



ORIGINAL ARTICLE

Prospective study of sexual dysfunction after proctectomy for rectal cancer



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KEYWORDS

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Summary *Background:* Although rectal cancer is a common malignancy and has an improved cure rate in response to oncological treatment, research on rectal-cancer survivors' sexual function remains limited.

Objective: The aim of this prospective study is to assess sexual dysfunction after rectal cancer surgery.

Patients and methods: Patients undergoing curative rectal cancer surgery were included in the study. Sexual function before and 6 months after the operation was measured using the validated questionnaires. Primary outcome was to determine the rates of Sexual dysfunction after rectal cancer surgery. Furthermore, the factors which can have an impact on sexual function after radical treatment have been assessed.

Results: A total of 187 patients [117 (63%) men and 70 (37%) women] with rectal cancer who underwent radical resection were included in the study. Sexual function has significantly decreased after surgery. Among male patients, sexual dysfunction increased from the baseline 4% (n = 5) up to 41% (n = 48) after the operation. Among female patients, sexual dysfunction increased from the baseline 53% (n = 37) up to 77% (n = 54) after the operation. A significant lower rate of laparoscopic surgery has been found in both males and females who reported sexual dysfunction after surgery. The patients who have locally advanced disease and those who received postoperative chemotherapy or radiotherapy have higher rates of sexual dysfunction.

Conclusion: This study, showed that sexual dysfunction is common in patients with rectal cancer after radical treatment. However, patients who underwent laparoscopic surgery have lower rates of sexual dysfunction than those who underwent open surgery.

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1. Introduction

The main treatment goals for rectal cancer are oncological cure and overall survival.¹ Treatment includes rectal resection and radio/chemotherapy in about 50% of all cases.² One of the most important advances in the treatment of rectal cancer is the concept of total mesorectal excision (TME), because it greatly reduces local recurrence.¹

With improved oncological results, functional results such as sexual function become increasingly important.³ However, the incidence of sexual dysfunction (SD) varies and depends on the surgical technique and extent of resection. Reported values range from 18 to 50%.⁴ A reason for variation lies in the assessment of sexual function, which has been inconsistent in most studies. The techniques differ greatly and include interviews, clinical tests and nonvalidated questionnaires.^{5,6} Many patients experience deterioration in sexual function, consisting of erectile dysfunction (ED) in men and vaginal dryness and dyspareunia in women, after rectal cancer treatment.³ Reduced sexual function is associated with lower quality of life in cancer survivors.⁷ In a previous study, we have shown that rectal cancer survivors had a high rate of SD, which was seldom treated.⁸ However, that study was retrospective, and no information was known about sexual (dys)function before the treatment of cancer, which limited the determination of the effect of the treatment on functioning or on the ability to correct for baseline functioning. Therefore, we think that prospective studies with an assessment point prior to surgical treatment are needed. Furthermore, factors such as age, gender, adjuvant therapy and type of surgery can also have an impact on sexual function, but studies measuring this effect in a prospective way remain limited. Therefore, this study aimed to assess the evolution of sexual functions over time after the treatment of rectal cancer.

2. Methods

2.1. Study design & setting

The study was planned as a prospective, single-arm cohort study. All cases of rectal cancer that involved surgery with curative intent at a university hospital were eligible to be included in the study. The Research Ethics Committee of Marmara University approved the study, and all patients signed a written informed consent form before their participation in the study.

2.2. Inclusion and exclusion criteria

Patients with rectal cancer who underwent a radical resection for any stage of rectal (with or without [neo] adjuvant therapy) were included. Patients who have benign rectal lesions, did not follow up, no sexual activity, previous rectal surgery and those who refused to complete the functional questionnaire were excluded from the study.

2.3. Surgical technique

TME was carried out for midrectal and low rectal cancer, whereas partial mesorectal excision removing 5 cm of mesorectum below the lower border of the rectal tumors was performed for high rectal tumors. In cases of neo-adjuvant treatment surgery was performed 6–8 weeks after the end of radiotherapy.

2.4. Assessment of sexual function

Evaluation was carried out before surgery (at the admission to the hospital for surgery), considered as the baseline status and 6 months after surgery by validated questionnaires, including the International Index of Erectile Function (IIEF-5), and the Index of Female Sexual Function (IFSF).

