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Original Article

Assessment of Long-Term Bowel Symptoms After Segmental Resection of Deeply Infiltrating Endometriosis: A Matched Cohort Study

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ABSTRACT **Study Objective:** To assess long-term bowel symptoms in women who underwent segmental bowel resection for deep-infiltrating endometriosis (DIE) compared with women who underwent resection of severe endometriosis without bowel resection.

Design: Cohort study with matched controls (Canadian Task Force classification II-2).

Setting: Cleveland Clinic.

Patients: 71 patients (36 cases and 35 controls).

Interventions: Patients who were at least 4 years out from undergoing segmental bowel resection due to DIE were matched with patients who had undergone resection of stage III/IV endometriosis without bowel resection. The patients completed validated questionnaires, and data were analyzed using the Wilcoxon rank-sum, χ^2, and Fisher exact tests.

Measurements and Main Results: The Bristol Stool Form Scale, Patient Assessment of Constipation Symptoms Questionnaire (PAC-SYM), and St Mark's Vaizey Fecal Incontinence Grading System were used to elicit information. The median duration of follow-up was 10.1 years (range, 4–18 years). The mean patient age and body mass index were comparable in the cases and the controls. A larger proportion of cases than controls reported new bowel symptoms (58% [21 of 36] vs 14% [5 of 35]; p = .001), as well as abdominal pain, incomplete bowel movements, and false alarms on the PAC-SYM questionnaire; however, total PAC-SYM and Vaizey Fecal Incontinence Grading System scores were similar in the 2 groups (median, 8 [interquartile range, 8–10] vs 8 [8–10]; p = .86). Similarly, the proportion of patients with normal stool consistency (Bristol Stool Form Scale score 2–6) was similar in the 2 groups (80.6% [29 of 36] vs 94.3% [33 of 35]; p = .59).

Conclusion: Segmental bowel resection for DIE may be associated with a higher incidence of new bowel symptoms (possibly due to abdominal pain, incomplete bowel movements, and/or false alarms), but not with worse constipation or fecal incontinence, compared with surgery without bowel resection. Journal of Minimally Invasive Gynecology (2016) 23, 753–759

Keywords: Constipation; Deep infiltrating endometriosis; Fecal incontinence; Segmental bowel resection; Severe endometriosis

Endometriosis is a significant cause of both infertility and pelvic pain. Deep infiltrating endometriosis (DIE) is a specific endometriotic lesion that extends more than 5 mm underneath the peritoneum [1]. Bowel endometriosis is a subtype of DIE and can be located in several locations along the intestines, including the rectum, rectosigmoid junction, colon, cecum, ileocecal junction, appendix, and small bowel [2]. The reported incidence of bowel endometriosis in women with endometriosis varies among studies, ranging from 5.3% to 12% [3,4].

The authors declare that they have no conflict of interest.

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Bowel endometriosis has been associated with gastrointestinal symptoms, such as diarrhea, constipation, rectal bleeding, proctitis, tenesmus, and colic rectal pain that can be chronic or menstrual-related. Bowel endometriosis also has been associated with noncyclic chronic pelvic pain [5]. Surgical removal of bowel endometriosis, often using a minimally invasive approach, can be offered to treat these symptoms [6].

Although bowel resection carriers significant risk to the patient, it can be offered to patients with DIE of the bowel who are experiencing severe symptoms. Bowel resection for endometriosis can be done open or with laparoscopic assistance, with similar outcomes [7]. Complications from the procedure can be considerable, including anemia requiring blood transfusion, anastomotic leakage, fistula formation, and bowel perforation or obstruction [8–10]. Given the significant morbidity associated with bowel resection, the symptomatic benefits need to outweigh the risks of surgery. Several studies with relatively short-term follow up (median <2 years) have shown that either operative technique can improve symptoms related to bowel endometriosis, with a resulting improved quality of life [7,9–11]; however, after bowel resection, patients may develop new bothersome symptoms related to the surgery, such as an increase in stools per day or, conversely, constipation or urinary retention [11,12]. Patients need to be informed of both the immediate operative risk and any long-term functional changes that could occur as a result of this procedure. The aim of this study was to evaluate the long-term (minimum 4 years) outcomes of patients who underwent segmental bowel resection due to DIE in comparison to controls. Primary outcomes included long-term bowel symptoms, and secondary outcomes included long-term outcome of endometriosis-related symptoms after bowel resection.

