

Original article

Evaluation of long-term symptoms and recurrence of bowel nodules after resection of deep bowel endometriosis: A retrospective cohort study

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Abstract: *Background* — Bowel endometriosis nodules (BEN) result from an abnormal growth of endometrial fragments located on intestine causing visceral pain, scars, and organ adhesions. Deep endometriosis operation (DEO) is performed in case of deep infiltrating endometriosis (DIE) as a routine procedure for BEN excision. In this retrospective cohort study, the authors aimed to investigate the long-term symptoms and the recurrence rate of BEN in DIE women.

Methods — The cases were pooled into two groups based on presence of surgery of bowel endometriosis (SBE, n=32) and absence of surgery of bowel endometriosis (no-SBE, n=44). Using inclusion and exclusion criteria, we selected 76 DIE women from Arash Women's Hospital (Tehran, Iran). General patient information and surgery-related data were extracted from medical histories of DIE patients (2018-2021). Two years of postoperative follow-up were part of our study, and endometriosis symptoms, pelvic pain, and BEN recurrence rate were assessed. Data were analyzed using SPSS (v.19), and statistical significance was assumed at $p < 0.05$.

Results — No statistically significant ($p = 0.54$) differences were detected between two groups (SBE and no-SBE) regarding pain recurrence. In SBE group, 28.1% of DIE women exhibited BEN recurrence, while this proportion was 9.4% in no-SBE women that had larger size of BEN. Changes in BEN sizes were not significant ($p = 0.6$) as compared with pelvic pain.

Conclusion — No significant differences were found between long-term symptoms and recurrence of BEN in women with DIE after SBE and without SBE. Excision of BEN during surgical procedures is not recommended clinically.

Keywords: long-term, symptom, bowel, nodule, recurrence, deep endometriosis, operation, deep infiltrating endometriosis, cohort, Iran.

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Introduction

Endometriosis is a chronic, estrogen-dependent disorder characterized by ectopic implantation of functional endometrial tissue into the peritoneal cavity. Although the exact etiology of endometriosis is not fully understood, several hypotheses have been proposed, including coelomic metaplasia, stem cell migration, Müllerian duct remnants, as well as vascular and lymphatic metastasis [1]. The clinical diagnosis of endometriosis is a menstrual cycle-dependent disorder characterized by chronic inflammation, systemic diseases, and severe pelvic pain [2]. Treatment options include a number of medications such as nonsteroidal anti-inflammatory drugs (NSAIDs), hormonal agents (GnRH analogs), and contraceptive methods. Other surgical protocols include procedures such as excision of endometrial implants, uterosacral nerve ablation via endocoagulation, and hysterectomy. Deep infiltrating endometriosis (DIE) includes lesions extending more than 5 mm under the peritoneum [3]. In addition, DIE as a surgical intervention associated with endometriosis can be performed in various pelvic locations

including cul-de-sac, uterosacral ligaments, vaginal wall, and bowel [4]. Bowel endometriosis is a subtype of DIE occurring in multiple locations on the outer surface of the intestines [5]. This condition can result in pelvic pain, constipation, diarrhea and painful bowel movements. The natural history of DIE is still unclear [6]; thus, patient symptoms are not well assessed in medical references [7]. Recurrent bowel endometriosis nodules (BEN) in DIE status refers to the presence of endometriotic nodules in the bowel as the main feature of DIE. Medical treatment of endometriosis with bowel involvement is complex. The first-line treatment is medical therapy, while surgery is recommended in case of severe pain, bowel obstruction and desire to preserve fertility [8]. Medical treatment does not completely affect the fibrous components of endometriosis lesions [8], and there are serious concerns about disease progression, risk of bowel obstruction and the need for more radical surgery [9].

Currently, there are no medical reports comparing the benefits or disadvantages between medical and surgical treatment of DIE [10]. There are also no definitive data regarding the need for BEN

excision during laparoscopic DIE surgery. Therefore, this retrospective study aimed to evaluate the long-term symptoms and recurrence of BEN in women with DIE who underwent laparoscopic surgery in two different groups: with a surgery of bowel endometriosis (SBE) and with no surgery of bowel endometriosis (no-SBE).

Methods

Ethical considerations

This retrospective cohort study was conducted based on the principles of the 1964 Declaration of Helsinki [11]. We carried out our study in the Endometriosis Referral Department (Arash Hospital, Tehran, Iran). The Ethics Committee of Tehran University of Medical Sciences approved the study (approval code: IR.TUMS.MEDICINE.REC.1402.085).