Validated self-reported psychometric questionnaires, such as IIEF and the IFSF, helped us to assess the impact of a specific treatment modality by evaluating different sexual function domains.^{9,10} Each IIEF item is scored on a 5-point ordinal scale, where lower values represent poorer sexual function. An abbreviated version of the IIEF, designated as the IIEF-5, has been developed and validated as a diagnostic tool for ED.¹¹ This index explores erectile function via 5 domains, including maintenance ability, erection confidence, maintenance frequency, erection firmness, and intercourse satisfaction. According to the IIEF-5, ED can be classified into five severity levels, ranging from none (22–25), to mild (17–21), mild-to-moderate (12–16), moderate (8–11), and severe (5–7).

The IFSF, a 9-item questionnaire, has been developed as a brief, multidimensional self-reporting instrument for assessing the key dimensions of sexual function in women.¹⁰ Specific domains analyzed in the IFSF included quality of sexual intercourse, desire, overall satisfaction with sexual function, orgasm, lubrication, and clitoral sensation. Specific questions analyzed included the degree of lubrication, the ability to achieve orgasm, and the degree of clitoral sensation, with responses graded on a scale of 1 (almost never or never) to 5 (almost always or always).¹⁰ A score of 0 indicated no attempt at intercourse. According to the IFSF, SD in women can be classified into four levels, ranging from none (≥ 35) to mild (26–35), moderate (16–25) and severe (≤ 15) in the Turkish female population.¹² The objective of this study was to assess the sexual function before and at 6 months after surgery for the men and women separately. For assessment of the factors that may have an impact on the development of SD after surgery, we have divided both male and female patients into two subgroups according to their SD scores. Participants who reported no problems or mild problems were categorized as not having sexual problems, while patients who reported moderate or severe problems were categorized as having sexual problems. The two groups were compared with each other.

2.5. Clinical data

Information on age, gender, histological diagnosis, surgical procedure, type of surgery (open vs laparoscopy), co-

morbidity, stoma status, pathological TNM stage, (neo) adjuvant treatment, Tumor distance from anal verge, Vascular invasion, Lymphatic invasion, Perineural invasion, and recurrence (distant metastasis) were obtained from the prospectively collected medical records.

2.6. Statistical analysis

Background clinical data were analyzed using the *t*-test or Mann–Whitney *U* for continuous data and Fisher exact test or the chi-square test for categorical data. Data for the total IIEF and IFSF scores and their domain scores were analyzed using a two-way analysis of variance. A multivariate logistic regression analysis with 95% confidence interval was used to identify factors associated with SD. Data were analyzed using SPSS ver. 17.0 (SPSS Inc., Chicago, IL, USA). All tests were two-sided, and *P*-values below 0.05 were considered statistically significant.

3. Results

3.1. Patient characteristics

Between November 2013 and January 2016 a total of 247 consecutive patients underwent rectal resection at our hospital. A total of 187 patients with rectal cancer were included into the study (Fig. 1). The study cohort consisted of 117 men (63%) and 70 women (37%) who completed the questionnaire. The median age of the patients was 63 (25–85) and all of them were diagnosed with an adenocarcinoma. None of the patients in the study cohort have received treatment for SD during 6 months follow up period.

The demographic and the clinical characteristics of the patients are shown in (Table 1).

3.2. Sexual function

3.2.1. Male patients

Among the male patients, 37 (32%) reported no SD, 40 (34%) reported mild, 35 (30%) reported mild-to-moderate, 4 (3%) reported moderate and 1 (1%) reported severe SD before surgery. However, after the surgery, 2 (2%) reported no SD, 25 (21%) reported mild, 42 (36%) reported mild-to-moderate, 30 (26%) reported moderate and 18 (15%) reported severe SD. In total, 4% (*n* = 5) male patients had moderate or severe SD before surgery. However, this rate increased significantly up to 41% (*n* = 48) after surgery ($p < 0.001$). This means that SD have developed after surgery in 38% (*n* = 43) of the male patients.

