



Deep Infiltrating Ileocecal Endometriosis: Surgical Outcome and Review of the Literature

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Abstract

Objective: To assess clinical features and surgical outcome of patients with deep infiltrating ileocecal endometriosis undergoing ileal or ileocecal resection, through minimally invasive technique (n = 16; laparoscopic 11, robotic 5) or laparotomy (n=5).

Methods: All consecutive patients with histologically proven deep infiltrating ileocecal endometriosis (infiltration into the muscularis propria or deeper) undergoing surgical treatment at Mayo Clinic Rochester and Arizona, between January 2006 and September 2018 were included. Data collected included; clinical, radiological, and surgical variables along with postoperative complications (Clavien-Dindo Classification) within 6 weeks.

Results: There were 16 patients with ileal endometriosis, 2 with cecal endometriosis, and 3 with ileocecal disease. The mean age was 43.7 years (range 22-66). Six (28.6%) patients presented with small bowel obstruction and underwent emergency surgery. In the remaining 15 (71.4%) patients, ileocecal endometriosis was detected during scheduled surgery. Preoperative diagnosis of deep infiltrating endometriosis was made in 4 (19.0%) patients by CT or MRI enterography. Concomitant rectosigmoidal endometriosis was documented in 6 (28.6%) patients who required rectosigmoid or sigmoid additional resections. Differences in surgical outcome including conversion rate and complications between the groups of emergency and elective surgery were not observed. No recurrences occurred after a median of follow-up of 21.4 months.

Conclusion: Infiltrating ileocecal endometriosis should be considered in premenopausal women presenting with symptoms of intestinal obstruction. Surgical resection is an effective treatment. Rectosigmoid involvement is present in almost one third of patients with ileocecal endometriosis.

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Introduction

Deep infiltrating endometriosis can affect the surrounding structures or organs, with rectosigmoidal involvement as the most common intestinal site, which has been reported in 56-63% of patients with deep pelvic endometriosis [1,2]. The small bowel and the right colon are rarely affected by endometriosis, and only 4% of women with deep infiltration endometriosis are found to have ileocecal (non-appendiceal) involvement [1]. Although ileocecal endometriosis is a rare condition, the ileocecal area should be systematically inspected for the presence of endometriosis as it is a potentially serious entity.

Ileocecal endometriosis has scarcely been reported in the literature, with most data extrapolated from small case series studies and single case reports dealing primarily with surgical treatment performed on an emergency basis or in the context of segmental resection for extensive endometriosis [3-7]. In the current study, therefore, we reviewed the clinical presentation and outcomes of a series of 21 surgically treated patients for ileocecal endometriosis. Also, data of these patients were compared with previous clinical series reported in the literature.

Methods

The medical records of all consecutive patients with histologically proven deep infiltrating ileocecal endometriosis (infiltration into the muscularis propria or deeper) undergoing surgical treatment at Mayo Clinic Rochester and Arizona between January 2006 and September 2018 were retrospectively reviewed. Patients with isolated appendiceal endometriosis and those with ileocecal endometriosis limited to the serosa were excluded. The study was approved by the Mayo Clinic Institutional Review Board, and all patients had provided written informed consent at the time of surgery.

Data collected from the patients' electronic medical records included demographics, Body Mass Index (BMI), hormonal status, previous surgery for endometriosis, hormonal medication within the previous 6 weeks of the index admission, clinical symptoms, radioimaging findings, site of endometriosis, details of the surgical procedure, intraoperative complications, pathological findings, postoperative complications (Clavien-Dindo classification [8]), and outcome at 6 weeks after operation.

All statistical analyses were performed with the Statistical Analysis Systems (SAS), version 9.4 (SAS Institute Inc., Cary, NC, USA). Categorical variables are expressed as frequencies and percentages and continuous variables (BMI and length of hospital stay) as median and range. Categorical variables were compared with the Fisher's exact test and continuous data with the Wilcoxon rank-sum test. All hypotheses were two-sided. A $p < 0.05$ was considered statistically significant.

