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ORIGINAL RESEARCH

Sexual Dysfunctions in Men and Women with Inflammatory Bowel Disease

The Influence of IBD-Related Clinical Factors and Depression on Sexual Function

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ABSTRACT

Introduction. Inflammatory bowel disease (IBD) is likely to have an impact on sexual function because of its symptoms, like diarrhea, fatigue, and abdominal pain. Depression is commonly reported in IBD and is also related to impaired sexual function. This study aimed to evaluate sexual function and its association with depression among patients with IBD compared with controls.

Methods. IBD patients registered at two hospitals participated. The control group consisted of a general practitioner practice population. The web-based questionnaire included the Female Sexual Function Index (FSFI) for women and the International Index of Erectile Function (IIEF) for men. Other variables evaluated were depression, disease activity, IBD-related quality of life, body image, and fatigue.

Results. In total, 168 female and 119 male patients were available for analysis (response rate 24%). Overall, patients with IBD did not significantly differ in prevalence of sexual dysfunctions from controls: female patients 52%, female controls 44%, male patients and male controls both 25%. However, men and women with an active disease scored significantly lower than patients in remission and controls, indicating impaired sexual functioning during disease activity. Significant associations were found between active disease, fatigue, depressive mood, quality of life, and sexual function for both male and female patients. The association between disease activity and sexual function was totally mediated by depression.

Conclusion. Male and female IBD patients with an active disease show impaired sexual function relative to patients in remission and controls. Depression is the most important determinant for impaired sexual function in IBD. **Bel LGJ, Vollebregt AM, Van der Meulen-de Jong AE, Fidder HH, Ten Hove WR, Vliet-Vlieland CW, ter Kuile MM, de Groot HE and Both S. Sexual dysfunctions in men and women with inflammatory bowel disease. The influence of IBD-related clinical factors and depression on sexual function. J Sex Med 2015;12:1557–1567.**

Key Words. Sexual Function; Depression; Fatigue; Quality of Life in IBD

[a]Both authors contributed equally to this work.

Introduction

Inflammatory Bowel Diseases (IBD), Crohn's disease (CD) and ulcerative colitis (UC), are characterized by a chronically relapsing course [1,2]. Because of symptoms like abdominal pain, fatigue, bloating, gas, and diarrhea, IBD is likely to have a substantial impact on body image, intimacy and sexuality [1,2]. Complications may include perianal disease, fistulae and abscesses. Surgery is frequently necessary, sometimes including the placement of a stoma or pouch. Furthermore, mood disorders, mainly depression, are reported to be common in IBD [3]. As sexual dysfunction is also known to be related to depression [4–9], depression may be an important determinant of sexual functioning in patients with IBD.

Studies about sexual functioning in IBD patients are scarce. Muller et al. [10] reported that 66.8% of the IBD patients felt that their body image was impaired due to the IBD. Timmer et al. [11] studied a male sample with IBD from a clinic and from a patients' organization group and compared them with general population means. She reported no differences on the International Index of Erectile Function (IIEF), compared with the general population, all scores were below the standard mean, but within 1 standard deviation (SD) for both groups. But both disease activity and depressive mood were associated with diminished sexual function. Moody et al. [12] reported that female patients with CD had significantly more dyspareunia and more often no sexual intercourse than age-matched controls. However, in a later study, Moody and Mayberry [13] reported no differences in the frequency of sexual intercourse between male patients with IBD and female patients with UC compared with controls. Timmer et al. [14] reported no differences between female patients with IBD and controls on the Brief Index of Sexual Function in Women, but female patients with an active disease felt less attractive and less feminine than patients in remission. In another study done by Timmer et al. [15] depression was the most important determinant of impaired sexual function for both male and female patients. Taken together, the knowledge about sexual dysfunctions in patients with IBD is limited, and so far, the studies have shown mixed results. However, the study results indicate that active disease is associated with impaired sexual function and that in particular, depression may be an important mediator of this association. We aimed to evaluate the prevalence of sexual dysfunctions in men and women with IBD, compared with the prevalence in an age-matched control group. Furthermore, we evaluated in patients the associations of disease activity, IBD-related quality of life, body image, fatigue and depression with sexual function, and tested whether quality of life, body image, fatigue, and depression were mediating variables in the association between active IBD and impaired sexual function. It was expected that: (i) patient with IBD would report more sexual problems than healthy controls; (ii) patients with active disease would report more sexual problems than patients in remission; and (iii) that in particular depression would mediate the association between active IBD and impaired sexual function.

