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The impact of laparoscopic deep endometriosis surgery on sexual functioning and distress

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ABSTRACT

Background: Sexual functioning is a complex phenomenon driven by multiple physical, psychological and social factors, necessitating comprehensive evaluation.

Objectives: To assess the impact of laparoscopic deep endometriosis (DE) surgery on sexual functioning and distress in comparison to healthy controls.

Methods: Retrospective cohort study including 125 sexually active women who underwent DE surgery and who completed patient-reported outcome measurements (PROMs) pre- and postoperatively. Postoperative data were compared to prospectively collected data from 134 healthy controls.

Main Outcome Measures: Postoperative female sexual function index (FSFI-9), including the FSFI-9 total score (percentage of best possible FSFI-9 score), and the Female Sexual Distress Scale-Revised score. Secondary outcomes included pain scores, depressive symptoms, quality of life (QoL), relational satisfaction and positive affect.

Results: Sexual functioning significantly improved across all domains (desire, arousal, lubrication, orgasm, satisfaction, pain, distress) after DE surgery. The FSFI-9 total score increased from 65% pre-operatively [mean 29.3 (27.2, 31.23)] to 75% at 3 months [mean 33.6 (32.3, 34.9), $P<0.001$)] and 74% at 6 months [mean 33.1 (31.0-35.0), $P<0.001$] after DE surgery, compared to 85% in healthy controls [mean 38.08 (37.21-38.87)]. In addition, an improvement in QoL, pain scores, depressive symptoms and positive affect was observed. Bowel surgery or reoperations did not affect postoperative sexual functioning. Compared to healthy controls, DE patients reported similar sexual functioning 3 months post-surgery, except for significantly lower sexual arousal, lubrication and pain. At 6 months, these differences persisted, with DE patients also reporting significantly lower sexual satisfaction, higher pain scores and poorer QoL across multiple domains compared to controls.

Conclusions: DE surgery (including bowel surgery) does significantly improve sexual functioning and distress. However, sexual functioning and distress remain inferior compared to healthy peers.

What is new? This study provides comprehensive pre- and postoperative PROMs to assess the impact of DE surgery on sexual functioning and to evaluate other key influencing factors.

Keywords: Sexual quality of life, laparoscopy, deep endometriosis, quality of life

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Introduction

Decreased sexual functioning is often observed in women with endometriosis.[1] Dyspareunia may be caused by endometriosis lesions located in the posterior vaginal fornix, the pouch of Douglas, the uterosacral ligaments or the rectum due to traction of scarred, inelastic and immobilised pelvic structures or pressure exerted on lesions within the fibrotic tissue.[2] Also, it is well-known that endometriosis is associated with pain symptoms, a reduced quality of life (QoL), social participation and mental health, which all may affect sexual functioning.[3-5]

While multiple studies demonstrate a positive effect of laparoscopic (deep) endometriosis resection on dyspareunia and sexual functioning, none provide a comprehensive view of the sexual and psychosocial functioning of either patients or healthy controls.[6-16] However, sexual functioning is a complex phenomenon driven by multiple physical, psychological and social factors which require holistic evaluation.[1,17] Hence, the methodology of the available studies, which often relied solely on the presentation of a single questionnaire to conclude on the sexual QoL, was identified earlier as an important weakness in the review on this topic.[17] This study aimed to examine the impact of deep endometriosis (DE) surgery, including bowel surgery, on sexual functioning and distress as primary outcomes, and on QoL, pain scores, relational satisfaction, depression and positive affect as secondary outcomes, in comparison to healthy controls.

Methods

This retrospective cohort study was conducted in a specialised endometriosis expertise centre in the Netherlands. All information for this study was obtained as part of standard clinical care and used for this research when informed consent was provided. Ethical approval was obtained from the Medical Ethics Committee Leiden Den Haag Delft (protocol number: P20.088, date: 30.05.2022).

Deep Endometriosis Patients

All women who 1) underwent DE surgery between January 2019 and December 2021, 2) completed the Female Sexual Functioning index-9 (FSFI-9) both before and after surgery, and 3) who consented to use of their patient-reported outcome measurements (PROMs) for research purposes, were selected. Inclusion criteria were: surgical confirmation of DE and being sexually active at the time of completing the FSFI-9 questionnaire before and after surgery. Exclusion criteria were: pregnancy and/or lactation, post-menopausal status, age <18 years, same-sex relationship, or cases where solely adenomyosis was diagnosed.

PROMs were sent (Questmanager, Philips) as part of the standard clinical care at the endometriosis expertise centre. All patients received questionnaires, an informed consent letter and explanatory information via email before their intake appointment. Patients were informed that questionnaires would be digitally sent at fixed intervals throughout their treatment trajectory and that the outcomes of the questionnaires would primarily be used for clinical purposes and secondarily for scientific research if the patient provided consent. Socio-demographic characteristics and clinical data were extracted from medical records, including surgical reports.

Healthy Controls

Healthy controls were recruited (December 2022-April 2023) through a database maintained by the department of sexology at the Leiden University Medical Centre, consisting of women (not patients) who expressed interest in participating in future medical research. They were sent an email with study information. In addition, participants were recruited through advertisement of the study (including a link to all study information) on social media platforms (the Instagram account of the Dutch Endometriosis Society and two sexologists). Responders were sent a digital link to an informed consent form, an inclusion and exclusion questionnaire and the PROMs using Castor EDC. The intake questionnaire was used to determine whether the healthy controls met the inclusion criteria: age 18-45, sexual activity in the preceding 4 weeks at time of completing the FSFI-9, no (prior) diagnosis of endometriosis, absence of (chronic) pain condition(s), a relationship with a heterosexual partner (for a minimum duration of three months) and understanding of the Dutch language. Exclusion criteria included pregnancy and/or lactation, post-menopausal status, malignancies and chronic diseases affecting the QoL. All women who met the inclusion criteria and who completed all questionnaires were offered a compensation of 10 euros.

Deep Endometriosis Surgery

Surgery was performed by experienced gynaecologists, abdominal surgeons and urologists, with more than 10 years of expertise. Laparoscopic DE resection was

performed according to the guidelines of the working group of the European Society for Gynaecological Endoscopy, European Society of Human Reproduction and Embryology and the World Endometriosis Society.[18] The goal of the surgery was to excise all (deep) endometriosis lesions, except for the uterus in cases of adenomyosis and a (future) wish to conceive, or when this was not deemed feasible (e.g., as determined by the surgeon), or when the patient did not consent to complete excision (e.g., in case of colorectal endometriosis). Whether complete resection of (deep) endometriosis was performed during the index surgery was documented and is presented in the results section. Bowel surgery was performed together with a specialised abdominal surgeon. Serosal shaving or superficial resection of endometriosis lesions from the bowel was performed in case the endometriosis was solely present within or on the serosa, without infiltrating the muscularis layer.[18] In case of infiltration of the muscularis, a more radical approach such as full thickness resection (discoid resection) or segmental bowel resection was necessary, depending on lesion(s) size, multifocality and the degree of infiltration.[18] During surgery, DE lesions were classified according to the #Enzian classification and the revised American Society for Reproductive Medicine.[19,20] Adenomyosis was diagnosed preoperatively through vaginal ultrasound based on the "Morphological Uterus Sonographic Assessment" criteria.[21] Postoperative complications were documented in accordance with the Clavien-Dindo (CD) classification, with CD IIIa-V considered as major complications.[22] The onset of a complication had to be within 6 weeks after surgery with the exception of lower anterior resection syndrome, which was also included as a post-operative complication, considering its impact on the patients' QoL.