Three patients who described moderate SD before surgery reported severe SD after surgery. The median age of those patients with moderate and severe SD (*n* = 5) before surgery was 75 (72–78). Except the patients with preoperative moderate and severe SD (*n* = 5), patients who reported moderate or severe SD after surgery (*n* = 43) were compared with those who reported no SD or mild problems (*n* = 69) (Table 2).

Univariate analysis showed a significant high rate of laparoscopic surgery among patients who did not reported

SD compared to those with SD after surgery [41% (*n* = 28) vs. 5% (*n* = 5), respectively; $P < 0.001$]. In other words SD was reported by only two (6%) of 30 patients who were undergone laparoscopic surgery while it was reported by 41 (50%) of 82 patients undergone open surgery ($P < 0.001$). Univariate analysis also showed a significant high rate of N2 stage among patients who reported SD compared to those without SD after surgery [30% (*n* = 13) vs 1% (*n* = 6), respectively; $p = 0.004$]. Univariate analysis also showed a significant high rate of postoperative radiotherapy among patients who reported SD compared to those without SD after surgery [49% (*n* = 21) vs 20% (*n* = 14), respectively; $p = 0.003$]. A significant high rate of postoperative chemotherapy among patients who reported SD was observed compared to those without SD after surgery [63% (*n* = 27) vs 42% (*n* = 29), respectively; $p = 0.03$]. This rate was correlated with N positive stage ($p < 0.001$).

A significant high rate of lymphatic/vascular invasion among patients who reported SD was observed compared to those without SD after surgery [67% (*n* = 29) vs 41% (*n* = 28), respectively; $p = 0.007$]. This rate was also significantly correlated with N positive stage ($p < 0.001$).

A significant high rate of recurrence (distant metastasis) among patients who reported SD was observed compared to those without SD after surgery [23% (*n* = 10) vs 1% (*n* = 4), respectively; $p = 0.007$]. No other significant difference was shown between the two groups regarding the other factors described in Table 2.

In the multivariate logistic regression analysis, the difference in rates of laparoscopic surgery between the two groups (one group with and the other without SD) was significant ($P = 0.001$). However the differences between the other variables which were significantly different in univariate analysis were found not significant in multivariate analysis (Table 3).

Other than SD no significant difference was showed between the patients with open surgery and those with laparoscopic surgery regarding demographic and clinical characteristics (Table 4).

3.2.2. Female patients

Among the female patients, 16 (23%) reported no SD, 17 (24%) reported mild, 27 (39%) reported moderate and 10 (14%) reported severe SD before surgery. After surgery, 4 (6%) patients reported no SD, 12 (17%) reported mild, 16 (23%) reported moderate and 38 (54%) reported severe SD. In total 53% (*n* = 37) of female patients had moderate or severe SD before surgery; however, this rate increased significantly up to 77% (*n* = 54) after surgery ($p < 0.001$). This means that SD have developed after surgery in 52% (*n* = 17) of the female patients. Except the patients with preoperative moderate and severe SD (*n* = 37), patients who reported moderate or severe SD exclusively after surgery (*n* = 17) were compared with those who reported no SD or mild problems (*n* = 16) (Table 5).

Univariate analysis showed a significant high rate of laparoscopic surgery among patients who did not reported SD compared to those with SD after surgery [100% (*n* = 16) vs 6% (*n* = 1), respectively; $P < 0.001$]. In other words SD was reported by only one (6%) of 17 patients who was undergone laparoscopic surgery while it was reported by all (100%) the patients (*n* = 16) who undergone open surgery