Materials and Methods

Setting and Sample

All patients registered in 2011 with CD or UC at the Gastroenterology departments of a tertiary referral center (Leiden University Medical Center) and a general hospital (Diaconessenhuis Leiden) in the Netherlands were invited to participate by regular mail. Patients were eligible for inclusion if they were 18–70 years of age, diagnosed with CD or UC, and had a stable heterosexual relationship for at least 3 months. The patients received written information about the study at their home address. In this information letter, patients were informed about the purpose and procedure of the study. Based on the written information, the patient could decide to fill in the web-based questionnaire or fill in that he/she was not interested to participate. All patients who did not return the questionnaire within 3 weeks received a reminder by regular mail. An age-matched control group of healthy men and women, registered at a general practitioner practice in the same region as the participating hospitals, were also invited to participate. The controls were eligible if they were 18–70 years of age, had a stable heterosexual relationship for at least 3 months and did not have bowel problems, like IBD or irritable bowel syndrome. Exclusion criteria for both patients and controls were pregnancy and lactation. If the questionnaire contained less than 75% of the answers, the questionnaire was not included for evaluation.

The study was approved by the ethics committee or the steering board of the participating medical centers. The gastroenterologists ware unaware which of the patients filled in the questionnaire. Only the medical researchers could reveal the patient number to look at the Montreal

classification in the medical records, in order to establish the severity of disease in patients.

Instruments

Assessment of Basic Characteristics

Both patients and controls received questions about socio-demographics. Data were collected about date of birth, the duration of their relationship, having children and level of education. There were also questions about height and weight for the calculation of the body mass index (BMI). Women received questions about use of contraceptives, pregnancy, lactation, and hormone suppletion. Both patients and controls received questions about having (other) chronic disease, use of medication [16] and history of lower abdominal surgery.

Assessment of Sexual Function

Sexual function in men was measured using the IIEF. The IIEF is a brief multidimensional self-report instrument consisting of five subscales: erectile function (five items), orgasmic function (two items), sexual desire (two items), intercourse satisfaction (three items), and overall satisfaction (two items). The score can range from 5 to 75. Higher scores indicate better sexual function. The IIEF has a good internal reliability and is able to differentiate well between clinical samples and non-dysfunctional controls [17]. To define patients with and without sexual dysfunction, in this study a cut-off score of 42.9, 1 SD below the mean of a healthy population [17,18] was applied. For erectile dysfunction, a cut-off score of 25 on the subscale erectile function was used [19].

Sexual function in women was assessed with the Female Sexual Function Index (FSFI) [20]. The FSFI is a brief multidimensional self-report instrument consisting of six subscales: desire (two items), arousal (four items), lubrication (four items), orgasm (three items), satisfaction (three items), and pain (three items). Total scores can range from 2 to 36. Higher scores indicate better sexual function. The FSFI has good internal reliability and is also able to differentiate between clinical samples and non-dysfunctional controls, using a cut-off score of 26.55 [20–22].

Assessment of Depression and Clinical Factors

Depression was evaluated using the 14-item Hospital Anxiety Depression Scale (HADS) [23]. The HADS has a good internal reliability and good test–retest reliability [24]. Total score for the subscale depression range from 0 to 21. A higher score indicates more depressive symptoms. A score 8 or above on the subscale depression, indicates presence of clinical depression [25].

The questionnaire for the IBD patients included disease-specific instruments and a fatigue inventory. The Short Inflammatory Bowel Disease Questionnaire (SIBDQ) [26] is a short disease-specific quality of life instrument and is able to measure clinical changes in health-related quality of life for both CD and UC [27]. A higher score indicates a better disease-related quality of life [26]. Disease activity was evaluated using the Simple Clinical Colitis Activity Index (SCCAI) [28] for patients with UC, and the Harvey–Bradshaw Index (HBI) [29] for patients with CD. For both questionnaires a score of 5 or more is an indication of an active disease [30–32].

The Multidimensional Fatigue Inventory-20 (MFI-20) [33] measured fatigue. It has a good internal consistency [34]. A higher score indicates more fatigue. Fatigue was defined as a general fatigue score above the 95th percentile mean score of healthy controls as used in the study from Minderhoud et al. [35]. From the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life questionnaire for Colorectal Cancer (EORTC-QLQ-CR38) [36] patients received three questions about body images (physical attractiveness, feeling masculine/feminine, and satisfaction about his/her body). A higher score means a less positive body image. Although this questionnaire has been used in research with IBD patients[11,14], it is neither designed nor validated for this patient group.