Calculating required sample size

According to the study by Vercellini et al., the incidence of BEN involvement in endometriosis conditions was 60%. Based on the significance level of 0.05 and the precision limit of 0.1, a minimum sample size of approved patients with DIE was estimated as 76 [6].

Inclusion and exclusion criteria

In the present study, data were collected from the medical records of women with DIE who underwent laparoscopic surgery for endometriosis in two groups: SBE and no-SBE. The data were collected between March 2018 and February 2021. The inclusion criteria were cases with approved endometriosis (18-45 years of age) and at least two years of endometriosis after surgery. In addition, cases with primary cancer or metastasis, pregnancy after surgery, previous history of surgery, bowel stenosis, and infertility were excluded from the study. DIE was defined as endometriosis lesions >5 mm covering the bowel. The study population included all patients with endometriosis with colorectal involvement [12].

General information of patients

Demographic data of the included female patients were collected through a checklist available in the mobile app, including: patient name, medical record number, phone number, age, gender, BMI, height, fertility status, gravidity, number of children, and parity.

Patient medical information

All endometriosis-related data were collected, including duration, time, and type of endometriosis surgery. All treatment types of cases were rechecked after patient visits. Critical

symptoms of endometriosis (dysmenorrhea, dyspareunia and dyschezia) were recorded using visual analogue scale (VAS) ranging from 0 to 10 before and at least 1 year after surgery [13]. In the present study, all cases with severe symptoms of DIE, as well as all patients not responding to medical treatment or contraindicated cases for medical treatment underwent laparoscopic surgery for endometriosis. In addition, laparotomy surgery was performed based on patient preference. The surgical protocol for BEN depended on the depth, size and location of the lesions and the level of luminal stenosis in three different stages. (1) Shaving or superficial excision (using laparoscopic scissors or ultrasonic harmonic scalpel). This procedure was used in cases with serous BEN lesions. In this process, the integrity of the bowel was assessed with methylene blue staining or bubble test (air leak test) after razor excision [14]. (2) Full-thickness discoid bowel excision (using scissors or harmonic scalpel) and repair procedure. In this method, the lesions and the full thickness of the surrounding bowel wall were completely excised and then sutured. This method was applied to those with lesions extending beyond the serosa, with bowel luminal stenosis < 60%, lesion infiltration < 50% of bowel circumference, and largest BEN diameter < 3 cm [15]. (3) Segmental bowel resection and anastomosis. In this process, the lesions and bowel segments were resected and then bowel anastomosis was performed. This procedure was carried out by laparotomy or laparoscopy for those with bowel luminal stenosis > 60%, lesion infiltration >50% of bowel circumference, and the diameter of the largest BEN >3 cm [16]. Verogest or oral contraceptives (for at least 2 years) were prescribed in hospital after endometriosis surgery (in cases with contraindications). The changes in lesion size in no-SBE women and BEN follow-up (in cases who underwent bowel surgery) were fully assessed by transvaginal ultrasonography (TVUS).

Statistical data processing

After data extraction, the Kolmogorov-Smirnov test was performed to confirm that the data were normally distributed. Comparisons were made using t-test and chi-squared test or Fisher's exact test. The data were analyzed using SPSS software (v.19), and statistical significance was assumed at p<0.05. Results were expressed as mean±SD [17].

Results

Patient sample

Applying inclusion and exclusion criteria, we selected 76 eligible patients with approved DIE diagnoses for demographic, follow-up, and ultrasonography evaluation.

Table 1. Demographic characteristics of study groups

Groups	Age *	Age at endometriosis diagnosis *	BMI *	TLH+BSO	NULIGRAVID **
No-SBE	41.02± 4.33	36.97±4.49	25.50± 3.88	18±40.9	6±13.6
SBE	40.25±5	37.53±12.97	24.92±4.5	5±15.6	6±18.8
P-value	0.47	0.79	0.55	0.01	0.06

* Mean±SD, Mann-Whitney U test; ** Percent (%), Chi-squared test. No-SBE, no surgery for bowel endometriosis; SBE, surgery for bowel endometriosis; BMI, body mass index; TLH+BSO, Total Laparoscopic Hysterectomy + Bilateral Salpingoophorectomy.