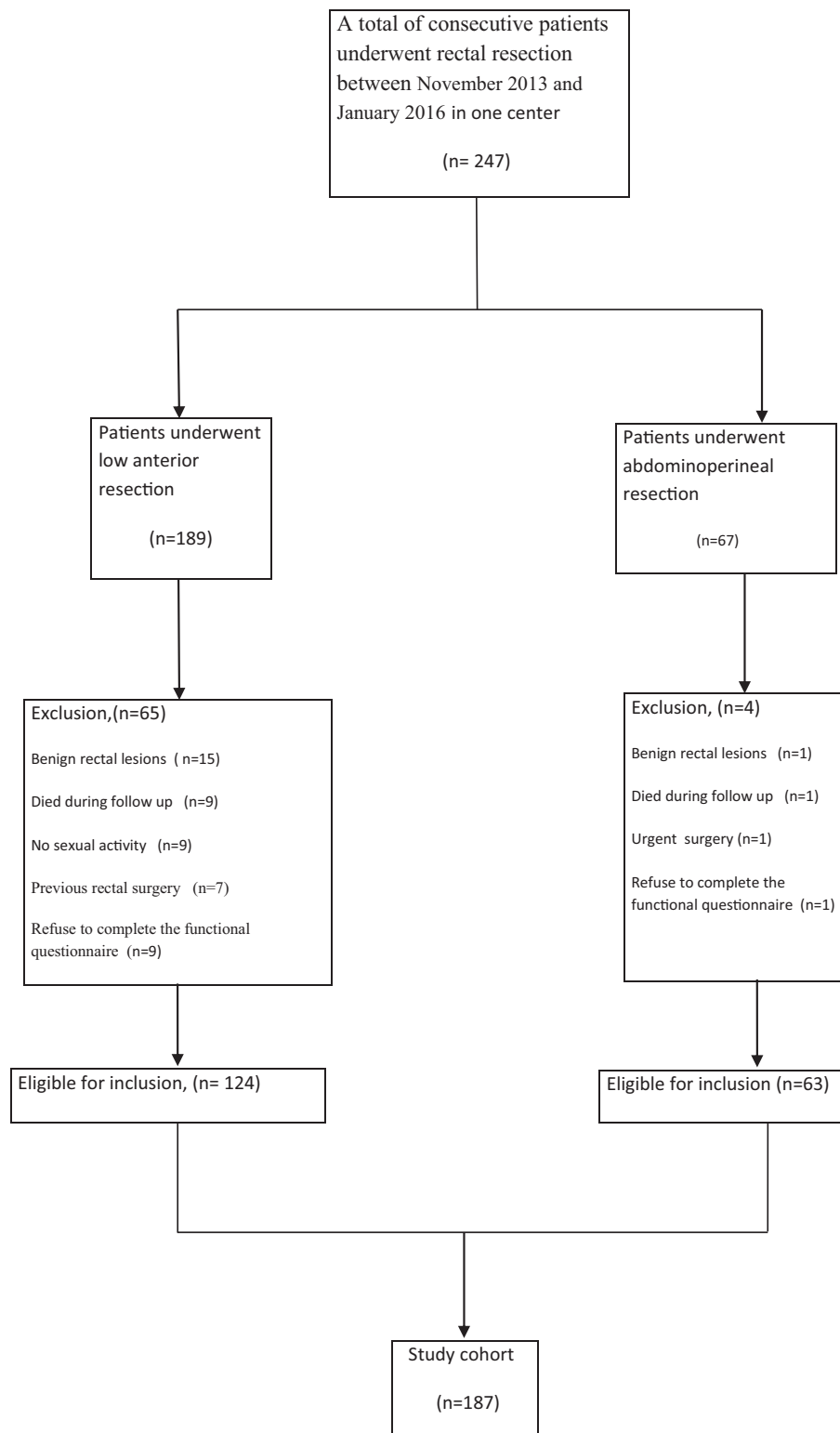


Figure 1 Flow-chart for inclusion in the study.

($P < 0.001$). Univariate analysis also showed a significant high rate of N positive stage among patients who reported SD compared to those without SD after surgery [71% ($n = 12$) vs 19% ($n = 3$), respectively; $p = 0.003$].

A significant high rate of postoperative chemotherapy among patients who reported SD was observed compared to

those without SD after surgery [94% ($n = 16$) vs 25% ($n = 4$), respectively; $p < 0.001$]. This rate was significantly correlated with N positive stage ($p < 0.001$). However no other significant differences were shown between the two groups regarding the other factors described in [Table 5](#).

Table 1 Patient characteristics (N = 187).