The Montreal Classification for the classification of CD and UC was received from the medical records.

Procedure

Participants were given written information about the study and gave informed consent before participation. The data were collected using the web-based software Netquestionnaire (NetQ Insights BV, Amsterdam, the Netherlands). All eligible patients were numbered consecutively. Data of each participant was entered in a database using a number. The number and data cannot be linked to participants. In this way, complete privacy is guaranteed. A list with the names of the participants, their study number, and their date of birth, was however stored by the investigator (separated from the collected data), as this information was needed to link the collected data to the medical records of the IBD patients.

Statistical Analyses

Statistical analyses were performed using SPSS (v. 20, SPSS, Inc., Chicago, IL, USA). First, sexual function, depression, quality of life, fatigue, and body image scores were analyzed separately for men and women, and for patients with active disease versus patients in remission and controls. Student's *t*- and χ^2 test were used to compare means and to test associations, analyses of covariance were used to correct for differences in baseline characteristics. Second, Z-scores were calculated for sexual function scores to examine the associations between disease activity, depression, quality of life, fatigue, and body image with sexual functioning within the male and female patient group using bivariate correlation analyses.

Furthermore, in order to test whether quality of life, fatigue, depression, and body image mediated the hypothesized association between disease activity and sexual functioning, sexual functioning was regressed upon, respectively, quality of life, fatigue, depression, body image, and disease activity. Relevant demographic variables were entered as control variables. Mediation occurs if: (i) disease activity significantly affects the mediator (IBD quality of life, fatigue, body image and depression); (ii) disease activity significantly affects sexual functioning in the absence of the mediator; (iii) the mediator has a significant and unique effect on sexual functioning; and (iv) the effect of disease activity on sexual functioning shrinks upon the addition of the mediator into the model [37]. To test whether putative mediators (partly) mediated the relationship of disease activity and sexual functioning, the standard error of the mediated effect was bootstrapped [38]. The macro for SPSS developed by Preacher and Hayes was used to generate estimates for the indirect effects in multiple mediator models [39]. The level of significance used was $P < 0.05$.

Results

Participants Basic Characteristics

In total, 1,581 patients and 1,018 controls were requested to participate. Response rate for the controls was 30% (n = 303) and for the patients 24% (n = 372). After age-matching, there were 168 female patients, 106 female controls, 119 male patients, and 91 male controls available for analysis. The other responders were excluded because they did not have a relationship, had a relationship shorter than 3 months, were pregnant or lactating, or they answered less than 75% of the questions. Basic characteristics of the study population are shown in Table 1. Female patients were comparable with controls on most characteristics. However, as expected, they had undergone more surgical procedures in the pelvis, had more systemic diseases other than IBD, had more diseases, and used more medication with possible influence on sexual function. Male patients and controls were comparable except for BMI with male controls having a higher BMI than male patients. The male patients were significantly older than the female patients, $t(279) = 5.27$, $P < 0.001$.

Disease Activity and Quality of Life

The Montreal Classification and disease activity are shown in Table 2. Male CD and UC patients scored comparable on the SIBDQ. Of the men with CD, 30.4% had an active disease (HBI > 5), versus 31.7% of the men with UC (SCCAI > 5) ($P > 0.05$). Women with CD scored significantly higher on the SIBDQ as compared with women with UC, $t(161) = -2.53$, $P < 0.05$. Of the women with CD, 43.9% had an active disease (HBI > 5), versus 28.4% of the women with UC (SCCAI > 5), χ^2 (1) = 4.09, $P < 0.05$.

Depression, Fatigue, and Body Image

Data on depression, fatigue, and body image are shown in Table 3. Patients (men as well as women) with an active disease had significantly more often a score indicating a depression than patients in remission and controls. Often, male patients in remission had significantly less scores indicating a depression than controls. Female patients in remission and controls scored comparably. Patients with active disease suffered significantly more often from fatigue and had a significant lower body image compared with patients in remission. This applied to men as well as women.