Questionnaires

Please see the Supplementary for a detailed description of all included PROMs.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics version 29. Data distribution was assessed using histograms. Normally distributed data were presented as mean and standard deviation (SD), whereas non-normally distributed data were presented as median and interquartile range. In case of skewed PROMs outcomes, logarithmic transformation was performed to achieve a more normal distribution and to enable parametric testing. The geometric mean and 95%-confidence intervals obtained from the transformed data (which were converted back to the original scale) were provided.

A paired t-test was performed to compare pre- and post-surgical PROMs outcomes within the DE cohort. The post-surgical outcomes of the DE patients were compared to the healthy controls using univariate and multiple regression analysis. Multiple regression was performed to adjust for observed significance differences in baseline variables between the DE patients and healthy controls. Both non-adjusted and adjusted *P*-values were provided. Univariate regression analysis was also performed to assess the effect of bowel surgery and major post-surgical complications on sexual functioning. Pre- and post-surgical binary outcomes within the DE cohort were compared using the McNemar test. A Fisher's exact test was used to compare binary outcomes between the DE cohort and healthy controls. A *P*-value of <0.05 was considered statistically significant.

We did not perform a priori sample size calculation due to lack of access to effect size estimates based on the FSFI-9, which would have been necessary to demonstrate within-individual differences in sexual functioning pre- and post-surgery. However, we did perform a post-hoc power analysis. With our sample size of 125 pairs, we had 77% power to detect a mean of paired differences of 2.7 (corresponding to a 10% increase from median starting value of 27 on the original scale), applying the observed SD of paired differences on the original scale of 11.15 and with a significance level (alpha) of 0.05 using a two-sided paired t-test.

Results

Population

Between January 2019 and December 2021, a total of 125 women underwent DE surgery, completed a FSFI-9 questionnaire both prior to and after surgery and consented to use their completed PROMs for research. Women were excluded for multiple reasons, including lack of informed consent, absence of DE, same-sex relationship or non-sexually active status. The selection process for the DE patients is illustrated by Supplementary Figure 1. Among the healthy controls, 177 women responded to the e-mail or advertisement and were sent a link to the online questionnaires. Of these, 142 provided consent and completed the questionnaires. Subsequently, 8 women were excluded because they reported a chronic illness, completed the questionnaires twice or reported

not to be sexually active during the last 4 weeks at the time of questionnaire completion. Supplementary Figure 2 outlines the selection process for the control group.

Socio-demographic characteristics, comorbidities, abdominal surgical history and information on hormone or analgesic usage among the DE patients are presented in Table 1. Compared to the healthy controls, DE patients were significantly older (33.0 vs. 30.5 years, *P*=0.02), more often in a longer relationship (9 vs. 5 years, *P*<0.001) and living together with their partner (86% vs. 77%, *P*=0.02). Additionally, fewer DE patients reported being employed (75% vs. 87%, *P*=0.04), and the level of education was significantly lower among DE patients compared to the control group (tertiary education 42% vs. 88%, *P*<0.001). The majority of DE patients expressed a desire for future pregnancy (62%), of whom 30% had experienced subfertility in the preceding year. In addition, 46% of these patients had undergone previous endometriosis surgery, 61% were using hormones, and 93% used analgesics prior to surgery.

With regard to the (surgical) DE classification, most patients were diagnosed with endometriosis affecting the ligaments (#Enzian B, left 69% and right 67%) and adenomyosis (63%) (Table 2). In addition, bowel endometriosis was present in the majority of patients (#Enzian C 50%, #Enzian FI 29%).

Table 1. Baseline characteristics.

	DE patients n=125	**Healthy controls n=134**	***P*-value**
Age[a] (years), median (IQR)	33.0 (29.0-38.5)	30.5 (28.0-36.0)	0.02
BMI (kg/m²), median (IQR)	23.8 (21.7-27.2)		
Male partner, n (%)	114 (91.2%)	134 (100%)	
Unknown[b], n (%)	11 (8.8%)	0 (0%)	
Living together with a partner, n (%)	107 (85.6%)	103 (76.9%)	0.02
Unknown[b], n (%)	4 (3.2%)	0 (0%)	
Duration of relationship (years), median (IQR)	9.0 (4.5-14.0)	5.0 (2.0-10.0)	<0.001
Unknown[b], n (%)	36 (28.8%)	1 (0.8%)	
Nulliparous, n (%)	87 (69.6%)	86 (64.2%)	0.36
Active or future pregnancy wish, n (%)	77 (61.6%)	71 (53.0%)	0.18
Unknown[b], n (%)	1 (0.8%)	0 (0%)	
Subfertility in the year prior to surgery, n (%)	37 (29.6%)		
Unknown[b], n (%)	1 (0.8%)		
Working, n (%)	94 (75.2%)	116 (86.6%)	0.04
Unknown[b], n (%)	2 (1.6%)	0 (0%)	
Highest education, n (%)			
Primary education[c]	0 (0%)	0 (0%)	
Secondary education[c]	54 (43.2%)	16 (11.9%)	<0.001
Tertiary education[c]	53 (42.4%)	118 (88.1%)	<0.001
Unknown[b], n (%)	18 (14.4%)	0 (0%)	
Comorbidities, n (%)			
Pain syndromes[1]	9 (7.2%)		
Rheumatoid arthritis	1 (0.8%)		
Gastro-intestinal[2]	24 (19.2%)		
Psychiatric[3]	25 (20%)		
Gynaecological[4]	2 (1.6%)		
Prior abdominal surgery (excluding endometriosis surgery), n (%)			
None	86 (68.8%)		

Table 1. Continued

	DE patients n=125	Healthy controls n=134	*P*-value
Laparoscopic surgery	30 (24.0%)		
1	28 (22.4%)		
2	2 (1.6%)		
Laparotomic surgery	17 (13.6%)		
1	15 (12.0)		
≥ 2	2 (1.6%)		
Prior endometriosis surgery, n (%)			
None	68 (54.4%)		
Laparoscopic surgery	56 (44.8%)		
1	40 (32.0%)		
≥ 2	16 (12.8%)		
Laparotomic surgery	2 (1.6%)		
1	2 (1.6%)		
Use of hormones prior to surgery, n (%)	76 (60.8%)		
Progestogen-only	11 (8.8%)		
COC	41 (32.8%)		
IUD[5]	7 (5.6%)		
GnRH analogue	18 (14.4%)		
Other[6]	2 (1.6%)		
Use of analgetic medication prior to surgery, n (%)	116 (92.8%)		
Paracetamol	99 (79.2%)		
NSAIDs	86 (68.8%)		
Opioids	14 (11.2%)		
Other[7]	5 (4.0%)		
Unknown[b], n (%)	3 (2.4%)		

[a]Age at the moment of filling in the FSFI-9 questionnaire prior to surgery. [b]Based on the electronic patient file. [c]Education levels are defined following the International Standard Classification of Education (ISCED), primary education is defined as ISCED level 1, secondary education as ISCED level 2-4 and Tertiary education as ISCED level 5-7. [1]Fibromyalgia (n=4), sciatica lumbago (n=4), hip dysplasia treated with a Ganz osteotomy surgery (n=1), chronic pain syndrome (n=1). [2]Irritable bowel syndrome (n=20), Crohn's disease (2), colostomy due to endometriosis (n=1), colostomy due to fistula formation (n=1), ileostomy due to ileus (n=1). [3]History of depression (n=10), anxiety and/or panic disorder (n=5), post-traumatic stress disorder (n=2), bipolar disorder (n=1), suicide attempt (n=1), burn-out (n=3), anorexia (n=2), under treatment of a psychiatrist or psychologist due to mood disorders (n=3). [4]Lichen sclerosis (n=1), pre-menstrual syndrome (n=1). [5]Levonorgestel-releasing IUD (n=6), copper IUD (n=1). [6]Clomid (n=1), etonogestrel/ethinyl estradiol vaginal ring (n=1). [7]Nerve block (n=1), cannabis (n=4).
BMI: Body mass index, COC: Combined oral contraceptive, GnRH: Gonadotropin-releasing hormone, FSFI: Female Sexual Functioning index, IQR: Interquartile range, IUD: Intrauterine device, NSAID: Non-steroidal anti-inflammatory drug, DED: deep endometriosis.