Variable	Data	%
Age (year) ^a	63 (25–85)	
Gender		
Male	117	63
Female	70	37
Co-morbidity	120	64
Surgical procedure		
Abdominoperineal resection	63	34
Low anterior resection	124	66
Surgical approach		
Open	134	72
Laparoscopy	53	28
Stoma status	127	68
Stoma reversal	6	3
Tumor stage		
T4	28	15
Nodal stage		
N1–N2	74	40
Preoperative radiotherapy	75	40
Postoperative radiotherapy	36	19
Postoperative chemotherapy	97	52
Tumor distance from anal verge		
≤6 cm	77	41
>6 cm	110	59
Vascular invasion	87	47
Lymphatic invasion	88	47
Perineural invasion	55	29
Recurrence (distant metastasis)	29	16
Patients received treatment for SD ^b	0	0

^a Values are median (range).

^b SD: Sexual dysfunction.

4. Discussion

This study, showed that sexual dysfunction (SD) is a common complaint in patients with rectal cancer after radical treatment in both males and females (38% and 52% respectively). Furthermore, patients who underwent open surgery have higher rates of SD than those who underwent laparoscopic surgery.

This study also showed a significant high rate of SD after surgery among the patients with N positive or N2 stage compared to those with N0 stage.

Conventionally, outcome assessments in colorectal cancer include mortality, morbidity, disease recurrence, and long-term survival. However, patient-reported outcomes (e.g., quality of life) are now also regarded as key measurements in assessing outcomes of interventions.¹³ Sexuality and intimacy are considered to be important aspects of quality of life.¹⁴

SD after rectal cancer treatment is common. Despite this, it is not often discussed in clinical practice. Patients are unlikely to mention these problems themselves either because they are embarrassed or because they do not relate their symptoms to their rectal cancer treatment.³ These complications can have a major impact on patients' psychological, social, and emotional functioning, as well as

Table 2 Comparing male sexual functions after surgery.

	Patients not having sexual dysfunction after surgery N = 69	Patients having sexual dysfunction after surgery N = 43	P value
Age (years) ^a	61 (34–80)	65 (25–85)	0.19 ^b
Co-morbidity (DM, hypertension, heart disease or others)	41 (59%)	30 (70%)	0.27 ^c
Surgical procedure			0.67 ^c
Abdominoperineal resection	19 (28%)	14 (33%)	
Low anterior resection	50 (72%)	29 (67%)	
Open surgery	41 (59%)	41 (95%)	<0.001 ^c
Laparoscopic surgery	28 (41%)	2 (5%)	
Stoma status	47 (68%)	29 (67%)	0.94 ^c
Stoma reversal	0 (0%)	0 (0%)	1.0 ^d
T4	12 (17%)	7 (16%)	1.0 ^d
N+	23 (33%)	22 (51%)	0.08 ^d
N2	6 (1%)	13 (30%)	0.004 ^d
Preoperative radiotherapy	31 (45%)	14 (33%)	0.19 ^c
Postoperative radiotherapy	14 (20%)	21 (49%)	0.003 ^d
Postoperative chemotherapy	29 (42%)	27 (63%)	0.03 ^c
Tumor distance from anal verge			0.84 ^c
≤6 cm	27 (39%)	16 (37%)	
>6 cm	42 (61%)	27 (63%)	
Vascular invasion	28 (41%)	29 (67%)	0.007 ^d
Lymphatic invasion	28 (41%)	29 (67%)	0.007 ^d
Perineural invasion	16 (23%)	16 (37%)	0.1 ^d
Recurrence (distant metastasis)	4 (1%)	10 (23%)	0.007 ^c
Patients received treatment for SD	0 (0%)	0 (0%)	1.0 ^d

DM: diabetes mellitus.

^a Values are medians (range).

^b *Mann–Whitney* for independent samples.

^c Chi squared test.

^d Fisher's exact test.

Table 3 Multivariate analysis for male patients.

Variable	95% C.I. for EXP (B)	P
Surgical procedure		
Abdominoperineal resection	0.01–0.36	0.001
Low anterior resection		
N2	0.46–7.68	0.377
Postoperative chemotherapy	0.39–3.05	0.818
Preoperative radiotherapy	0.81–6.82	0.112
Vascular invasion	0.6–4.3	0.334
Recurrence (distant metastasis)	0.62–12.6	0.18

Table 4 Comparing male patients with open surgery and those with laparoscopic surgery.