Sexual Function

Overall, men and women with IBD scored comparable with controls on the IIEF and the FSFI (see Tables 4 and 5). However, male patients with active disease reported more orgasm problems and were less satisfied compared with controls, and reported more erectile problems, more orgasm problems, less sexual desire, and were less satisfied compared with patients in remission (see Table 4). In the total group of male patients with IBD, 25.2% had a sexual dysfunction (score of <42.9) and in the control group this was 25.3%. Of the male patients with an active disease, 36.1% had a sexual dysfunction, in comparison with 18.8% of

Table 1 Participants characteristics—demographics and other general information

	Female patients N = 168	Female controls N = 106	*P* value	Male patients N = 119	Male controls N = 91	*P* value
Age (years)*	42.9 (12.9)	43.8 (12.8)	0.58	51.1 (12.8)	52.4 (12.7)	0.47
BMI (kg/m^2)	21.0 (4.5)	20.8 (3.2)	0.71	23.0 (3.1)	24.0 (3.4)	0.03
Relationship duration (years)	17.2 (13.5)	18.1 (14.0)	0.59	23.2 (14.3)	24.6 (15.0)	0.47
Children (yes)	97 (57.7%)	72 (68.6%)	0.07	94 (79.0%)	81 (89%)	0.05
Education			0.66			0.58
Basic level	20 (11.9%)	16 (15.1%)		13 (10.9%)	14 (15.4%)	
Medium level	89 (53.0%)	57 (53.8%)		53 (44.5%)	36 (39.6%)	
High level	59 (35.1%)	33 (31.1%)		53 (44.5%)	41 (45.1%)	
Hormonal contraception (yes)	64 (38.1%)	43 (40.6%)	0.68			
Estrogen medication (yes)	4 (2.4%)	6 (5.7%)	0.16			
Operations in pelvis (yes)†	68 (40.5%)	2 (1.9%)	0.000	48 (40.3%)	31 (34.1%)	0.35
Medication with possible influence on sexual function‡			0.000			0.24
None	106 (63.1%)	96 (90.6%)		71 (59.7%)	64 (70.3%)	
Minor	38 (22.6%)	10 (9.4%)		25 (21.0%)	16 (17.6%)	
Major	24 (14.3%)	0 (0.0%)		23 (19.3%)	41 (45.1%)	
Systemic disease			0.000			0.18
None	128 (76.2%)	102 (96.2%)		102 (85.7%)	74 (81.3%)	
Minor	31 (19.0%)	4 (3.8%)		11 (9.2%)	15 (16.5%)	
Major	8 (4.8%)	0 (0.0%)		6 (5.0%)	11 (12.1%)	
Disease with possible influence on sexual function§ (yes)	15 (8.9%)	1 (0.9%)	0.006	10 (8.4%)	9 (9.9%)	0.71

*M (SD).
†Ten of the male controls underwent vasectomy.
‡Antihypertensive medication, antidepressants, antiepileptics, antipsychotics, benzodiazepines, statins, antacids, digoxin, and corticosteroids. Minor = 1, major = ≥2.
§Female patients: MS N = 1, hypo/hyperthyroid N = 5, DM type II N = 1, COPD N = 1, renal insufficiency N = 1, hypertension N = 4, Morbus Sheehan N = 1, depression N = 1. Female controls: MS N = 1. Male patients: Parkinson N = 1, heart disease N = 5, DM type II N = 5, COPD N = 1. Male controls: DM type II N = 5, hypertension N = 6.
BMI = body mass index; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; MS = multiple sclerosis; SD = standard deviation.

the male patients in remission, χ^2 (1) = 4.09, $P < 0.05$, and 25.3% in the control group, χ^2 (1) = 1.49, $P > 0.05$. In the total group of male patients with IBD, 46.2% had erectile dysfunction (score < 25) and in the control group this was 40.7%, χ^2 (1) = 0.65, $P > 0.05$. Of the male patients with active disease, 58.3% had erectile dysfunction, in comparison with 40% of the male patients in remission, χ^2 (1) = 3.36, $P > 0.05$, and 40.7% in the control group, χ^2 (1) = 3.25, $P > 0.05$).

Female patients with active disease reported more lubrication problems and more dyspareunia compared with patients in remission and controls (see Table 5). In the total group of women with IBD, 51.2% had sexual dysfunction, against 44.3% of the control group, χ^2 (1) = 1.22, $P > 0.05$. Of the women with an active IBD, 63.1% had sexual dysfunction (total score < 26.55), against 44% of women in remission, χ^2 (1) = 5.74, $P < 0.05$, and 44.3% of the control group, χ^2 (1) = 5.66, $P < 0.05$.

Associations with Sexual Functioning in Patients

Table 6 reports correlations between sexual function, age, relationship duration, gender, disease activity, and the putative mediating factors, quality of life, fatigue, depression, and body image. Age and relationship duration were significantly correlated with sexual function. Patients with higher age and longer relationship duration reported more sexual problems. Also, as expected, disease activity was significantly associated with sexual function. Patients with more active disease reported more sexual problems. The putative mediating variables quality of life, fatigue, depression, and body image were all significantly correlated with sexual functioning. Patients reporting higher quality of life reported less sexual problems, and patients scoring higher on fatigue, depression, and negative body image reported more sexual problems.

