($P < 0.05$). In all analyses ($P < 0.05$) was considered significant.

RESULTS

In our study 121 patients who were hospitalized at the Department of General and Colorectal Surgery and provided written consent to take part in the study were enrolled. In the final analysis 100 patients who correctly fulfilled the anonymous study questionnaire were included.

The analyzed group included 40 women at mean age of 50.9 ± 8.3 years and 60 men at mean age of 53.1 ± 7.3 years. Detailed demographic characteristics with analysis of differences between the gender groups are presented in Table 1.

Most patients ($n = 64$) expressed that LAR operation has strongly affected their QoSL, 32 patients reported mild decrease in QoSL, while only 4 patients stated that they did not experience any changes in QoSL. The mean value of QoSL was assessed in 3 different periods of time: before operation, 1 month after and 6 months after the operation (22.6 ± 3.7 vs. 11.3 ± 7.9 vs. 17.0 ± 6.3 ; $P < 0.0001$ respectively) (Fig.1.).

No statistically significant relationship was found between age of patients and change in score of QoSL before and 6 months after the operation ($P = 0.804$; $r = -0.025$).

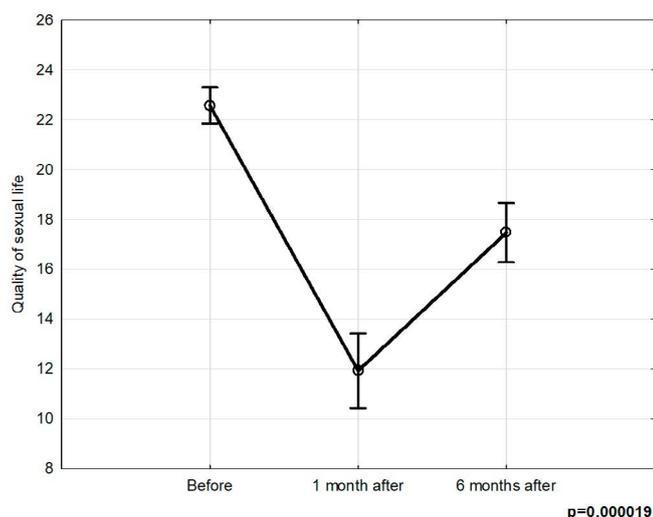


Fig. 1. Mean value of QoSL in patients before, 1 and 6 months after low anterior resection of the rectum ($P = 0.000019$).

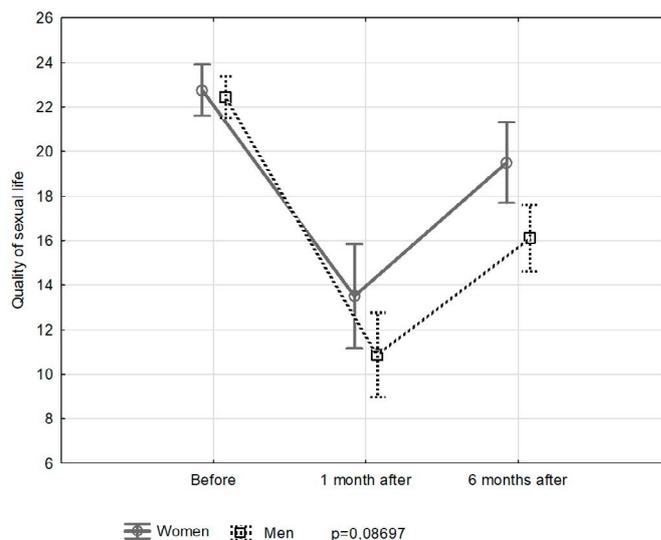


Fig. 2. Mean value of QoSL before, 1 and 6 months after low anterior resection in relation to gender of the patients ($P = 0.08697$).

The analysis demonstrated that men developed slightly greater decrease in QoSL after operation and worse improvement in QoSL in the post-operative period compared to women ($P = 0.0869$; Fig 2.). This difference was (before operation: ♂ = 22.5 vs. ♀ = 22.7; 1 month after operation: ♂ = 10.9 vs. ♀ = 13.5; 6 months after: ♂ = 16.1 vs. ♀ = 19.5; $P = 0.469$) (Fig. 2). However, the QoSL one month after surgery was significantly lower in patients with diagnosed hypertension (7.8 vs. 16.5; $P = 0.0283$). In case of other comorbidities, such as diabetes, these correlations were not observed (7.3 vs. 13.1; $P = 0.4434$). A higher BMI significantly impaired the improvement in QoSL (difference of QoSL before and 6 months after the operation) in the post-operative period ($r = 0.279$; $P = 0.005$). In our study no significant relationship between the level of education, professional activity and place of residence and the QoSL after LAR was observed ($P = 0.891$; $P = 0.761$; $P = 0.321$).