Materials and Methods

This was a matched cohort study involving women who underwent surgical resection of endometriosis between 1993 and 2007 at the Cleveland Clinic. The study protocol was approved by the Cleveland Clinic's Institutional Review Board (IRB 10-899). Procedure and diagnostic codes were used to perform a search for all patients undergoing surgery with a diagnosis of endometriosis between 1993 to 2007 at our institution. A separate electronic search was done to capture patients with endometriosis who underwent bowel resection with a diagnosis of endometriosis during the same time frame. The electronic or paper medical charts of all identified patients were reviewed. Cases were confirmed by reviewing operative and pathology reports. Additional cases that were missed from the initial electronic search were identified through manual review of the charts. Patients who had undergone bowel resection less than 4 years from the date of data collection were excluded. (At least 4 years of follow-up time were required for the study.) Also excluded were any patients who subsequently developed a primary or metastatic pelvic or abdominal malignancy. Potential controls were identified from the chart review and were used for the matching process.

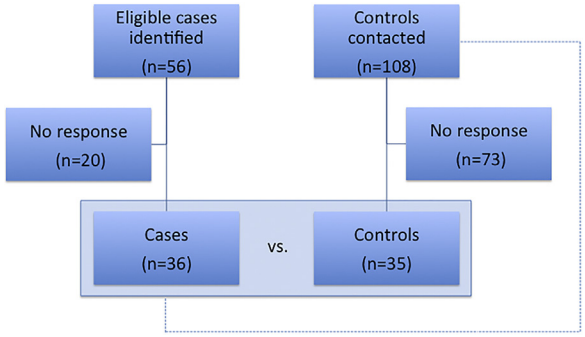
The control group consisted of patients with stage III/IV endometriosis who underwent surgical removal of disease without a bowel resection. These patients had no known endometriosis-related bowel disease and served to evaluate the overall long-term bowel function of patients with severe endometriosis. As with the cases, controls who had undergone surgery less than 4 years from the start of the study were excluded, as were those who subsequently developed a primary or metastatic pelvic or abdominal malignancy. If a patient had undergone more than 1 surgery for endometriosis, the most recent operation was used for matching purposes.

After demographic data were collected, a detailed questionnaire was sent by mail to the identified cases. Patients who did not respond to the initial contact attempt were sent a second questionnaire by mail and were contacted by telephone when this information was available. When the information obtained was incomplete, patients were subsequently contacted by telephone to obtain the missing information. The questionnaire elicited general information regarding indications for the initial surgery and whether additional medical and surgical treatment had been required since the bowel resection. Cases were then asked to rate the severity of symptoms related to endometriosis, such as dysmenorrhea and chronic pelvic pain, both before their surgery and currently. Finally, the survey contained validated and reliable questionnaires pertaining to current bowel function.

Three separate validated questionnaires were incorporated into the patient survey: the Bristol Stool Form Scale, the St. Mark's Vaizey Fecal Incontinence Grading System, and the Patient Assessment of Constipation Symptoms Questionnaire (PAC-SYM). The Bristol Stool Form Scale is a 7-point descriptive visual scale used to assess a patient's most common stool consistency. The patient selects his or her most common stool consistency based on images and text descriptions of the different stool forms, ranging from a separate hard lump to entirely liquid stool. The Bristol Scale Stool Form is a reliable assessment of stool consistency and has been found to correlate with complete gut transit time [13]. The St. Mark's Vaizey Fecal Incontinence Grading System is a standardized scoring system for assessing the severity of fecal incontinence. The questionnaire enquires about the frequency of incontinence of gas, liquid stool, and solid stool. It also assesses the frequency of urge, the use of pads or plugs, and the use of constipating medications to prevent incontinence. The responses are graded to provide an overall severity of fecal incontinence symptoms that have been found to be reproducible and sensitive to changes produced by treatments [14]. The third validated questionnaire included in the patient survey, the PAC-SYM, is designed to assess the severity of constipation. The patient answers 12 questions pertaining to constipation, including assessing for symptoms of incomplete emptying, small bowel movements, hard bowel

Fig

Patient flow diagram.



movements, straining, false alarms, and rectal bleeding. The PAC-SYM has found to be a highly reliable and valid tool for assessing constipation symptoms in adults [15]. Permission to use the PAC-SYM questionnaire in our survey was granted by the Janssen Research Foundation.