Mediators of the Association of Disease Activity with Sexual Function

In order to test whether quality of life, fatigue, depression, and body image mediated the association between disease activity and sexual functioning, sexual functioning was regressed upon, respectively, quality of life, fatigue, depression, body image, and disease activity. In each of these mediation analyses, gender, age, and relationship duration were entered as control variables. In the mediation analysis with gender, age, relationship duration, quality of life, and disease activity being included together in the regression equation,

Table 2 Montreal Classification and disease activity

Montreal classification	Crohn's disease		Ulcerative colitis	
	Men N = 57	Women N = 98	Men N = 62	Women N = 70*
Age at diagnosis (years)				
A1 (<17)	5 (8.8%)	7 (7.1%)		
A2 (17–40)	42 (73.7%)	78 (79.6%)		
A3 (>40)	10 (17.5%)	13 (13.3%)		
Location				
L1 (ileal)	19 (33.3%)	18 (18.4%)		
L2 (colonic)	7 (12.3%)	22 (22.4%)		
L3 (ileocolonic)	31 (54.5%)	58 (59.2%)		
+L4 (upper digestive)	9 (15.8%)	4 (4.1%)		
+P (perianal disease modifier)	20 (35.1%)	31 (31.6%)		
Behavior				
B1 (non-stricturing, non-penetrating)	23 (40.4%)	52 (53.1%)		
B2 (stricturing)	13 (22.8%)	18 (18.4%)		
B3 (penetrating)	10 (17.5%)	12 (12.2%)		
B2 + B3 (both stricturing as penetrating)	11 (19.3%)	16 (16.3%)		
Extend colitis				
E1 (proctitis)			6 (9.7%)	16 (22.9%)
E2 (left-sided UC)			14 (22.6%)	17 (24.3%)
E3 (wxtensive UC)			42 (67.7%)	35 (50.0%)
Disease severity				
S0 (remission)			41 (66.1%)	46 (65.7%)
S1 (mild)			10 (16.1%)	8 (11.4%)
S2 (moderate)			3 (4.8%)	3 (4.3%)
S3 (severe)			0	0
Patients with a IPAA			8 (12.9%)	13 (18.6%)
Disease activity				
HBI score	3.98 (2.55)	4.74 (4.01)		
SCCAI score			3.30 (3.31)	3.39 (2.55)
SIBDQ score	5.50 (0.99)	4.98 (0.99)	5.72 (1.07)	5.35 (0.88)

*For two UC patients, the extent of the disease missed.
HBI = Harvey–Bradshaw Index; IPAA = ileal pouch anal anastomosis; SCCAI = Simple Clinical Colitis Activity Index; SIBDQ = Short Inflammatory Bowel Disease Questionnaire; UC = ulcerative colitis.

quality of life was a significant predictor, $\beta = 0.32$, $t = 4.84$, $P < 0.001$, and the relationship between sexual functioning and disease activity decreased in strength, from $\beta = -0.17$, $t = -2.95$, $P < 0.01$ to $\beta = -0.01$, $t = -0.18$, $P = 0.86$. In the mediation analysis with gender, age, relationship duration, fatigue, and disease activity being included together in the regression equation, fatigue was a significant predictor, $\beta = 0.33$, $t = -5{,}61$, $P < 0.001$, and the relationship between sexual functioning and disease activity decreased in strength, from $\beta = -0.17$, $t = -3.03$, $P < 0.01$ to $\beta = -0.04$, $t = -0.61$, $P = 0.54$. Similarly, in the mediation analysis with gender, age, relationship duration, depression, and disease activity being included together in the regression equation,

Table 3 Depression, fatigue, and body image

	Controls	Active disease	Remission	Active versus remission t/χ^2 value	Active versus controls χ^2 value	Remission versus controls χ^2 value
Men						
Depression N (%)	17 (18.7)	15 (41.7)	4 (5)	24.37*	7.23**	7.40**
Fatigued patients N (%)		24 (66.7)	19 (23.8)	19.60*		
Body image mean score (SD)		5.61 (2.31)	3.82 (1.33)	–5.25*		
Women						
Depression N (%)	11 (10.4)	16 (25.8)	12 (11.7)	5.50***	6.64***	0.14
Fatigued patients N (%)		48 (73.8)	52 (52)	7.88**		
Body image mean score (SD)		6.20 (2.78)	4.58 (1.68)	–4.65*		

*$P < 0.001$, **$P < 0.01$, ***$P < 0.05$.
SD = standard deviation.