DISCUSSION

Sexual disorders after LAR are a very important issue, underestimated in everyday practice. Although it is known that sexual function is significantly lower after APR compared to LAR the QoSL after LAR is still an important issue [11, 13, 14].

In our study we have shown that QoSL is significantly lower after LAR. Based on previous studies the impair of QoSL after LAR is probably related to intraoperative damage of hypogastris and pelvic nerves [10]. In our study QoSL was especially significantly lower 1 month after surgery (22.6 ± 3.7 vs. 11.3 ± 7.9 ; $P < 0.0001$) which was also found in other studies [11, 14].

Ali Zedan et al. estimated that overall surgical incidence of sexual and urinary dysfunctions after LAR may range from 22% to 45%. It is related to avulsion or direct injury to pelvic autonomic nerves. Despite the autonomic nerve-preserving techniques in total mesorectal excision the bladder and sexual dysfunction, such as retrograde ejaculation, may be observed in up to 12% and 35% of patients. Ali Zedan et al. also considered total mesorectal excision as a technique preserving the autonomic nerves and therefore reducing the incidence of urinary (from 10–30% to 0–5%) and sexual dysfunction (from 40–60% to 10–35%) [21]. We also observed

a 30-day mortality/morbidity in 3%/25% respectively, urinary dysfunction in 9.9%, and sexual dysfunction in 15.8% [10].

Eveno et al. also showed that patients after rectal resection suffered from a different type of sexual disorders. Of those patients undergoing surgery, 69% of all men and 43% of males with pre-operative normal sexual activity had an abnormal international index of erectile function (IIEF score) after surgery. Among females, 62% overall and 39% of those with pre-operative normal sexual activity had abnormal female sexual function index (FSFI score) [3].

Evano et al. in his study showed that urgency and incontinence were reported by 77% and 63% of respondents, respectively. Vaginal dryness, dyspareunia and reduction of vaginal dimensions occurred in 72, 53 and 29%, respectively, and 69% reported that they had little/no sexual desire. Preoperative radiotherapy was associated with voiding difficulties (OR = 1.63, 95% CI 1.09–2.44), reduced vaginal dimensions (OR = 4.77, 95% CI 1.97–11.55), dyspareunia (OR = 2.76, 95% CI 1.12–6.79), lack of desire (OR = 2.22, 95% CI 1.09–4.53) and reduced sexual activity (OR = 0.55, 95% CI 0.30–0.98). Bowel dysfunction was associated with bladder storage difficulties (OR = 1.64, 95% CI 1.01–2.65), lack of sexual desire (OR = 2.69, 95% CI 1.21–5.98), sexual inactivity (OR = 0.48, 95% CI 0.24–0.96) and sexual dissatisfaction (OR = 0.40, 95% CI 0.20–0.82). Eveno et al. showed that bowel dysfunction after operation is associated with reduction in sexual desire, activity and satisfaction [2]. In our study, most patients (64%) expressed that LAR operation strongly affected their QoSL, and 32 patients reported mild decrease in QoSL. Only 4 patients stated that they did not experience any changes in QoSL.

In our study we also found correlation between gender, BMI, hypertension and QoSL after LAR. Our analysis demonstrated that men developed a slightly higher decrease in QoSL after operation and worse improvement in QoSL in the post-operative period compared to women ($P = 0.0869$). Moreover, QoSL one month after surgery was significantly lower in patients with diagnosed hypertension ($P = 0.0283$).

Duran et al. conducted a study investigating urinary and sexual dysfunction rates following rectal cancer surgery. They estimated

Tab. I. Detailed demographic characteristics with analysis of gender differences in patients enrolled in the study.

		WOMEN (n = 40)	MEN (n = 60)	P
Age		50,9 ± 8,3	53,1 ± 7,3	P
BMI		24,8 ± 3,6	27,1 ± 2,4	0.11
Education	Basic	7	15	<0.001
	Secondary	10	16	0.5984
	Higher	23	29	0.2733
Coexisting diseases		5	12	0.8512
	1	26	41	
	≥2	9	7	
Place of residence	Village	2	1	
	< 50000 residents	7	12	
	50000–200000 residents	13	23	
	> 200000 residents	18	24	

pre-operational sexual dysfunctions of the patients by using the questionnaires prepared according to the International Prostate Symptom Score (IPSS) and International Index of Erectile Function (IIEF) in men and Index of Female Sexual Function (IFSF) in women. The average post-treatment sexual dysfunction score of both men and women was decreased by 27.5 and 17.8%, respectively. They concluded that patients should be informed about sexual dysfunctions in the pre-operative consultations [3].