Once the surveys were returned by the case patients, matching was performed to identify adequate control patients. A logistic regression model was fit to the data using age and year of surgery as the independent variables and X as the dependent variable. Propensity scores were calculated from the model. Matching was performed using the R package "matching" under several different conditions; the caliper for matching was varied from 0.5 to 1.5 in increments of 0.25. Matching was done by ratios of 1-to-1, 2-to-1, 3-to-1, and 4-to-1, and subjects were matched without replacement. Each of these matched datasets was evaluated using Rubin's rules. Based on these evaluations, the 2-to-1

Table 1

Patient baseline characteristics

	Cases (n = 36)	Controls (n = 35)	p value
Age, yr, median (IQR)	37 (30.8–39)	34 (29.5–41.5)	.74*
BMI, median (IQR)	25 (22.3–30)	26.8 (21.9–31.5)	.90*
Race, n			.02†
Caucasian	25	31	
African-American	10	2	
Asian	0	0	
Hispanic	1	0	
Other/none listed	0	2	
Reason for surgery, n‡			
Dysmenorrhea	24	26	.66§
Chronic pelvic pain	17	12	.39§
Infertility	12	20	.07§
Bowel pain	24	11	.006§
Dysuria	6	3	.48†
Other	2	5	.26†

BMI = body mass index; IQR = interquartile range.
* Wilcoxon rank-sum test with continuity correction.
† Fisher exact test for count data.
‡ Multiple answers allowed in the questionnaire.
§ Pearson χ^2 test with Yates continuity correction.

Table 2

Symptom-specific questionnaire in relation to surgery

	Cases, n	Controls, n	p value*
Dysmenorrhea			.58
Improved	14	8	
Worsened	2	1	
Unchanged	2	3	
Chronic nonmenstrual pain			.15
Improved	20	12	
Worsened	3	1	
Unchanged	3	3	
Rectal bleeding			.04
Improved	11	3	
Worsened	3	1	
Unchanged	1	5	
Pain with bowel movement			.07
Improved	18	10	
Worsened	6	2	
Unchanged	2	4	
Constipation			.01
Improved	14	11	
Worsened	13	3	
Unchanged	2	5	
Lower back pain			.89
Improved	17	17	
Worsened	1	4	
Unchanged	4	3	
Diarrhea			.28
Improved	7	7	
Worsened	7	2	
Unchanged	2	5	

* Fisher exact test for count data.

Table 3

Postoperative status questionnaire

Question	Cases, n/N (%)	Controls, n/N (%)	p value
After surgery have you had:			
New bowel symptoms?	21/36 (58)	5/35 (14)	.001*
New urinary symptoms?	13/36 (36)	10/35 (29)	.67*
Diagnosis of irritable bowel syndrome?	6/36 (17)	5/35 (14)	.99†
Diagnosis of cancer?	1/36 (3)	1/35 (3)	.99†
Would you have the same surgery?	30/36 (83)	29/35 (83)	.74†

* Pearson χ^2 test with Yates continuity correction.
† Fisher exact test for count data.

Table 4

Bristol Stool Form Scale and PAC-SYM scores

Variable	Cases	Controls	p value
Normal Bristol Stool Form Scale (2–6), n/N (%)	29/36 (81)	33/35 (94)	.59*
Total PAC-SYM score, median (IQR)	9 (6–18.75)	4 (0–13)	.029†
PS discomfort in abdomen, n			.21*
Absent	15	19	
Mild	14	7	
Moderate	3	6	
Severe	4	2	
Very severe	0	1	
PS pain in abdomen, n			.005*
Absent	20	23	
Mild	12	3	
Moderate	0	6	
Severe	4	3	
Very severe	0	0	
PS bloating in abdomen, n			.63*
Absent	15	16	
Mild	11	7	
Moderate	5	8	
Severe	2	3	
Very severe	3	1	
PS stomach cramps, n			.11*
Absent	19	23	
Mild	12	5	
Moderate	1	5	
Severe	3	1	
Very severe	1	1	
PS painful bowel movements, n			.95*
Absent	19	23	
Mild	12	5	
Moderate	1	5	
Severe	3	1	
Very severe	1	1	
PS rectal burning, n			.34*
Absent	29	28	
Mild	3	4	
Moderate	1	3	
Severe	3	0	
Very severe	0	0	
PS rectal bleeding, n			.84*
Absent	28	29	
Mild	4	3	
Moderate	1	2	
Severe	2	0	
Very severe	1	1	
PS incomplete bowel movements, n			.017*
Absent	9	22	
Mild	11	6	
Moderate	11	4	
Severe	4	2	
Very severe	1	1	
PS hard bowel movements, n			.061*
Absent	14	21	
Mild	6	5	
Moderate	6	7	
Severe	9	1	
Very severe	1	1	
PS small bowel movements, n			.46*
Absent	14	17	
Mild	8	11	
Moderate	10	4	
Severe	3	2	
Very severe	1	1	
PS straining bowel movements, n			.21*
Absent	9	18	
Mild	8	5	
Moderate	10	8	
Severe	6	3	
Very severe	3	1	
PS false alarms, n			.015*
Absent	15	25	
Mild	12	3	
Moderate	4	6	
Severe	4	1	
Very severe	1	0	

IQR = interquartile range; PAC-SYM = Patient Assessment of Constipation Symptoms Questionnaire; PS = patient symptom.
* Fisher exact test for count data.
† Wilcoxon rank-sum test with continuity correction.

matching with a caliper of 1 provided the best match; however, because we could not guarantee that all subjects would respond to the survey, we performed 3-to-1 matching (Fig).