Results

Baseline characteristics

Of a total of 241 patients with intestinal involvement of endometriosis diagnosed during the study period, 21 (8.7%) had deep infiltrating endometriosis of the ileocecal region. The mean age of the patients was 44 years (range 22-66). Ileal endometriosis was noted in 16 patients; 2 had lesions isolated to the cecum and 3 patients had both ileal and cecal involvement. Two patients had pathological diagnosis of Crohn's disease in the surgical specimen in addition to endometriosis. Salient characteristics of these 21 patients are shown in Table 1.

Seventeen patients were premenopausal and 3 menopausal. The hormonal status was unknown in the remaining woman. Eleven premenopausal women were on hormonal treatment during the 6 months prior to surgery, but none of the postmenopausal women were on hormonal replacement therapy. Eight (38.1%) patients had history of previous surgery for endometriosis, which was performed at a mean of 62.9 months (range 3.0-3.7) prior to ileocecal surgery.

Intestinal symptoms were recorded in 61.9% of women, while gynecologic symptoms suspicious for endometriosis were the primary complaint in 23.8% of cases. Three patients were asymptomatic. The majority of gastrointestinal symptoms were nonspecific, 7 patients presenting with pain in the right lower quadrant, and 1 with epigastric pain. Obstructive symptoms were present in 10 (47.6%) patients. Preoperatively, 20 (95.2%) patients were evaluated with radiologic imaging (Figure 1A), but ileocecal endometriosis was suspected in only 4 (19%) of them. These 4 patients had undergone either CT or MRI enterography. Colonoscopy was performed in 8 (38.1%) patients, but the diagnosis of ileocecal endometriosis based on colonoscopy findings was made in only 1 patient.

Operative procedures

Six (28.6%) patients underwent urgent surgery due to small bowel obstruction. In the remaining 15 (71.4%) patients, ileocecal endometriosis was detected during scheduled surgery (Figure 1B). History of previous obstructive symptoms was present in 5 (83.3%) patients undergoing urgent operation as compared with 5 (33.3%) patients in the scheduled surgery group ($p = .063$). Details of surgical procedures are shown in Table 2. Ileal segmental resection with ileoileostomy was performed in 8 patients, ileocectomy in 11, and modified right colectomy with ileocolostomy in 2. A minimally invasive technique was used in 16 patients (laparoscopic 11, robotic 5) and laparotomy in 5. The ileocecal valve was preserved in eight patients. Conversion to open surgery was necessary in five patients (three in the urgent surgery group). The median size of the largest lesion was 2.7 cm (range 1.8-3.5). The most frequent segment affected was the ileum. There was only one patient with ileal mucosal involvement. Six cases had submucosal involvement, and muscularis infiltration was present in the remaining patients.

Follow-up and outcome

The median length of hospital stay was 3.5 days (range 2-15). Patients were followed for a median of 21.4 months. Two patients presented a Clavien-Dindo >III complication within 6 weeks of surgery (1 in the urgent surgery group, 1 in the scheduled surgery group). No ileocecal recurrence was noted in 16 patients evaluated radiologically during the follow-up period (3 MRI, 5 CT, 4 CT enterography, 3 MRI enterography, and 1 abdominal ultrasound). Subsequent surgery for endometriosis was required in 3 patients from the urgent surgery group (50%) and in none of the scheduled surgery group ($p = .015$). In these 3 patients rectosigmoid endometriosis was found, with concomitant ovarian endometriosis in 2 of them. At follow-up, pelvic pain recurrence was diagnosed in 4 (19%) of patients and nonspecific gastrointestinal symptoms in 7 (33.3%). No obstructive episodes were observed. Only one of the patients with ileocecal valve resection developed chronic diarrhea. Finally, the type of surgery, urgent vs. scheduled was not associated with differences in length of stay or postsurgical gynecological and gastrointestinal symptoms.

Table 1: Clinical characteristics of 21 patients diagnosed with deep infiltrating ileocecal endometriosis.