Table 4 Mean International Index of Erectile Function scores (standard deviation) of patients with an active disease, patients in remission and controls

	Patients with active disease† N = 36	Patients in remission N = 80	Controls N = 91	Active versus control *t* value	Active versus remission *t* value	Remission versus control *t* value
Erectile function	20.17 (9.63)	23.95 (8.00)	22.30 (9.95)	1.83	–2.13*	–0.12
Orgasm	6.89 (3.69)	8.71 (2.73)	8.16 (3.41)	2.24*	–3.09**	–0.93
Sexual desire	6.11 (2.23)	7.39 (1.70)	6.86 (1.98)	–1.85	3.39**	1.87
Sexual satisfaction	7.92 (4.94)	9.36 (4.47)	9.04 (5.08)	1.65	–1.80	0.01
Overall Satisfaction	6.28 (2.49)	7.54 (2.09)	7.47 (2.41)	–2.49*	2.83**	0.19
Total score	47.36 (20.60)	56.95 (16.69)	53.84 (20.39)	2.04*	–2.59*	–0.40

*$P < 0.05$, ** $P < 0.01$
†Active disease meant a Simple Clinical Colitis Activity Index total score or a HBI total score ≥5

Table 5 Mean Female Sexual Function Index scores (standard deviation) of patients with an active disease, patients in remission and controls

	Patients with active disease† N = 65	Patients in remission N = 100	Controls N = 106	Active versus Control *t*-value	Active versus remission *t*-value	Remission versus control *t*-value
Desire	3.03 (1.16)	3.09 (1.18)	3.19 (1.24)	–0.87	0.33	–0.61
Arousal	3.50 (1.96)	3.82 (1.88)	3.95 (1.78)	–1.54	1.04	–0.52
Lubrication	3.77 (2.15)	4.32 (2.21)	4.51 (2.20)	2.64**	–2.10*	0.48
Orgasm	3.71 (2.20)	4.08 (2.14)	4.17 (2.07)	1.54	–1.33	0.17
Satisfaction	4.14 (1.66)	4.46 (1.57)	4.41 (1.58)	0.89	–1.17	–0.34
Pain	3.25 (2.44)	4.39 (2.32)	4.33 (2.38)	3.33**	–3.48**	–0.22
Total score	21.39 (10.04)	24.16 (10.20)	24.34 (10.15)	2.30*	–2.13*	0.20

*$P < 0.05$, ** $P < 0.01$.
†Active disease meant a Simple Clinical Colitis Activity Index total score or a Harvey–Bradshaw Index total score ≥5. For one control, the lubrication score missed, and for eight controls, the satisfaction score

depression was a significant predictor, $\beta = -0.35$, $t = -6.26$, $P < 0.001$, and the relationship between sexual functioning and disease activity decreased in strength, from $\beta = -0.17$, $t = -3.03$, $P < 0.01$ to $\beta = -0.04$, $t = -0.81$, $P = 0.41$. And finally, in the mediation analysis with gender, age, relationship duration, body image, and disease activity being included together in the regression equation, body image was a significant predictor, $\beta = -0.20$, $t = -2.12$, $P < 0.001$, and the relationship between sexual functioning and disease activity decreased in strength, from $\beta = -0.16$, $t = -2.84$, $P < 0.01$ to $\beta = -0.08$, $t = -1.46$, $P = 0.15$. Bootstrapping the indirect effects of these univariate mediators on sexual functioning using 5.000 bootstrap samples, indicated that quality of life, fatigue, depression, and body image all significantly mediated the relationship between sexual functioning and disease activity. When, however, as a next step, these four mediating variables were entered together in one

Table 6 Correlations between sexual function, demographic variables, disease activity, and putative mediators in male and female patients

	Sexual function	Quality of life	Fatigue	Depression	Body image
Age	–0.31**	0.21**	–0.05	–0.01	–0.18**
Gender	–0.03	–0.24**	0.15*	0.02	–0.18**
Relationship duration	–0.29**	0.21**	–0.09	–0.01	–0.18**
Disease activity	–0.18**	–0.51**	0.43**	0.36**	0.38**
Quality of life	0.25**	—	–0.34**	–0.63**	–0.67**
Fatigue	–0.34**	–0.76**	—	0.69**	0.55**
Depression	–0.37**	–0.63**	0.69**	—	0.54**
Body image	–0.19**	–0.67**	0.55**	0.54**	—