Table 2. Bowel nodule characteristics before and after surgery in study groups

Indices	Study Groups		P-value
	No-SBE	SBE	
Nodule Characteristic			
Nodule size before surgery	29.18±1.6	25.84±1.9	0.23**
Muscle involvement	30±6.8	30±2.9	0.03*
Mucous layer involvement	4±0.95	13±0.4	<0.001*
Serosa involvement	44±4.2	32±5.9	0.21*
Site of bowel endometriotic lesions	Upper rectum	20±2.6	0.60*
	Rectosigmoid	14±3.1	
Nodule size post-surgery	19.13±1.3	21±3.2	-
Recurrence / Increase in nodule size	4±0.9	9±0.2	0.03*
Reduction in nodule size	11±0.25	-	-
Recurrence / Increase in nodule size	With TLH+BSO	0	0.17
	Without TLH+BSO	4±0.1	5±0.5

* Mean±SD, Mann–Whitney U test; ** Percent (%), Chi-squared test; No-SBE, no surgery for bowel endometriosis; SBE, surgery for bowel endometriosis; TLH+BSO, Total Laparoscopic Hysterectomy + Bilateral Salpingo-oophorectomy.

Table 3. Symptoms of endometriosis in partisans before and after surgery in study groups

Symptoms of endometriosis	Groups		p-value	
	No-SBE (Mean±SD)	SBE (Mean±SD)		
Pelvic Pain	Before surgery	7.13±2.30	7.43±2.48	0.6*
	Post-surgery	1.06±2.54	1.59±2.87	0.22*
	Better	41±9.32	27±8.44	0.10**
	Worth	3±0.68	1±0.03	
	No change	0	2±0.63	
Dysmenorrhea	Before surgery	8.59±1.60	8±0.02	0.17*
	Post-surgery	1.31±0.31	1.43±2.34	0.38*
	Better	38±8.64	28±8.75	0.86**
	Worth	4±0.91	2±0.63	
	No change	2±0.45	2±0.54	
Dyspareunia	Before surgery	6.4±0.24	6.61±2.31	0.72*
	Post-surgery	0.58±0.01	1.68±0.25	0.72*
	Better	28±0.93	19±0.95	0.70**
	Worth	2±0.06	2±0.09	
Dyschezia	Before surgery	5.88±0.18	5.50±1.78	0.53*
	Post-surgery	0.76±1.67	1.10±1.94	0.68*
	Better	16±0.80	15±0.78	0.14**
	Worth	0	3±0.15	
	No change	2±0.10	1±0.05	
Appear	2±0.10	0		

* Visual analogue score, Mean±SD, Mann–Whitney U test; ** Percent (%), Chi-squared test. No-SBE, no surgery for bowel endometriosis; SBE, surgery for bowel endometriosis.

Table 4. Comparison of endometriosis recurrence symptoms between study groups and patients with intestinal nodule recurrence

Variables	Recurrence of endometriosis symptoms		p-value *
Groups	No-SBE	11 (25)	0.54
	SBE	10 (31.3)	
Bowel nodule recurrence	Yes (n=13)	2 (15.4)	0.49
	No (n=63)	11 (84.6)	

* Percent (%), Chi-squared test. N=22.

Demographic data

The mean follow-up period of patients was 2.84±0.81 years for the included DIE women. Laparoscopic surgery for no-SBE patients was performed in 57.9% (n=44) of study subjects and 78.3% (n=18) in total laparoscopic hysterectomy + bilateral salpingo-oophorectomy (TLH+BSO) cases. For SBE group, 18.4% (n=14), 5.3% (n=4), 11.8% (n=9) and 6.6% (n=5) of DIE patients underwent shaving, discoid excision, resection anastomosis and laparotomy procedures, respectively. For TLH+BSO cases, these numbers were 17.4% (n=4), 0%, 0% and 4.3% (n=1) respectively. According to

[Table 1](#), the mean age of the patients was 41.02±4.33 years and 40.25±5 years in the no-SBE and SBE groups, respectively. The mean BMI was 25.50±3.88 kg/m² and 24.92±4.5 kg/m² in the no-SBE and SBE cases, respectively. We detected no statistically significant differences between groups in terms of age (p=0.47), BMI (p=0.55), nulliparous status (p=0.06), and endometriosis duration (p=0.79) ([Table 1](#)).

Results of ultrasonography

The most common reason for deep endometriosis operation (DEO) was reported pain: 96.2% in the no-SBE group and 96.4% in the SBE group. The mean BEN size was 29.18±16.14 mm in the no-SBE group and 25.84±10.99 mm in the SBE group, which was not, however, statistically significant (p=0.23). After ultrasound evaluation, the most common location of BEN was the upper rectum in both the SBE and no-SBE groups. After DEO, the BEN size increased by 9.1% in no-SBE individuals. In addition, BEN was found in 28.1% of women with SBE ([Table 2](#)).