Once the control group surveys were returned, comparisons were performed using the Wilcoxon rank-sum test and the χ^2 test. In cases of small frequencies, comparisons were made using the Fisher exact tests. Results were considered statistically significant at a p value $\leq .05$. Univariate and multivariate analyses were conducted using R version 3 (R Project for Statistical Computing, Vienna, Austria). A linear mixed-effects model with matched groups serving as a random effect was applied for the multivariate analysis.

Results

The study population comprised 71 patients, including 36 cases and 35 controls. The overall response rate to the surveys was 43% (64% for cases and 32% for controls). The median duration of follow-up was 10.1 years (range, 4–18 years) for the cases and 10.2 years (range, 4–18 years) for the controls. The mean patient age and body mass index

(BMI) were comparable in the 2 groups (Table 1). The proportion of patients that were African-American patients was higher in the case group (27.8% [10 of 36] vs 5.7% [2 of 35]; p = .02). The proportion of patients with preoperative dyspareunia was comparable in the 2 groups (36.1% [13 of 36] vs 40% [14 of 35]; p = .80). The symptoms that patients listed as the reason of the surgery were similar in the 2 groups, except that more cases reported bowel pain as a reason (66.7% [24 of 36] vs 31.4% [11 of 35]; p = .006).

According to the questionnaire evaluating the progression of specific symptoms in relation to surgery, a larger proportion of cases had improved rectal bleeding compared with controls (30.6% [11 of 36] vs 8.6% [3 of 35]; p = .04) (Table 2). In addition, a larger proportion of cases reported worsened constipation (36.1% [13 of 36] vs 8.6% [3 of 35]; p = .04).

Analysis of the postoperative status questionnaire revealed a significantly higher proportion of new bowel symptoms in cases compared with controls (58.3% [21 of 36] vs 14.3% [5 of 35]; p = .001) (Table 3). Importantly, the proportion of patients stating that they would undergo the same surgery again was similar in the 2 groups (83.3% [30 of 36] of cases vs. 82.9% [29 of 35] of controls; p = .74). In addition, there were no significant between-group differences in the incidence of new urinary symptoms and in the diagnosis of irritable bowel syndrome or cancer.

The proportion of patients with normal stool consistency as rated by the Bristol Stool Form Scale Score of 2 to 6 was similar in the 2 groups (80.6% [29 of 36] of cases vs 94.3% [33 of 35] of controls; p = .59) (Table 4). Univariate analysis revealed a statistically higher total PAC-SYM score in the cases compared with the controls (median, 9 [interquartile range (IQR), 6–18.75] vs 4 [IQR, 0–13]; p = .029). Abdominal pain, incomplete bowel movements, and false alarms were statistically more frequent in the cases (Table 4); however, the median total PAC-SYM score was similar in the 2 groups when a linear mixed-effects model with matched groups serving as a random effect was applied (Table 5). The Vaizey Fecal Incontinence Grading System score was also similar in the cases and controls (median, 8 [IQR, 8–10] vs 8 [IQR, 8–10]; p = .86) (Table 6). Correspondingly, there were no differences in the individual symptoms reported on the Vaizey questionnaire and after application of the linear mixed-effects model (Table 5).

Table 5

Comparison of cases and controls using a univariate analysis vs a linear mixed-effects model with matched groups used as a random effect

	p value	
Variable	Univariate analysis	Linear mixed-effects model
New bowel symptoms	.001*	.001†
Normal Bristol Stool Form Scale score (2–6)	.59‡	.083†
Total PAC-SYM score, median	.029§	.36¶
Vaizey Fecal Incontinence Grading System score, median	.86§	.70¶

PAC-SYM = Patient Assessment of Constipation Symptoms Questionnaire.
* Pearson χ^2 test with Yates continuity correction.
† Generalized linear mixed-effects model (odds ratio, cases vs controls).
‡ Fisher exact test for count data.
§ Wilcoxon rank-sum test with continuity correction.
¶ Linear mixed-effects model (mean difference, cases vs controls).