N varies from 274 to 281, *$P < 0.05$, **$P < 0.01$

Table 7 Regression models with only control variables included, control variables plus disease activity included, and control variables, disease activity, plus putative mediating variables included

Predictor	Beta	*t*-value	*P* value
Model 1			
Constant		2.28	0.023
Gender	0.13	2.10	0.036
Relationship duration	–0.09	–0.99	0.324
Age	–0.25	–2.44	0.015
Model 2			
Constant		2.68	0.008
Gender	0.12	1.93	0.055
Relationship duration	–0.13	–1.28	0.201
Age	–0.22	–2.20	0.028
Disease activity	–0.16	–2.84	0.005
Model 3			
Constant		1.32	0.189
Gender	0.09	1.56	0.119
Relationship duration	–0.13	–1.35	0.179
Age	–0.25	–2.57	0.011
Disease activity	0.01	0.06	0.950
Quality of life	0.02	0.71	0.476
Fatigue	–0.15	–1.65	0.101
Depression	0.07	–3.00	0.003
Body image	–0.23	0.32	0.747

Total model 1 $R^2 = 0.10$, $F(3,270) = 10,34$, $P < 0.001$; total model 2 $R^2 = 0.13$, $F(4,269) = 9.97$, $P < 0.001$; total model 3 $R^2 = 0.25$, $F(8,265) = 11.25$, $P < 0.001$.

model, depression appeared as the only significant mediator (see Table 7). In fact, the model with gender, age, relationships, and depression entered explained an equal amount of variance, $R^2 = 0.25$, $F(5,277) = 18.17$, $P < 0.001$, compared with the model with the control variables and quality of life, fatigue, depression, and body image entered, $R^2 = 0.25$, $F(8,273) = 11.25$, $P < 0.001$. Bootstrapping the indirect effects of depression on sexual functioning using 5.000 bootstrap samples, depression proved to be a significant mediator of disease activity in sexual functioning, while controlling for gender, age, and relationship duration. The results indicate that the differences in sexual functioning between patients with and without active disease were totally mediated by depression.

Discussion

The present study does not show a higher prevalence of sexual dysfunction in patients with IBD compared with controls. However, significantly more male and female patients with active IBD scored within the sexual dysfunctional range compared with patients in remission or healthy controls. More male patients with active disease had a sexual dysfunction, in comparison with male patients in remission. Male patients with active disease scored lower on orgasm and overall sexual satisfaction compared with controls, and scored lower on erectile function, orgasm, desire, and sexual satisfaction compared with patients in remission. More female patients with active disease had a sexual dysfunction compared with patients in remission and controls. Female patients with active disease scored lower on the FSFI lubrication and pain domains compared with patients in remission and controls, indicating more problems with lubrication and pain during intercourse. The association of disease activity and sexual function was totally mediated by depression.

In our IBD patient group (both CD and UC), a relatively high percentage of patients had active disease (31% of the men and 39% of the women). Other studies reported comparable percentages of patients with active disease (26% of the men and 35% of the women) [11,14]. The response rates in the tertiary referral center and general hospital were 26% and 20%.

Our findings support the results reported in other studies. Timmer et al. [11] reported that disease activity had a significant influence on sexual functioning. The greatest influence was found on the subscales orgasm and sexual desire. It was also previously reported that male patients in remission scored comparably on the IIEF as controls [15]. Moody reported more dyspareunia in female CD patients, which is in accordance with our study, in which we found that women with an active disease reported more complaints of pain during intercourse [5].

In agreement with the results of studies from Timmer et al. [11,14,15], we found that depressive symptoms are strongly associated with sexual dysfunction. Depression was even the only factor that significantly mediated the association between disease activity and sexual function. Although patients with active disease reported, apart from higher levels of depressive mood, also higher levels of fatigue, lower disease-related quality of life, and a more negative body image, and these variables were all associated with worse sexual functioning, the effect of active disease on sexual functioning was mediated only by depression. This indicates that active IBD impacts sexual functioning mainly through the impact of active disease on mood, corroborating with other studies pointing to an important role of depression in the negative effects of chronic somatic disease on sexual functioning [5,40,41]. Depression may possibly, through the effect of negative thinking, influence the percep-

tion and also reporting of sexual functioning. However, it likely affects sexual functioning via various cognitive, neurobiological, interpersonal, and intrapersonal mechanisms, which are to date largely unknown.