In 2013 Luca et al. performed a study about the impact of robotic surgery on sexual and urinary functions after fully-robotic nerve-sparing total mesorectal excision for rectal cancer. The research was performed from April 2008 to December 2010. As many as 74 patients who underwent a fully-robotic resection for rectal cancer were involved. Sexual dysfunctions affecting quality of life were assessed with individual questionnaires in all patients undergoing robotic total mesorectal excision (RTME). The effect was calculated with confirmed scoring systems and statistically analyzed. The analyses of the questionnaires completed by 74 patients who underwent RTME showed that sexual function and general sexual satisfaction decreased significantly 1 month after intervention: 19.1 ± 8.7 versus 11.9 ± 10.2 ($P < 0.05$) for erectile function and 6.9 ± 2.4 versus 5.3 ± 2.5 ($P < 0.05$) for general satisfaction in men; 2.6 ± 3.3 versus 0.8 ± 1.4 ($P < 0.05$) and 2.4 ± 2.5 versus 0.7 ± 1.6 ($P < 0.05$) for arousal and general satisfaction, respectively in women. Afterwards, both parameters increased progressively, and 1 year after surgery, the values were comparable to those measured before surgery. Luca et al. showed that RTME allows for protection of urinary and sexual functions. This is probably due to the superior movements of the wristed instruments that simplify fine dissection, and a magnified view that helps in recognizing the inferior hypogastric plexus [4].

Asoglu et al. conducted another study about the impact of laparoscopic surgery on bladder and sexual function after total mesorectal excision for rectal cancer. In this research 63 of the 116 patients who underwent surgery for rectal cancer from 2002 to 2006 were included. Male sexual functions were assessed with a questionnaire on the basis of the International Prostatic Symptom Score (IPSS) and International Index of Erectile Function (IIEF). Impotency after surgery was experienced by 6 of 17 preoperatively sexually active males (29%) in group 1 and 1 of 18 males (5%) in group 2 ($P = 0.04$). Similarly, 5 of 10 women (50%) in group 1 and

1 of 14 women (7%) in group 2 felt that their general level of sexual function had decreased as a result of surgery ($P = 0.03$). In our study 96% of patients after LAR reported decrease in QoSL (32% reported mild decrease). Only 4% of patients stated that LAR did not affect their QoSL. Asoglu et al. concluded that laparoscopic rectal cancer surgery offers an important benefit with regard to preservation of postoperative sexual function and constitutes a true progress in rectal cancer surgery as compared with the open technique. The proposed advantages can be assigned to improvement in visibility thanks to magnification offered by laparoscopic surgery. As a result, Duran et al. concluded that open rectal cancer resection is associated with a higher rate of sexual dysfunction [7].

J. Traa et al. in their research claimed that preoperatively, the percentage of sexually active men varied from 37% to 79% across studies [17]. The percentage of preoperatively potent men that experienced sexual dysfunction postoperatively varied from 5% to 88% [17]. Compared with preoperative scores, a postoperative increase in erectile/ejaculatory dysfunction was almost always reported. What is more, J. Traa et al. proved that sexual desire decreased postoperatively [17]. The percentage of preoperatively sexually active women on the other hand ranged from 27% to 78% [17]. Women who were sexually active before the operation remained sexually active postoperatively. Women most often reported sexual dysfunction such as dyspareunia and vaginal dryness. Twelve months after treatment, sexual desire remained unchanged in women [17]. In our study we also observed a significant decrease in QoSL in 64% of surveyed patients both male and female.

Results from studies of all mentioned authors emphasize the fact that LAR is strongly connected with lower QoSL, especially 1 month after surgery. After that period QoSL gradually improves. Those theses are also proven in our study. Summing up, colorectal cancer is a disease that mostly affects the elderly. There has been an ongoing debate on whether or not sexual dysfunction in a higher age is normal or pathological [16]. Den Oudsten B.L., Traa M.J., Roukema J.A. et al. reported lower sexual functioning for patients with colorectal cancer compared with an age-matched general population [18]. This may indicate that colorectal cancer has an additional negative effect on sexual functioning.

It is an important task for researchers to provide more information on the potential effects of a colorectal cancer diagnosis and effects of treatment to health professionals so that they in turn can inform patients on the possible outcomes of multimodality treatment. Information about the treatment, including the side-effects (especially decrease in postoperative QoSL) that can occur, gives patients a possibility to include sexual issues in the decision-making process [19]. Nevertheless, only 10% of patients remembered discussing possible sexual effects of treatment before surgery [20]. If a professional surgeon initiated such a discussion, this could even change patient's decision on the operation.

CONCLUSIONS

Sexual disorders after LAR for rectal cancer are often underestimated and it is very important to be aware of them. In our study, it was determined that male sex, higher BMI and hypertension are related to impair of sexual function after LAR. We observed that the most severe complaints related to sexual activity occur one

month after the procedure, while after 6 months in most of the patients sexual disorders were decreased approaching the initial state. The patients should be informed about the treatment before

surgery, their questions should be answered and the approach to treatment of the functional impairments observed in the follow-up should be multi-disciplinary.

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