Discussion

Our findings in this study suggest that undergoing segmental bowel resection for DIE may be associated with a higher incidence of new bowel symptoms (possibly due to abdominal pain, incomplete bowel movements, and/or false alarms), but not with worse constipation or fecal incontinence compared with surgery without bowel resection. The treatment for severe endometriosis, particularly in patients with DIE involving the bowel, is often complex and may require a multidisciplinary surgical approach for symptomatic patients who do not improve with medical treatment [16–18]. Several case series involving segmental bowel resection for DIE have been reported in the literature, but these have been limited owing to a lack of validated questionnaires, small sample size, or absence of a control group that did not undergo bowel surgery [10,19–28]. Moreover, some studies have lacked long-term follow-up [23,28]. The purpose of the present study was to compare the long-term outcomes of patients who underwent bowel resection for DIE and matched patients with severe endometriosis using validated condition-specific questionnaires.

The present study suggests that most patients who underwent surgical treatment for endometriosis (with [cases] or without [controls] bowel resection) experienced improvement in dysmenorrhea, chronic nonmenstrual pain, pain with bowel movements, and lower back pain. This improvement in symptoms was not statistically significantly different between the cases and the controls, however. In contrast, a larger proportion of cases than controls experienced reduced rectal bleeding after surgery. When patients were specifically asked about worsened constipation, a larger proportion of cases than controls reported this finding; however, assessment of these symptoms using a valid and reliable questionnaire (PAC-SYM) revealed no significant differences between the 2 groups. In addition, the cases and controls reported a similar proportion of normal stools as evaluated by the Bristol Stool Form Scale, indicating similar stool consistency and transit times. With respect to stool incontinence (Vaizey Fecal Incontinence Grading System), patients who underwent bowel resection did not report a higher incidence of fecal incontinence compared with controls.

Table 6

Vaizey Fecal Incontinence Grading System results

Variable	Cases	Controls	p value
Vaizey score, median (IQR)	8 (8–10)	8 (8–10)	.86*
Incontinence for solid stools, n			.25†
Never	28	32	
Rarely	0	1	
Sometimes	2	1	
Weekly	4	1	
Daily	2	0	
Incontinence for liquid stools, n			.21†
Never	27	30	
Rarely	2	4	
Sometimes	3	0	
Weekly	2	1	
Daily	2	0	
Incontinence for gas, n			.85†
Never	17	14	
Rarely	4	7	
Sometimes	7	6	
Weekly	2	3	
Daily	6	5	
Altered lifestyle, n			.23†
Never	27	32	
Rarely	3	2	
Sometimes	3	0	
Weekly	1	1	
Daily	2	0	
Pad or plug use, n			.11†
Yes	4	0	
No	32	35	
Constipating medication use, n			.36†
Yes	4	1	
No	32	34	
Inability to defer defecation for 15 min, n			.28†
Yes	12	7	
No	24	28	

IQR = interquartile range.
* Wilcoxon rank-sum test with continuity correction.
† Fisher exact test for count data.

Regarding patient satisfaction, a similar proportion of cases and controls reported that they would undergo the same surgery again. Nevertheless, the cases were more likely than the controls to report new bowel symptoms. Presumably, these symptoms were abdominal pain, incomplete bowel movements, and false alarms, which were statistically more frequent in the cases (Table 4). Before undergoing bowel resection, patients should be counseled about the risk of developing these new symptoms after surgery.

Limitations of the present study include the potential for selection or recall bias owing to the study's retrospective and single-institution design, relatively small sample size, and low response rate to the surveys. The small sample size was due to the strict inclusion criteria, that required at least a 4-year follow-up. Nonetheless, it is possible that this study was underpowered to detect smaller, clinically significant differences, or that these symptoms diminished over time after surgery. Moreover, other surgical modalities for treating DIE involving the bowel, such as shaving or discoid resection of lesions, were not performed and thus are not included in our analysis.

The low overall response rate to the surveys (43%) occurred despite systematic attempts to contact both cases and controls. An important contributing factor was the inability to contact many patients at the available address or a forwarding address, given the study's long time span (14 years).

Despite these limitations, however, this study represents an important addition to the literature given the distinctive strengths of long-term follow-up (median follow-up >10 years), use validated questionnaires, and inclusion of matched controls.

Future studies to evaluate the role of bowel surgery for DIE should consider including pain scores as well as overall quality of life markers in addition to validated bowel function questionnaires.

In conclusion, segmental bowel resection for DIE appears to be associated with a higher incidence of new bowel symptoms compared with surgery for advanced endometriosis without bowel resection (possibly owing to abdominal pain, incomplete bowel movements, and/or false alarms). The incidence of constipation or fecal incontinence is similar in these 2 groups of patients, however.

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