Surgical Characteristics

Complete resection of all DE lesions was performed in 94% of surgeries (Table 2). Incomplete resection was performed due to the following reasons: the patient did not consent to the resection of bowel endometriosis (3.2%), and the need to remove diaphragm endometriosis and DE in two separate surgeries (2.4%). In addition, among patients who underwent bowel surgery (56%), segmental resection was performed in 69% of cases. A hysterectomy was performed in 28% of DE patients. In 36% of patients, an adenomyotic uterus was left *in situ* due to a (future) desire for children. Following surgery, 42% used hormonal medication. In total, 21 women (17%) experienced post-surgical complication(s), with 9 women (7%) who had a major post-surgical complication requiring re-operation (CD IIIb) (Supplementary Table 1).

Table 2. Characteristics of deep endometriosis (surgery).

	n=125
Indication surgery, n (%)	
Pain	95 (76.0%)
Combination pain and subfertility	28 (22.4%)
Subfertility	1 (0.8%)
Stenotic ureter lesion	1 (0.8%)
#Enzian classification surgical, n (%)	
A(vagina)[a]	41 (32.8%)
<1 cm	3 (2.4%)
1-3 cm	12 (9.6%)
>3 cm	26 (20.8%)
B (ligaments) left[a]	86 (68.8%)
<1 cm	2 (1.6%)
1-3 cm	51 (40.8%)
> 3 cm	33 (26.4%)
B (ligaments) right[a]	84 (67.2%)
<1 cm	2 (1.6%)
1-3 cm	50 (4.0%)
>3 cm	32 (25.6%)
C (rectum)[a]	62 (49.6%)
<1 cm	5 (4.0%)
1-3 cm	18 (14.4%)
>3 cm	39 (31.2%)
Pre-operative FA (adenomyosis) according to MUSA criteria	79 (63.2%)
FB (bladder)	31 (24.8%)
FI (intestinal)	36 (28.8%)
FU (ureter)	26 (20.8%)
FO (diaphragm)	6 (4.8%)
FO (sciatic nerve)	1 (0.8%)
Presence of endometrioma(s), n (%)	47 (37.6%)
Pathological confirmation of endometriosis*, n (%)	123 (98.4%)
rASRM classification surgical[b], n (%)	
1	18 (14.4%)
2	24 (19.2%)
3	28 (22.4%)
4	53 (42.4%)
Opening of the vagina during surgery, n (%)	53 (42.4%)
Women who underwent hysterectomy	35 (28.0%)
Bowel surgery, n (%)	70 (56.0%)
Shave	20 (16.0%)
Disc resection	2 (1.6%)
Segment resection	48 (38.4%)
Complete resection during surgery, n (%)	118 (94.4%)
Underwent additional endometriosis surgery in follow-up period after surgery, n (%)	23 (18.4%)
Median follow-up period in months, median (IQR)	17.0 (7.0-32.0)
Hormonal therapy after surgery, n (%)	53 (42.4%)
Unknown[d]	7 (5.6%)

[a]Not available (n=3). [b]Not available (n=2). [c]Separate video-assisted thoracoscopic surgery to remove endometriosis from diaphragm (n=2), to prevent fistula formation, a lower anterior resection and resection of endometriosis lesions in the vagina and bladder were performed in 2 separate surgeries (n=1). [d]Based on the electronic patient file. *Only coagulation was performed during the index surgery (n=1); no endometriosis was found in the provided tissue (n=1).
rASRM: Revised American Society for Reproductive Medicine, MUSA: Morphological Uterus Sonographic Assessment, IQR: Interquartile range.

The Impact of DE Surgery on Sexual Functioning and Distress

Figure 1 and Supplementary Table 2 illustrate the FSFI-9 and sexual distress scores both before and after DE surgery at 3 (n=125) and 6 (n=65) months of follow-up in comparison to healthy controls.

3 Month Follow-Up

Patients reported significant improvements in sexual functioning across all domains of the FSFI-9. At 3 months post-surgery, significantly fewer DE patients were classified as having low sexual functioning or having high sexual distress. While DE patients had similar post-surgical scores for sexual desire, orgasm, satisfaction and distress compared to healthy controls, healthy controls reported a significantly higher total FSFI-9 score, along with significantly better scores for sexual arousal, lubrication and pain. Furthermore, fewer women in the healthy control group were classified as having low sexual functioning compared to DE patients (Figure 1 and Supplementary Table 2).

6 Month Follow-Up

At the 6-month follow-up, 53% of DE patients completed the FSFI-9 questionnaire. Significant improvements in sexual functioning were observed across all domains of the FSFI-9 compared to baseline. However, the significant improvement in low sexual functioning or having high sexual distress, compared to the pre-surgical situation

and 3-month follow-up, was no longer observed. In comparison to the healthy controls, DE patients reported similar scores for sexual desire, orgasm and distress 6 months following DE surgery. However, DE patients reported significantly lower FSFI-9 total scores, as well as significantly worse scores for sexual arousal, lubrication, satisfaction and pain compared to healthy controls. In addition, the number of women reporting high sexual distress and classified as having low sexual functioning was significantly higher 6 months following DE surgery compared to controls.

The FSFI-9 total score of 65% pre-surgically [mean 29.3 (27.2, 31.23)], increased to 75% at 3 months [mean 33.6 (32.3, 34.9)] and 74% at 6 months [mean 33.1 (31.0-35.0)] after DE surgery. In comparison, healthy controls reported a percentage of 85% on the FSFI-9 total score [mean 38.08 (37.21-38.87)].

The Impact of DE Surgery on Pain Scores, QOL, Relational Satisfaction, Depression and Positive Affect

Figure 2 and Supplementary Table 3 illustrate the pain scores, QoL scores, scores for relational satisfaction, depression and positive affect at 3 and 6-month follow-up in comparison to healthy controls.

DE patients reported significantly lower scores for dysmenorrhea, dyspareunia, chronic pelvic pain, dyschezia, dysuria and depression 3 and 6 months post-surgery (Figure 2 and Supplementary Table 3). In addition, three months post-surgery, QoL had significantly improved across all domains of the Endometriosis Health Profile (EHP)-30. However, at 6-month follow-up, the significant improvements in the social support and self-image domains of the EHP-30 were no longer observed.