	Open surgery N = 82	Laparoscopic surgery N = 30	P value
Age	61 ± 11	63 ± 11	0.72
T4	16 (20%)	3 (10%)	0.235
N +	37 (45%)	8 (27%)	0.078
N2	16 (20%)	3 (10%)	0.235
Neoadjuvant chemotherapy	28 (34%)	7 (23%)	0.27
Postoperative chemotherapy	44 (53%)	12 (40%)	0.2
Preoperative radiotherapy	33 (40%)	12 (40%)	0.98
Co-morbidity (DM, hypertension, heart disease or others)	53 (65%)	18 (60%)	0.65

on their overall well-being.¹⁵ Most of the Studies in literature regarding SD are retrospective. This study fills this gap and highlights the less discussed issue of SD.⁷ It is also a prospective study with an assessment point prior to surgical treatment.

The design of our study was in accordance with the criteria from Ho et al including the use of validated instruments, inclusion of at least 30 patients for both men and women, obtaining data from 2 time points, and reporting incidence of sexual dysfunction, baseline data, item response rates, and mean/median data for subscales or domains.¹⁶

This study has some limitations that need to be acknowledged. First, the study population is a cohort of surviving rectal cancer patients who were treated in a single center. Therefore, results may not be generalizable to all patients undergoing rectal cancer surgery. Second, procedure subgroups were not randomly assigned and differed in their tumor characteristics as well as their treatments. Third, obtaining data from only 2 time points rather than 1 year or beyond. The final limitation is the small number of female patients. In a previous study, we have shown that rectal cancer survivors had a high rate of SD. However, that study was retrospective, all cases of rectal cancer that involved surgery with curative intent at from January 2012 to September 2013 were selected from a database of all colorectal cancer operations and no information was known about sexual (dys)function before surgery, which limited the determination of the effect of the surgery on functioning or on the ability to correct for baseline functioning. This was proved in this study that some patients reported SD before surgery. Widely varying rates of SD after rectal surgery have been reported in the literature, and comparisons between studies are difficult due to the different exclusion criteria and outcome measures used in those studies.^{17,18} This study showed lower rates of SD among the patients who were undergone laparoscopic surgery compared with those who were undergone open surgery. The introduction of laparoscopic surgery,

Table 5 Comparing female sexual functions after surgery.

	Patients not having sexual dysfunction after surgery N = 16	Patients having sexual dysfunction after surgery N = 17	P value
Age (years) ^a	54 (40–71)	48 (26–72)	0.87 ^b
Co-morbidity (DM, hypertension, heart disease or others)	7 (44%)	10 (59%)	0.39 ^c
Surgical procedure			
Abdominoperineal resection	6 (37%)	10 (59%)	0.22 ^c
Low anterior resection	10 (63%)	7 (41%)	
Open surgery	0 (0%)	16 (94%)	<0.001 ^c
Laparoscopic surgery	16 (100%)	1 (6%)	
Stoma status	9 (56%)	14 (82%)	0.14 ^d
Stoma reversal	1 (6%)	0 (0%)	0.49 ^d
T4	1 (6%)	2 (12%)	1.0 ^d
N+	3 (19%)	12 (71%)	0.003 ^c
Preoperative radiotherapy	6 (38%)	9 (53%)	0.37 ^c
Postoperative radiotherapy	3 (19%)	4 (24%)	1.0 ^d
Postoperative chemotherapy	4 (25%)	16 (94%)	<0.001 ^c
Tumor distance from anal verge			
≤6 cm	5 (41%)	11 (65%)	0.06 ^c
>6 cm	11 (69%)	6 (35%)	
Vascular invasion	3 (19%)	6 (35%)	0.44 ^d
Lymphatic invasion	3 (19%)	6 (35%)	0.44 ^d
Perineural invasion	3 (19%)	4 (24%)	1.0 ^d
Recurrence (distant metastasis)	2 (12%)	3 (18%)	1.0 ^d
Patients received treatment for SD	0 (0%)	0 (0%)	1.0 ^d

DM: diabetes mellitus; SD: Sexual dysfunction.

^a Values are medians (range).