Variables	No. patients (%)
Age, years, median (range)	44 (22-66)
Body mass index (BMI), kg/m ² , median (range)	24.3 (17.4-44.0)
Hormone status	
Premenopausal	17 (85.0)
Menopausal	3 (15.0)
Missing	1
Previous surgery for endometriosis	
One operation	3 (14.3)
Two operations	3 (14.3)
Three operations	2 (9.5)
Hormonal medication (previous 6 months)	
Oral contraceptive pill	5 (23.8)
Progesterone (no IUD)	3 (14.3)
GnRh agonist	2 (9.5)
Other	1 (4.8)
Symptoms	
Asymptomatic	3 (14.3)
Acute/subacute bowel obstruction	10 (47.6)
Diffuse abdominal pain	8 (38.1)
Dysmenorrhea	7 (33.3)
Pain in the right lower quadrant	7 (33.3)
Diarrhea	4 (19.0)
Pelvic pain	3 (14.3)
Constipation	3 (14.3)
Dyspareunia	2 (9.5)
Epigastric pain	1 (4.8)
Site of involvement	
Ileum	16 (76.2)
Cecum	2 (9.5)
Both	3 (14.3)
Pathologic findings	
Muscularis propria	14 (66.7)
Submucosa	6 (28.6)
Mucosa	1 (4.8)
Intraoperative bladder injury	1 (4.8)
Postoperative complications (within 6 weeks after surgery)	
Clavien-Dindo type III A	1 (4.8)
Clavien-Dindo type IV A	1 (4.8)

IUD: Intrauterine Device; GnRh: Gonadotropin-Releasing Hormone. Data expressed as frequencies and percentages in parenthesis unless otherwise stated.

Table 2: Details of surgical procedures in 21 patients diagnosed with deep infiltrating ileocecal endometriosis.

Surgical procedures	No. patients (%)
Bowel resection	21 (100)
Segmental ileal resection	8 (38.1)
Ileocecectomy	11 (52.4)
Modified right hemicolectomy	2 (9.5)
Additional resections	6 (28.6)
Rectosigmoid resection	5 (23.8)
Sigmoid local excision	1 (4.8)
Diverting ileostomy	3 (14.3)
Ileocecal valve preservation	8 (38.1)
Ovarian cystectomy	2 (9.5)
Bilateral salpingo-oophorectomy	5 (23.8)
Hysterectomy	7 (33.3)
Modified radical parametrectomy	1 (4.8)
Abdominal wall resection	1 (4.8)

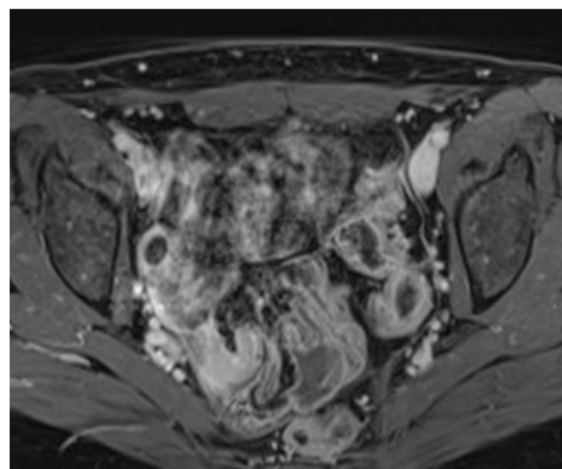
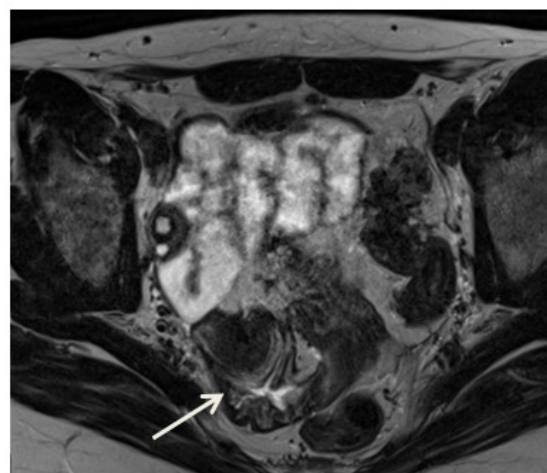


Figure 1: (A): Axial TSE T2 MR image shows a large T2 hypointense crescent shaped mass and “Mushroom Cap” configuration involving a pelvic ileal small bowel loop in the right lower pelvis (arrow). That demonstrates delayed enhancement after contrast administration. **(B):** Surgical resection confirmed a deep endometriotic implant.