Among those who remained in a relationship during the treatment trajectory, relational satisfaction remained stable. In some cases, the relationship was ended post-

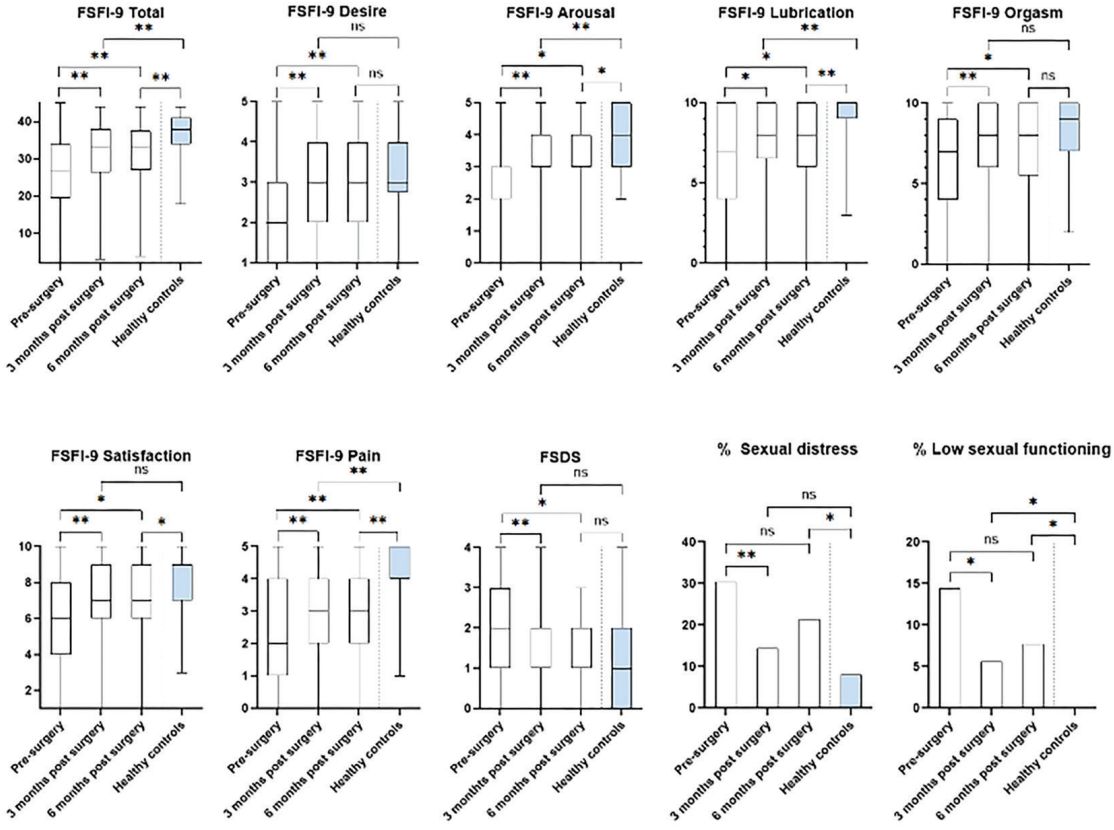

Figure 1. Sexual functioning and distress pre- and post-deep endometriosis surgery in comparison to healthy controls. Boxplots are illustrated. The adjusted p-values from the statistical analysis comparing deep endometriosis (DE) patients and controls are presented (see Supplementary Table 1). *P*-value controls vs. DE patients 3 and 6 months post-surgery were adjusted for age, living together (yes or no), duration of relationship, nulliparous (yes or no), future wish to conceive (yes or no), working (yes or no), and secondary education (yes or no) using multiple regression analysis.

FSFI-9: Female Sexual Functioning index-9, FSDS: Female Sexual Distress scale.

surgery (Supplementary Table 3). Furthermore, following surgery, DE patients experienced a significant increase in positive affect at 3 months post-surgery. However, this improvement was no longer observed at 6 months post-surgery. Despite all these improvements in PROMs among DE patients, most scores remained significantly lower in comparison to the control group, except for emotional well-being 3 and 6 months post-surgery, self-image 3 months post-surgery, depression 3 and 6 months post-surgery and positive affect 6 months post-surgery (Figure 2 and Supplementary Table 3). Relational satisfaction was significantly higher among DE patients 3 months post-DE surgery, but at 6 months, both groups reported similar scores for relational satisfaction.

Furthermore, post-operative sexual functioning was not negatively affected by bowel surgery, nor was it affected by the occurrence of major post-operative complications when compared to their peer DE patients (Supplementary Table 4).

Discussion

Our results demonstrate a significant improvement in sexual functioning 3 and 6 months after DE surgery. This was accompanied by improvement in pain scores, QoL, depressive symptoms, positive affect and stable relational satisfaction. In comparison to healthy controls, post-surgical DE patients reported similar scores in several domains of sexual functioning (desire, orgasm,