Regarding depressive symptoms, we observed a difference in the prevalence of depression between IBD patients with active disease and controls, which is similar to a review from 2009, where depression was more often found in IBD patients than in controls [1]. This review discussed population-based studies as well as studies comparing clinical samples with controls, and there was no statement made about the severity of the disease.

Regarding fatigue, our results are in agreement with the study by Minderhoud et al. [35], who also found significant differences with the MFI-20 between patients with an active disease and patients in remission. And Jelsness-Jorgensen [42] reported that half of the patients with IBD experienced substantial fatigue, measured with the Fatigue Questionnaire (FQ). Taken together, it seems that more patients with active IBD suffer from fatigue, are depressed, and have sexual problems. Unfortunately the FQ was not presented to the control population, so it is difficult to draw conclusions about the extent of fatigue in comparison with a general population. As patients in remission score comparable with—or even better than—controls on depression and sexual function, it is likely that the emotional and sexual problems patients experience while their disease is active decrease when disease activity decreases. Strikingly, the data indicate that in men, mood and sexual functioning are even better in patients in remission compared with healthy controls. Possibly male patients in remission compare their mood and sexual functioning with their mood and sexual functioning during active disease and perceive their functioning more positive because of a contrast effect. Another explanation may be that male patients in remission take advantage of their better physical condition, by employing more pleasurable activities and sexual activities, which may facilitate mood and sexual satisfaction.

We should discuss several limitations of our study. One limitation is the low response rate for both the patients and the controls. This impairs the generalizability of the study results. Since no information was obtained about the demographic characteristics of the patients or controls not willing to participate, we do not know whether specific groups were less represented in our study groups. It should also be noted that in our study, a high proportion of controls reported sexual problems. A possible explanation for this high fraction could be self-selection bias. Possibly, mainly individuals with sexual problems decided to participate because they recognize the importance of research on sexual functioning. However, this may also be the case in the IBD patients. The female control group scored 20% lower on the FSFI than the control group in the Rosen et al. study [20]. And in comparison with a European control group, our female control group scored 16% lower on the FSFI [43]. The same is for the male control group, our control group scored 10% lower than the control group of Rosen [17]. It cannot be ruled out that the exceptional high percentage of our controls reporting sexual problems may have obscured a difference in prevalence of sexual dysfunction between patients with IBD and healthy persons. However, our results are in agreement with other studies in which no difference was observed in sexual function scores between patients with IBD and healthy controls, and where sexual dysfunction was more often present only in patients with IBD with an active disease [11,14,15]. In addition, it is remarkable that no significant difference was found in sexual desire scores between female patients with active disease and controls, while these patients had more often depressive symptoms than controls. An explanation could be that desire problems are generally the most reported sexual problem in women [44–46], and that because of low desire scores in both patients and controls, a floor effect hampered the observation of significant differences among groups. It seems that in the female patient population, active disease had the strongest effect on lubrication and pain. Possibly, complaints such as gas and diarrhea, cause increased tension in the pelvic floor muscles, which may result in pain during intercourse, and possibly because of fear of pain, in lubrication problems [47]. To examine the possible effect of active disease on pelvic floor functioning and sexual complaints, it will be interesting to include a measure of pelvic floor hyperactivity in future studies [48].

Another limitation of our study is that people without a steady relationship were excluded from participation, because not having a relationship can influence the scores on the sexual function questionnaires. The validated questionnaires that were used are more suitable to people with stable heterosexual relationships. Especially the FSFI, where women who did not have intercourse in the

last 4 weeks score very low, which will be seen as sexual dysfunction. It is however possible that there is a group of patients lacking a relationship because of their sexual problems. In that case, there could be an underestimation of sexual problems in the patient population. Also, the exclusion of patients lacking a relationship may have resulted in a relatively old study population, as younger people are more often without a steady partner. It could be that sexual problems play a bigger role in young patients who just started to be sexually active, and these patients may be underrepresented in our study. In addition, it should be noted that the IIEF, although presently the best validated and most widely used questionnaire for male sexual dysfunction, has a relative strong focus on erectile function. It may be less suited to measure other specific sexual dysfunctions, for example premature ejaculation. Therefore, it should be noted that orgasmic problems in the male subjects may have been detected less due to the use of the IIEF.

In conclusion, our data show that patients with active IBD can experience depressive feelings and that these are associated with sexual dysfunction. Depressive feelings and an impaired sexual function have an important impact on quality of life. It is important to ask patients about fatigue, mood, and sexual function, and refer them for psychological or sex-therapeutic treatment when needed.

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