^b *Mann–Whitney* for independent samples.

^c Chi squared test.

^d Fisher's exact test.

where magnification of the view facilitates identification of the nerves and, therefore, may increase preservation of urogenital function.¹⁹ However, evidence is lacking and clinical data are confusing. Two randomized trials demonstrated a worse urogenital function after laparoscopic rectal excision compared with open surgery.^{20,21} Whereas 2 recent comparative nonrandomized series showed a better function after laparoscopic surgery.^{22,23} In one multicentric retrospective study Jones et al reported lower rates of SD among the male patients who were undergone laparoscopic surgery.²⁴

This study also showed a significant high rate of N positive or N2 stage among patients who reported SD compared to those without SD after surgery which means that locally advanced tumor stage may be a predictive factor of worse

sexual function after surgery. Similar result have been reported by Adam et al²⁵ However he has proved it for tumor stage T3 and T4 not for nodal stage. To our knowledge, this prospective study is the first to show the predictive value of nodal stage for worse sexual function after surgery. Interestingly this study showed a significant high rate of lymphatic/vascular invasion among patients who reported SD. However lymphatic/vascular invasion rates were significantly correlated with N positive stage. The influence of gender on sexual function after rectal surgery was analyzed in very few studies. Engel et al²⁶ and Camilleri-Brennan and Steele²⁷ found male gender to be associated with worse sexual function than female gender after surgery for rectal cancer. However, Mannaerts et al²⁸ studied patients with advanced rectal cancer and found the same extent of impaired sexual function (50%) in male and female patients after comprehensive treatment for rectal cancer. Furthermore, some studies show that sexual function after rectal resection seems to be better in women than in men.²⁶ Thus gender distribution should be adjusted when conducting research on that subject. In this study gender distribution was adjusted and we found female gender to be associated with worse sexual function than male gender after surgery for rectal cancer. While a number of studies have examined rates of SD after surgery for rectal cancer, the primary focus has been on the male sexual issue of ED. Research on female rectal cancer survivors' sexual function remains limited, and generally it is ignored during surgery.^{29–31} Moreover, female SD after surgery for rectal cancer has been relatively ignored¹³ due in part to the reluctance of women with rectal cancer to respond to questions about their sexuality.³² In studies where surgery was combined with radiotherapy, the rate of reported sexual dysfunction increased independent of type of surgery.^{17,33} Rather unexpected in this study was the finding that neoadjuvant radiotherapy was not significantly associated with SD. Considering that radiotherapy is one of the most robust findings in the literature, our contradictory finding is noteworthy. However in this study sexual functions were not assessed in the patients before neoadjuvant radiotherapy, that may make the assessment of radiotherapy on SD is difficult. However this study showed a significant high rate of postoperative radiotherapy among patients who reported SD compared to those without SD after surgery. Recently randomized studies showed that chemotherapy does not increase the risk of male SD,³⁴ adjuvant pelvic radiotherapy or chemoradiation does increase the rate of erectile dysfunction.³⁵

In this study stoma status and type of resection were not significantly different between the groups with and without SD. Milbury et al³⁶ reported that neither having a stoma nor type of resection was significantly related to SD for women. Prospective studies indicate that other indices of quality of life typically improve over time, yet sexual function remains impaired.^{27,37}

In conclusion, this study, showed that SD is a common complaint in patients with rectal cancer after radical treatment. However, patients who underwent laparoscopic surgery have lower rates of SD than those who underwent open surgery. Furthermore, nodal stage was found as a predictive factor for worse sexual function after rectal

surgery. These results imply that attention needs to be drawn to SD among male and female survivors of rectal cancer in both research and clinical practice.

Authors' contributions

Wafi Attaallah: conception and design, acquisition of data, analysis and interpretation of data; drafting the article, revising it critically for important intellectual content; and final approval of the version to be published.

Suleyman Caglar Ertekin: acquisition of data, analysis and interpretation of data; drafting the article or revising it critically for important intellectual content; and final approval of the version to be published.

Cumhur Yegen: analysis and interpretation of data; drafting the article, revising it critically for important intellectual content; and final approval of the version to be published.

Conflict of interest

Authors declare no conflict of interest.

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