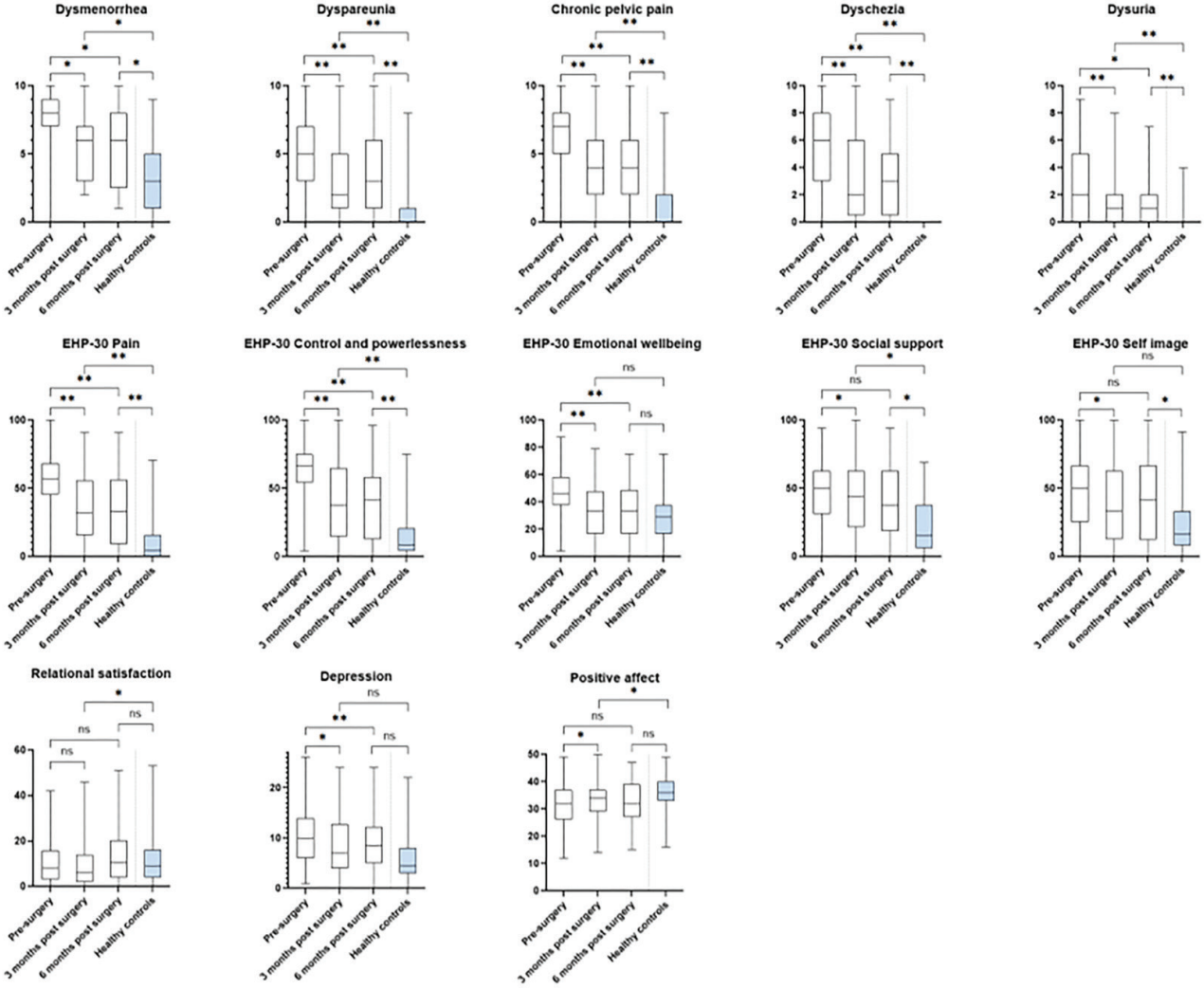

Figure 2. Numeric rating scale pain scores, quality of life (EHP-30), relational satisfaction, depression and positive affect pre- and post-deep endometriosis surgery in comparison to healthy controls. Boxplots are illustrated. The adjusted *P*-values from the statistical analysis comparing deep endometriosis (DE) patients and controls are presented (see Supplementary Table 2). *P*-value controls vs. DE patients 3 and 6 months post-surgery were adjusted for age, living together (yes or no), duration of relationship, nulliparous (yes or no), future wish to conceive (yes or no), working (yes or no), and secondary education (yes or no) using multiple regression analysis. EHP: Endometriosis Health Profile.

distress) 3 and 6 months after surgery. However, in other domains (arousal, lubrication, pain), DE patients scored significantly lower.

Sexual functioning is of importance for overall well-being and should therefore always be addressed when counselling patients (and their partners) for DE surgery.[1] Consistent with our findings, multiple studies demonstrate improvements in sexual functioning following (deep) endometriosis surgery.[9,14,15,23,24] However, these studies often lack data on relational satisfaction and psychosocial well-being and comparison against healthy controls, which may compromise the reliability of their results.

Whilst we observed a significant improvement in sexual functioning and distress following surgery, scores of DE patients remained significantly worse across several domains of sexual functioning compared to healthy controls. In contrast to our study, Martínez-Zamora et al.[6] demonstrated similar sexual and health-related QoL in DE patients compared to controls 6 months following surgery. This difference could be explained by more disease progression in our cohort compared to the study of Martínez-Zamora, as indicated by the relatively high percentage of patients who underwent bowel resection surgery in the current cohort (38%) compared to the cohort of Martínez-Zamora et al.[6] (9%). In addition, they excluded patients undergoing hysterectomy, which may also indicate less disease progression (no adenomyosis). However, direct comparison of classified disease severity is not possible as no endometriosis classification system was provided. Another explanation could be that their control group reported worse outcomes compared to those in our cohort.

Strengths and Limitations

Strengths of the current study are the use of a large number of PROMs in order to provide a holistic perspective on the overall well-being of the patients and controls, which is important to evaluate when assessing sexual functioning.[1] Furthermore, to our knowledge, no studies on this topic use the #Enzian criteria for surgical classification of DE.[6-17,19] This lack of standardisation makes clinical interpretation of the data challenging and hampers comparison between study cohorts.

Our study has several limitations that should be taken into account when interpreting the results. First, there is missing data in the endometriosis group (Supplementary Table 3). The burden of questionnaire completion may have been too high for some patients. This could explain why only 53% of DE patients completed the FSFI-9 questionnaire 6 months following surgery. Consequently, we cannot demonstrate whether the effect of DE surgery remains stable at 6 months follow-up, and it is questionable whether these results are representative of the entire cohort, as patients experiencing more severe symptoms may be more motivated to complete questionnaires. In addition, women who were not sexually active pre-surgically due to severe pain symptoms were not included in this study (no FSFI score available), while the effect of DE surgery would have been particularly interesting in this patient population. Considering the aforementioned limitations, had these patients been included and the follow-up completed, the effect of DE surgery would likely have been even more pronounced. Therefore, the results presented in this study might underestimate the true effect of DE surgery on sexual functioning and distress. This applies also to women in whom the adenomyosis was left *in situ*, given their future desire to conceive. Second, although our follow-up time is comparable to previous studies,[12,14] we recognise that it is relatively short and that a longer follow-up would be preferable. Third, information on other types of menstrual disorders beyond dysmenorrhea and on medications (e.g., antidepressants) affecting sexual function would have been of added value, as both may negatively impact sexual outcomes.[25,26] Nevertheless, these conditions are not primarily influenced by surgery. Finally, some of the observed postoperative sexual dysfunction may reflect non-endometriosis-related problems that were already present at baseline.

Conclusion

DE surgery significantly improves sexual functioning (FSFI-9 total from 65% to 75%, compared to 85% in healthy controls) and distress, independent of the occurrence of major post-operative complications and/or bowel surgery in the first six months after surgery.

Despite the significant improvement, sexual functioning in post-surgical DE patients does not reach the level observed in healthy controls. Future research is necessary to determine whether a holistic approach can optimise post-surgical sexual QoL of DE patients even further, aiming to achieve scores comparable to those of healthy controls. Surgery addresses the physical aspects affecting the sexual functioning of DE patients as demonstrated in our results. An additional holistic approach also focusing on psychological and social factors may further enhance overall outcomes, e.g., through consultation with a pelvic

floor physiotherapist and/or sexologist. Our findings are important to use during the counselling process in order to inform the patient on outcomes and expectations regarding sexual functioning and overall health following DE surgery.

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Data sharing: The data supporting this study will be made available upon reasonable request to the corresponding author.

Transparency: Hereby, I affirm (as corresponding author) that this manuscript is an honest, accurate, and transparent account of the study being reported. No important aspects of the study have been omitted. Discrepancies from the study as planned have been explained.

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Supplementary Data

Included Questionnaires

Sexual functioning was assessed using the FSFI-9, including six domains (desire, arousal, lubrication, orgasm, satisfaction and pain).[27] One more question was added to determine whether patients were sexually active around the time of completion. The total FSFI-9 score ranges from 2 to 45, with a higher score indicating better sexual functioning. Low sexual functioning was defined as a total score <15.[27.] To make findings applicable to usage in clinical practice, we calculated the FSFI-9 total score pre- and post-surgery as a percentage of the maximum possible score (45.0). To assess sexual distress, one item based on the Female Sexual Distress Scale-Revised (FSDS-R) was used: "How many times have you felt stressed or unhappy about your sex life in the past 4 weeks?". This was answered on a 5-point Likert scale from 0 (never) to 4 (always).[28] Sexual distress was defined as an FSDS-R score ≥3.