Table 3: Details studies of deep infiltrating ileocecal endometriosis with more than five patients published in the literature in comparison with the present series.

Variables	First author, year of publication [reference]				
	Ruffo, 2011 [6]	Fedele, 2013 [7]	Rousset, 2014 [10]	López-Carrasco, 2016 [9]	Suarez-Salvador, present series
No. patients	31	8	33 (9 ileocecal lesions)	7	21
Rate of ileocecal DIE	10.3% (31/301)	3.3% (8/241)	21.2% (9/33)	4.7% (7/150)	8.7% (21/241)
Age, years, median (range)	34 (25-40)	29-43	35 (21-46)	35 (31-41)	44 (22-66)
Preoperative diagnosis	0	25% (2/8)	100% (9/9)	57.1% (4/7)	19% (4/21)
Technique	Barium	Barium + colonoscopy	3.0 T MRI enterography	MRI + barium	MRI/CT enterography
Surgical approach	Laparoscopy	Laparotomy	Laparoscopy/laparotomy	Laparoscopy/laparotomy	Laparoscopy/laparotomy
Urgent surgery	0	12.5% (1/8)	0	14.3% (1/7)	28.6% (6/21)
Rectosigmoid involvement	94%	100%	57%	42.8%	28%
Surgical procedure	Segmental resection	Segmental resection	Segmental resection	Segmental resection	Segmental resection
Infiltration	Not reported	Not reported	Muscularis propria	Not reported	Muscularis propria
Postoperative complications Clavien-Dindo > III	6.5%	12.5%	Not reported	28%	9.5%
Follow-up, months, median	27 months	96 months	6 months	Not reported	21.4 months
Recurrence	5.5%	Not reported	Not reported	Not reported	0%

DIE: Deep Infiltrating Ileocecal Endometriosis.

Discussion

Infiltrating ileocecal endometriosis is a rare and serious condition, requiring bowel resection and with a significant impact on the patients' quality of life. The present series of 21 women diagnosed with deep infiltrating ileocecal endometriosis is one of the largest series reported in the literature, and contributes to elucidate clinical presentation of the disease, work up studies and surgical procedures that may be needed for the adequate treatment of these patients. Previous reports of deeply infiltrating ileocecal endometriosis are mostly limited to descriptions of individual cases. As far as we are aware, only four clinical series (two surgical series and two radiological series) including more than five patients each have been published until now, with a total of 55 patients [6,7,9-11] to which the present series of 21 patients are added. The characteristics of these studies are summarized in Table 3.

Though the number of patients is limited, the varied presentations may help us understand the clinical spectrum of the disease from a multidisciplinary perspective. While typical pelvic endometriosis symptoms involve dysmenorrhea and cyclic pelvic pain, intestinal involvement can present with nonspecific symptoms of noncyclic abdominal pain, constipation, and diarrhea. In severe cases, obstructive symptoms and emergent situations like bowel perforation may occur. Due to the rare nature of the disease, along with the focus of gynecologic surgeons on the reproductive organs, ileocecal endometriosis may not fall into the differential diagnosis when seeing patients with these nonspecific symptoms.

Cyclic symptoms are less frequently encountered with gastrointestinal endometriosis, but are highly suggestive of endometriosis when present. Unfortunately, catamenial symptoms are often overlooked by healthcare providers outside of gynecology, and at times even by the patient. When the patient's chief complaints are gynecological, such as dyspareunia and

dysmenorrhea, abdominal symptoms are often non-specific and overlooked. Gynecologic symptoms were the main complaint in one in four patients in these series. However, it is remarkable that 47.6% of patients had previous episodes of occlusive symptoms. This rate rose to 83.3% in the case of patients who required urgent surgery. Bowel symptoms should not be disregarded in the context of patients with possible endometriosis as endometriosis may be more widespread than initially suspected. None of the menopausal women requiring surgery presented with gastrointestinal symptoms. This could be related to the progressive course of the disease during the childbearing age, and the lack of hormonal stimulation during menopause.