Table 5. Information of the patients in bowel surgery group based on type of operation

Surgical Methods	Number	Bowel nodule size	Pelvic pain	Dysphasia	Serosa involvement	Mucous layer	Muscle involvement
Shave	14	19.42±3.79	6.5±2.23	7.2±2.04	14±1.00	6±4.29	12±0.85
Discoid	4	36.50±15.58	7.5±2.88	6.5±1.73	4±0.10	0	4±0.10
Anastomose	14	29.12±11.29	8.21±2.48	5.85±2.96	14±1.00	7±0.50	14±0.10
P-value	-	0.03*	0.13*	<0.001	-	0.19	0.25

* Kruskal-Wallis one-way analysis, Mean±SD.

Table 6. Information regarding the individuals in bowel surgery group based on bowel nodule recurrence

	No recurrence N=23	Recurrence N=9	P-value
Age *	39.43±4.52	42.33±5.85	0.14
BMI*	24.49±4.75	26.10±3.78	0.39
Gravidity *	1.26±0.75	1.66±1.1	0.24
Age at endometriosis diagnosis *	37.15±15.38	38.33±5.91	0.82
Pelvic pain*	7.52±2.48	7.22±2.63	0.76
Dyspareunia*	6.50±2.25	7.00±2.73	0.68
Dichasia*	5.92±1.65	3.66±1.15	0.05
Oophorectomy** total	1±4.3	4±44.4%	<0.001
	Yes	No	
	22±9.57	5±55.6	
Nodule size of bowel *	26.17±10.89	25.00±11.86	0.79
Muscle involvement**	21±1.93	9±0.10	0.36
Mucous layer involvement**	7±30.4	6±66.7	0.06
serosa involvement**	23±1.00	9±1.00	0.66
	Shave	10±43.5	4±44.4
	Discoid	4±17.4	0
Bowel surgery**	Anastomose	6±26.1	3±33.3
	Laparotomy	3±0.13	2±22.2

* Mean±SD, Mann–Whitney U test; ** Percent (%), Chi-squared test.

Clinical symptoms

All the symptoms of endometriosis including dysmenorrhea, dyspareunia, dyschezia and pelvic pain were significantly ($p=0.001$) increased in both groups during the follow-up period. Increased dyspareunia status was observed in 6.7% in the no-SBE group and 9.5% in the SBE cases. Some patients (6.8%) in the no-SBE group and 9.4% of those with SBE experienced increased pelvic pain after surgery, while 15.7% of those with SBE exhibited higher levels of dyschezia after surgery and 10% of women without SBE had dyschezia after surgery with no change during the follow-up period (Table 3). Nearly 28.9% of all included women experienced pain recurrence, including 31.3% in cases with SBE and 25% in cases without SBE. We found no statistically significant difference ($p=0.54$) between both groups regarding pain recurrence in endometriosis (Table 4). Of the 22 individuals with pain recurrence, 15.4% of the cases exhibited BEN recurrence. This finding implied that pain did not significantly ($p=0.13$) correlate with BEN recurrence. All study participants were assessed for diarrhea, hematochezia, low caliber stool, anastomotic leakage, fecal incontinence, and flatus incontinence before and during patient visits. Only 7.1% of SBE women reported fecal incontinence. A total of 32 cases underwent SBE, and 28.1% of patients in these groups experienced recurrence of endometriosis nodules during the follow-up period, while 44.4% of them underwent TLH+BSO. Table 5 presents the data of individuals who underwent SBE. During this period, the SBE group of individuals was compared in terms of BEN recurrence (Table 5). The results revealed no statistically significant differences between the two groups with regard to age ($p=0.14$), gravidity ($p=0.24$), BMI ($p=0.39$), age at endometriosis diagnosis ($p=0.82$), pelvic pain ($p=0.76$), dyspareunia ($p=0.68$), characteristics of intestinal

endometriosis nodules ($p=0.79$ for size, $p=0.36$ for nodule involvement, $p=0.06$ for mucus involvement, and $p=0.66$ for serosa involvement), and type of intestinal nodule surgery ($p=0.56$) (Table 6).

Discussion

The goal of this study was to investigate the long-term outcome of DEO involving the bowel and to determine how endometriosis symptoms and associated changes in bowel nodules occur in women with and without SBE. According to the results of this study, after 2 years of postoperative endometriosis assessment, the severity of endometriosis symptoms decreased in all subjects with SBE and without SBE. The incidence of women with high pain levels during the follow-up period showed little difference between both study groups. BEN recurrence was observed in 28.1% of women with SBE. In addition, 9.1% of women without SBE had elevated BEN levels. However, larger BEN size did not correlate with pain severity. We suggest that some loose adhesions were misdiagnosed as nodule recurrence in patients with SBE.