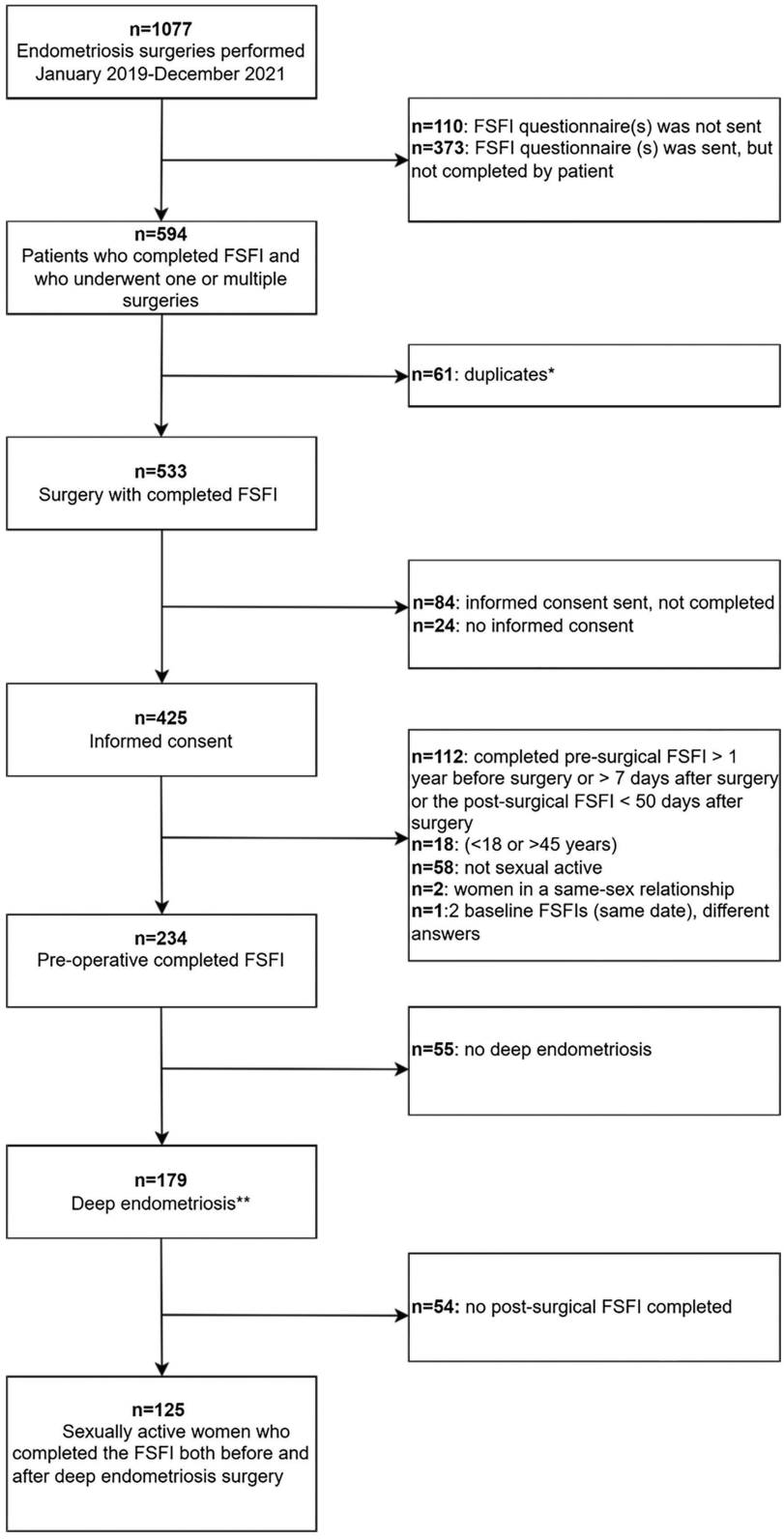
Endometriosis-associated QoL was examined using the Endometriosis Health Profile-30 (EHP-30) questionnaire, containing 5 domains: pain (11 items), control and powerlessness (6 items), emotional well-being (6 items), social support (4 items) and self-image (3 items), with the outcome ranging on a scale of 0 to100, with lower scores representing better QoL. For the healthy controls, the standard question "Because of your endometriosis, how often did you ..." was adjusted into "How often did you ...," as suggested by van de Burgt et al.[29]

Pain symptoms were assessed using the numeric rating scale scores for dysmenorrhea, dyspareunia, dyschezia, dysuria and chronic pelvic pain. The scale ranges from 0 (no pain) to 10 (worst pain imaginable).

Depressive symptoms were measured using the Patient Health Questionnaire-9. The total score ranges from 0 to 27 and can be classified in the following categories: no depression (0-4 points), mild depression (5-9 points), moderate depression (10-14 points), moderate to severe depression (15-19 points) and severe depression (20-27 points).[30]

Relational satisfaction was measured using the Maudsley Marital Questionnaire vsubscale, including 10 questions, with each item rated on a scale ranging from 0 (satisfied) to 8 (dissatisfied).[31]

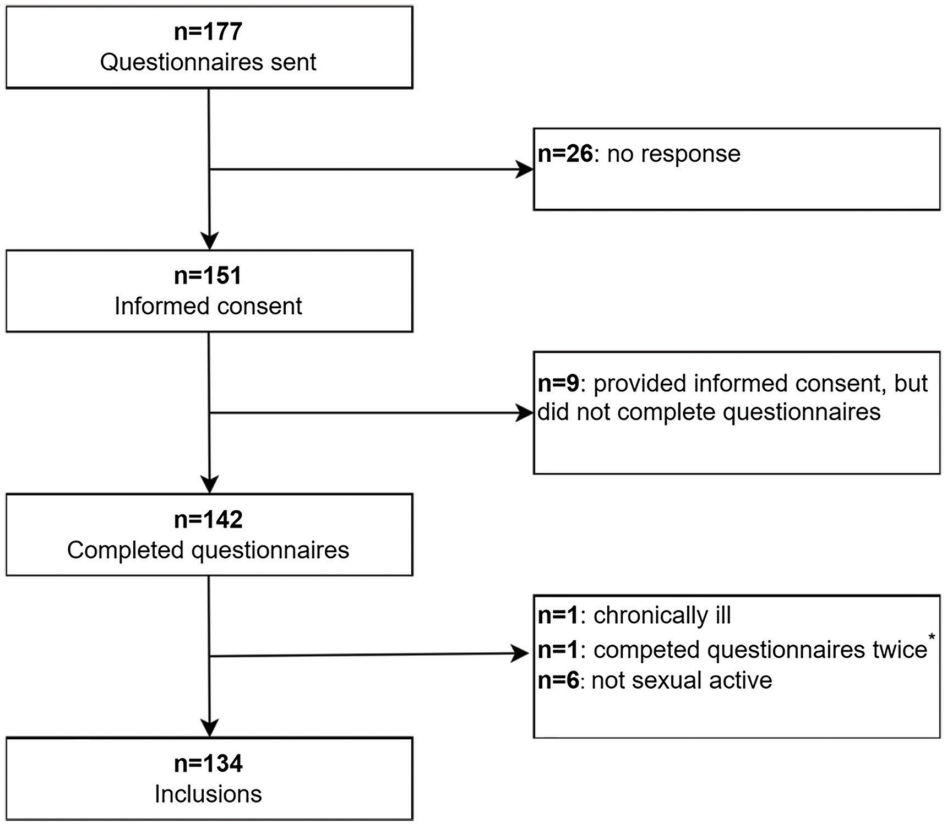
Positive affect was measured using the 10 items on positive affect which are part of Positive and Negative Affect Schedule.[32] Total scores range from 10 to 50, with higher scores representing more positive affect.



Supplementary Figure 1. Flow selection deep endometriosis patients.

*The same patient underwent multiple surgeries and completed the FSFI questionnaire before one single surgery (55 patients: 2 surgeries, 3 patients: 3 surgeries). **Deep endometriosis was confirmed during surgery.

FSFI: Female sexual functioning index.



Supplementary Figure 2. Flow selection healthy controls. *The most recently filled in questionnaires were used in the analysis.

Supplementary Table 1. Intra- and postoperative complications.		
	Total n=125	
Intraoperative complications, n (%)	**n=3 (2.4%)**	
Visceral	n=2 (1.6%)	
Other	n=1 (0.8%)	
Postoperative complications, n (%)	**n=21 patients (16.8%)** **n=29 post-operative complications**	**Clavien-Dindo classification***
Vaginal cuff dehiscence	n=2 (6.9%)	Grade IIIb
Urinary infection	n=4 (13.8%)	Grade II
Pyelonephritis	n=2 (6.9%)	Grade II
Pelvic abscess	n=1 (3.4%)	Grade II
Lower anterior resection syndrome	n=3 (10.3%)	Grade I
Infection of unknown cause treated with antibiotics	n=2 (6.9%)	Grade II
Pneumonia	n=1 (3.4%)	Grade II
Postdural puncture headache	n=2 (6.9%)	Grade II
Hydronephrosis	n=2 (6.9%)	Grade IIIb
Postoperative acute kidney injury	n=2 (6.9%)	Grade I
Ureterovaginal fistula	n=1 (3.4%)	Grade IIIb
Rectovaginal fistula	n=1 (3.4%)	Grade IIIb
Bowel injury	n=1 (3.4%)	Grade IIIb
Bladder injury	n=1 (3.4%)	Grade I
Hypotonic bladder	n=1 (3.4%)	Grade I
Acute endometritis**	n=1 (3.4%)	Grade IIIb
Infected hematoma	n=1 (3.4%)	Grade IIIb
Thrombophlebitis	n=1 (3.4%)	Grade II
*Complications were classified according to the Clavien-Dindo classification as described elsewhere.[22] **Laparoscopic surgery was done to rule out bowel injury.		

Supplementary Table 2. Sexual functioning and distress pre- and post-deep endometriosis surgery in comparison to healthy controls.

	Min-Max score	DE patients' prior surgery (n=125)	3 months post-surgery (n=125)	*P*-value	6 months post-surgery (n=65)	*P*-value	Healthy controls (n=134)	Non-adjusted *P*-value HC vs. DE 3 months post-surgery	Adjusted *P*-value HC vs. DE 3 months post-surgery	Non-adjusted *P*-value HC vs. DE 6 months post-surgery	Adjusted *P*-value HC vs. DE 6 months post-surgery
Days before or after surgery, median (IQR)		11.0 (6.0-13.0) 0.4 months	81.0 (71.0-185.0) 2.7 months		193.0 (171.5-357.5) 6.3 months						
FSFI-9, geometric mean (95% CI)											
Total score	2-45	29.31 [27.15,31.23]	33.62 [32.16,34.94]	<0.001[a]	33.13 [31.02,34.95]	<0.001[b]	38.08 [37.21,38.87]	<0.001[c]	<0.001[d]	<0.001[e]	<0.001[f]
Desire	1-5	2.46 [2.25,2.66]	3.02 [2.82,3.21]	<0.001[a]	3.05 [2.81,3.29]	<0.001[b]	3.21 [3.05,3.36]	0.12[c]	0.39[d]	0.27[e]	0.66[f]
Arousal	0-5	2.87 [2.62,3.11]	3.39 [3.20,3.57]	<0.001[a]	3.31 [3.03,3.57]	0.002[b]	3.98 [3.83,4.13]	<0.001[c]	<0.001[d]	<0.001[e]	0.001[f]
Lubrication	0-10	7.55 [7.02,8.01]	8.18 [7.81,8.51]	0.007[a]	8.19 [7.60,8.69]	0.02[b]	9.32 [9.15,9.49]	<0.001[c]	<0.001[d]	<0.001[e]	<0.001[f]
Orgasm	0-10	7.13 [6.56,7.64]	8.10 [7.69,8.48]	<0.001[a]	8.02 [7.40,8.56]	0.009[b]	8.52 [8.20-8.82]	0.096[c]	0.21[d]	0.11[e]	0.25[f]
Satisfaction	1-10	6.44 [5.93,6.91]	7.53 [7.14,7.90]	<0.001[a]	7.42 [6.87,7.92]	0.002[b]	8.52 [8.26,8.76]	<0.001[c]	0.11[d]	<0.001[e]	0.046[f]
Pain	0-5	2.80 [2.47,3.10]	3.45 [3.19,3.69]	<0.001[a]	3.28 [2.90,3.62]	<0.001[b]	4.58 [4.46,4.70]	<0.001[c]	<0.001[d]	<0.001[e]	<0.001[f]
FSDS-R, geometric mean (95% CI)	0-4	1.72 [1.94,1.52]	1.28 [1.47,1.10]	<0.001[a]	1.40 [1.69,1.14]	0.02[b]	1.0 [1.17,0.85]	0.03[c]	0.25[d]	0.01[e]	0.16[f]
								***P*-value**		***P*-value**	
Low sexual function[a], n (%)		n=18 (14.4%)	n=7 (5.6%)	0.01[g]	n=5 (7.7%)	0.07[h]	n=0 (0%)	0.01[i]		0.003[j]	
High sexual distress[b], n (%)		n=38 (30.4%)	n=18 (14.4%)	<0.001[g]	n=14 (21.5%)	0.06[h]	n=11 (8.2%)	0.120[i]		0.01[j]	

[a]Paired t-test 3 months post-surgery vs. baseline. [b]Paired t-test 6 months post-surgery vs. baseline. [c]Unadjusted *P*-value controls vs. DE patients 3 months post-surgery, univariable regression analysis. [d]*P*-value controls vs. DE patients 3 months post-surgery, adjusted for age, living together (yes or no), duration relationship, nulliparous (yes or no), future wish to conceive (yes or no), working (yes or no), secondary education (yes or no), multiple regression analysis. [e]Unadjusted *P*-value controls vs. DE patients 6 months post-surgery, univariable regression analysis. [f]*P*-value controls vs. DE patients 6 months post-surgery adjusted for age, living together (yes or no), duration relationship, nulliparous (yes or no), future wish to conceive (yes or no), working (yes or no), secondary education (yes or no), multiple regression analysis. [g]McNemar test 3 months post-surgery vs. baseline. [h]McNemar test 6 months post-surgery vs. baseline. [i]Fisher's exact test controls vs. DE patients 3 months post-surgery. [j]Fisher's exact test controls vs. DE patients 6 months post-surgery. HC: Healthy controls, DE: Deep endometriosis, FSDS: Female Sexual Distress scale, IQR: Interquartile range, CI: Confidence interval.

Supplementary Table 3. PROM outcomes pre- and post-deep endometriosis surgery in comparison to healthy controls.