This research is one of the first studies to evaluate the long-term outcome of DIE surgery in two patient groups (no-SBE and SBE). There is currently a debate regarding the treatment of DIE, with the main focus on the effects of local excision using laparoscopy or segmental bowel resection. Furthermore, there are limited studies on the medical treatment of DIE [18] and most of them are case series of the no-SBE group. In a recent study by Vercellini et al., symptom improvement was similar in both the medical treatment and laparotomy groups, and over two-thirds of patients were satisfied with the medical treatment after 3 years of follow-up [6]. The natural history of endometriosis has not been clearly defined yet; hence, and it is questionable how endometriosis lesions progress. There is no clear evidence that small lesions progress to cystic lesions or DIE. However, it is logical to assume that large BEN may progress over time [19]. Similarly, it is likely to see small lesions regressing [20]. In addition, it is unclear whether the presence of these lesions indicates recurrence of the pathology or simply residual lesions [7]. In our study, recurrence of intestinal endometriosis was observed in 28.1% of the SBE group using the ultrasonography procedure. Generally, recurrence of endometriosis in studies with more than 2 years of follow-up was reported in 4.9–25% of cases [21]. In our study, 9.1% of women without SBE had large nodules. Andres et al. reported BEN size increased by 10% 6 months after medical treatment (238 women with rectosigmoid endometriosis) [22]. In our study, larger BEN in the no-SBE group and their recurrence in patients with SBE did not have any effect on patient symptoms, which was consistent with the results of other studies [22]. Complications in SBE group included dyschezia and fecal incontinence. Dyschezia was observed in the no-SBE group, which is consistent with the results of other published studies [23]. In this study, most women who underwent surgery also received long-

term medical treatment with oral contraceptive pills or progestin. Therefore, the effect of surgery on bowel and pelvic pain symptoms was overestimated because it was not possible to distinguish the effects of both treatment components in combination. This important caveat was identified as the main limitation of our study. In addition, postoperative DIE information based on ultrasonography was not evaluated: only BEN ultrasonography data were examined. In our study, BEN recurrence was considered a far-fetched phenomenon. It is possible that BEN were falsely observed due to the presence of adhesions. Although this is a retrospective study, all information was accurately recorded in the hospital database. However, the experience of the surgeons may have been lower in the early stages of the study vs. the later stages. In addition, the methods of bowel nodule removal (shaving, discoid excision and anastomotic resection) and surgical techniques (laparotomy vs. laparoscopy) were not identical among individuals with SBE in this study. Still, the quality of imaging methods for follow-up of patients, the duration of follow-up (on average, 24 months), and before-and-after surgery comparisons are undoubtedly strengths of the present study. Also, the clinical center from which patients were selected for the study trained radiologists performing TVUS according to published protocols for the effective diagnosis of DIE affecting rectosigmoid lesions.

Conclusion

The recurrence rate of endometriosis symptoms and BEN were similar in both groups (no-SBE and SBE). However, the size of BEN was high in a small number of women without SBE. On the other hand, recurrence and increased size of BEN did not correlate with the severity of symptoms. In addition, clinical examinations and ultrasonography are recommended in the follow-up of patients. We revealed no statistically significant difference in the recurrence of endometriosis-related clinical symptoms and bowel nodules in both SBE and no-SBE groups. In patients with BEN without any contraindications (such as bowel obstruction or severe pain) and unresponsive to medical treatment, surgical procedure of BEN is not recommended. At present, a more comprehensive study with a larger sample population is strongly recommended to reach a solid conclusion regarding DEO in patients with endometriosis.

Limitations

Since the patients were included in this study from all regions of Iran, its major limitation was a difficulty experienced by patients in terms of accessing a clinical unit, which resulted in the complete loss of some data. Therefore, the small number of patients is the main limitation of our study.

Abbreviations

DEO: deep endometriosis operation; DIE: deep infiltrating endometriosis; BEN: bowel endometriosis nodules; SBE: surgery of bowel endometriosis; no-SBE: No surgery of bowel endometriosis, NSAIDs: nonsteroidal anti-inflammatory drugs; VAS: visual analog scale, TLH+BSO: total laparoscopic hysterectomy + bilateral salpingo-oophorectomy; TVUS: transvaginal ultrasonography.

Conflict of interest

The authors declare no conflicts of interest.

Informed consent

Formal consent is not required for this type of study.

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Author contributions

RH carried out the primary animal manipulation. ZA performed the reproductive assays. ZV and NH were involved in case management and data processing. Also, ZV initiated this study and served a corresponding author. The manuscript was written by NR and AE, and its accuracy was checked and approved by all authors.

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