	DE patients' prior surgery (n=125)	**3 months post-surgery**	***P*-value**	**6 months post-surgery**	***P*-value**	**Healthy controls (n=134)**	***P*-value HC vs DE 3 months post-surgery**	**Adjusted P-value HC vs DE 3 months post-surgery**	***P*-value HC vs DE 6 months post-surgery**	**Adjusted *P*-value HC vs DE 6 months post-surgery**
NRS pain scores	n=117	n=105		n=65						
Days before or after surgery, median (IQR)	10.0 (6.0-13.0)	81.0 (72.0-184.5)		193.0 (173.5-357.5)		NA				
	Min score: 0 (positive)	Max. score: 10 (negative)								
Dysmenorrhea, geometric mean [95% CI]	6.55 [5.75,7.43]	5.10 [4.40,5.89]	0.004[a]	4.91 [3.75,6.36]	0.003[b]	2.27 [1.91,2.67]	<0.001[c]	0.002[d]	<0.001[e]	0.008[f]
Dyspareunia	3.84 [3.22,4.54]	2.03 [1.61,2.51]	<0.001[a]	2.64 [2.01,3.40]	<0.001[b]	0.63 [0.46,0.82]	<0.001[c]	<0.001[d]	<0.001[e]	<0.001[f]
Chronic pelvic pain	5.80 [5.16,6.50]	3.28 [2.77,3.88]	<0.001[a]	3.74 [3.07,4.53]	<0.001[b]	0.72 [0.54,0.93]	<0.001[c]	<0.001[d]	<0.001[e]	<0.001[f]
Dyschezia	4.08 [3.43,4.82]	2.09 [1.63,2.62]	<0.001[a]	2.05 [1.50,2.72]	<0.001[b]	0.55 [0.40,0.71]	<0.001[c]	<0.001[d]	<0.001[e]	<0.001[f]
Dysuria	1.53 [1.17,1.94]	0.98 [0.72,1.28]	<0.001[a]	0.96 [0.66,1.31]	0.001[b]	0.07 [0.02,0.12]	<0.001[c]	<0.001[d]	<0.001[e]	<0.001[f]
EHP-30 core questionnaire	n=107	n=109		n=64						
Days before or after surgery, median (IQR)	127.0 (24.0-220.0)	81.0 (72.0-181.0),		182.5 (172.3-357.3)		NA				
	Min score: 0 (positive)	**Max score: 100 (negative)**								
EHP-30 Pain, geometric mean [95% CI]	51.02 [45.68,56.98]	22.87 [17.85,29.23]	<0.001[a]	18.59 [13.02,26.35]	<0.001[b]	3.58 [2.58,4.86]	<0.001[c]	<0.001[d]	<0.001[e]	<0.001[f]
EHP-30 control and powerlessness	60.25 [55.51,65.40]	26.66 [21.29,33.34]	<0.001[a]	25.26 [18.45,34.46]	<0.001[b]	7.91 [6.33,9.83]	<0.001[c]	<0.001[d]	<0.001[e]	<0.001[f]
EHP-30 emotional well-being	47.94 [44.84,51.03]	34.21 [30.12,38.31]	<0.001[a]	32.68 [27.61,37.75]	<0.001[b]	27.39 [24.75, 30.04]	0.50[c]	0.98[d]	0.91[e]	0.37[f]
EHP-30 social support	38.52 [32.19,46.07]	26.91 [21.17,34.13]	0.03[a]	24.46 [17.19,34.63]	0.13[b]	10.65 [8.11,13.90]	<0.001[c]	0.02[d]	<0.001[e]	0.007[f]
EHP-30 self-image	28.48 [22.04,36.71]	18.82 [13.88,25.40]	0.003[a]	21.21 [14.14,31.57]	0.122[b]	10.66 [8.18,13.80]	0.005[c]	0.20[d]	0.004[e]	0.02[f]
MMQ	n=112	n=119		n=68						
Days before or after surgery, median (IQR)	11.0 (6.0-13.0)	81.0 (71.0-182.0)		181.0 (172.0-356.5)		NA				

Supplementary Table 3. Continued

	DE patients' prior surgery (n=125)	3 months post-surgery	*P*-value	6 months post-surgery	*P*-value	Healthy controls (n=134)	*P*-value HC vs DE 3 months post-surgery	Adjusted P-value HC vs DE 3 months post-surgery	*P*-value HC vs DE 6 months post-surgery	Adjusted *P*-value HC vs DE 6 months post-surgery
	Min score: 0 (positive)	**Max. score: 80 (negative)**								
Relational satisfaction, geometric mean [95% CI] No relation	6.65 [5.34,8.22] n=0	5.88 [4.63,7.41] n=12	0.25[a]	8.36 [6.16,11.24] n=6	0.24[b]	7.77 [6.46,9.32]	0.06[c]	0.003[d]	0.67[e]	0.86[f]
PAS, median (IQR)	n=115	n=110		n=64						
Days before or after surgery, median (IQR)	10.0 (6.0-13.0)	81.0 (72.0-182.3)		216.5 (175.0-357.8)		NA				
	Min. score: 10 (negative)	**Max. score: 50 (positive)**								
Total score, mean [95% CI]	31.26 [29.90,32.62]	32.63 [31.25,34.00]	0.02[a]	32.36 [30.49,34.23]	0.10[b]	35.95 [34.94,36.96]	<0.001[c]	0.02[d]	<0.001[e]	0.07[f]
PHQ-9, median (IQR)	n=64	n=64		n=46						
Days before or after surgery, median (IQR)	11.0 (6.0-13.0)	78.0 (72.0-130.8)		178.0 (171.8-323.8)		NA				
	Min. score: 0 (positive)	**Max. score: 27 (negative)**								
Total score, geometric mean [95% CI] No depression, n (%) Mild depression, n (%) Moderate depression, n (%) Moderate severe depression, n (%) Severe depression, n (%)	9.25 [7.83,10.90] n=7 (10.9%) n=23 (35.9%) n=20 (31.3%) n=5 (7.8%) n=9 (14.1%)	6.76 [5.51,8.25] n=18 (28.1%) n=20 (31.3%) n=17 (26.6%) n=7 (10.9%) n=2 (3.1%)	0.001[a]	7.23 [5.65,9.18] n=9 (19.6%) n=17 (37.0%) n=14 (30.4%) n=3 (6.5%) n=3 (6.5%)	<0.001[b]	4.66 [4.07,5.31] n=67 (50.0%) n=46 (34.3%) n=14 (10.4%) n=4 (3.0%) n=3 (2.2%)	0.002[c]	0.11[d]	0.001[e]	0.053[f]

[a]Paired t-test 3 months post-surgery vs. baseline. [b]Paired t-test 6 months post-surgery vs. baseline. [c]Unadjusted *P*-value controls vs. DE patients 3 months post-surgery, univariable regression analysis. [d]*P*-value controls vs. DE patients 3 months post-surgery adjusted for age, living together (yes or no), duration relationship, nulliparous (yes or no), future wish to conceive (yes or no), working (yes or no), secondary education (yes or no), multiple regression analysis. [e]Unadjusted *P*-value controls vs. DE patients 6 months post-surgery, univariable regression analysis. [f]*P*-value controls vs. DE patients 6 months post-surgery adjusted for age, living together (yes or no), duration relationship, nulliparous (yes or no), future wish to conceive (yes or no), working (yes or no), secondary education (yes or no), multiple regression analysis. HC: Healthy controls, DE: Deep endometriosis, IQR: Interquartile range, CI: Confidence interval, EHP: Endometriosis health profile, Min: Minimum, Maximum, NRS: Numerical rating scale, MMQ: Maudsley Marital Questionnaire, PAS: Perceived anxiety scale, PHQ-9: Patient health questionnaire-9.

Supplementary Table 4. The impact of major postoperative complication(s) and bowel surgery on sexual functioning.

Surgical variable		n	FSFI-9 total score, 3 months post-surgery Geometric mean [95% CI]	*P*-value	n	FSFI-9 total score, 6 months post-surgery Geometric mean [95%CI]	*P*-value
Major postoperative complication(s) (CD 3B)	No	116	33.89 [32.39, 35.24]	0.17[a]	60	33.34 [31.12, 35.24]	0.46[a]
	Yes	9	29.68 [21.61, 35.19]		5	30.35 [19.60, 36.88]	
Bowel endometriosis surgery	No	55	33.52 [31.27, 35.45]	0.90[a]	26	32.97 [29.16, 35.96]	0.90[a]
	Yes	70	33.70 [31.65, 35.49]		39	33.23 [30.48, 35.52]	

[a]Univariate regression analysis. CD: Clavien-Dindo, FSFI-9: Female sexual function index-9, CI: Confidence interval.