Ileum involvement carries a greater risk of obstruction. In our series, patients presented with occlusive symptoms, all had endometriosis located in the ileum. In the series of eight patients with deep infiltrating ileocecal endometriosis reported by Fedele et al. [7], seven patients underwent scheduled surgical treatment and all of them had cecal endometriosis. Endometriosis involving the ileum and cecum can cause diagnostic confusion with Crohn's disease. Some authors have pointed out the coexistence of both diseases and the difficulty for the differential diagnosis [12,13]. Two patients in our database presented with simultaneous diagnosis of Crohn's disease and ileocecal endometriosis, and in both cases the ileal involvement by endometriosis was limited to the serosa, and the symptomatology was related to Crohn's disease.

Transvaginal ultrasound and pelvic MRI have been shown to be sensitive techniques to detect deep infiltrating endometriosis. A limitation of these techniques is that imaging can only detect lesions in the field of view of the study and ileocecal endometriosis if not suspected is outside of the field. However, symptomatology is useful to direct preoperative imaging. CT or MRI enterography are most helpful if suspecting ileocecal in-

involvement. CT enterography is a powerful tool in the evaluation of small bowel disease affecting the mucosa and bowel wall. Deep intestinal endometriosis typically presents as wall thickening due to muscle proliferation and fibrosis. In a prospective study of 33 patients, 3.0-T MR enterography showed sensitivities of 92% for one reader and 96% for a second reader, with 100% specificity for the preoperative diagnostic accuracy of DIE lesions located above the rectosigmoid junction [10]. Biscaldi et al. [14] proposed multislice computed tomography combined with colon distension by water enteroclysis (MSCTe) to diagnose ileal endometriosis, since there is retrograde opacification of the terminal ileum, and most ileal endometriosis lesions are within 10 cm of the ileocecal valve. In our study, CT enterography and MRI enterography were diagnostic of ileal endometriosis in all 4 patients who had this examination performed. Further studies are needed to better understand the clinical picture of ileocecal endometriosis, and to guide the clinician as to when and what type of additional imaging should be considered.

Coexistence of gastrointestinal lesions involving large and small intestine in patients with pelvic endometriosis varies from 28% to 100% depending on the surgical or clinical presentation [2,6,7]. In our series 28% of patients had rectal or sigmoid colon endometriosis in addition to the ileocecal lesion. This rate is different from rates of 94% and 100% reported in two previous clinical series, in which only patients undergoing surgery in the context of extensive endometriosis were included [6,7]. Known or suspected rectosigmoid endometriosis should raise the suspicion for multifocal lesions, and thorough intraoperative inspection of the bowel should be performed. Given the multifocal potential of endometriosis [14,15], the gynecologic surgeon should thoroughly evaluate the pelvis, small bowel, appendix, and all peritoneal surfaces including the upper abdominal diaphragmatic surfaces.

The diagnosis of deep ileocecal endometriosis is established by pathological confirmation of involvement of the intestinal wall beyond the serosa. Endometriosis of the intestinal tract is usually an extra-luminal lesion, and can cause severe stenosis of the intestinal lumen. Mucosal involvement for endometriosis is extremely rare, so macroscopic diagnosis through colonoscopy is rarely performed. Endoscopy biopsies many times are not deep enough to get histopathologic diagnosis. No conclusive histological patterns are usual in endoscopic biopsies [17]. At the pathologic analysis endometriotic foci, although much more common in the muscularis propria, and submucosa were seen in all layers of the bowel wall in the current series.

Segmental resection could be necessary in patients with deep intestinal endometriosis. Although the decision of the type of surgery (radical or conservative) depends on factors such as the size and depth of the lesion and the percentage of circumference affected, factors studied for the large intestine are not applicable to the involvement of the small intestine [17]. This cohort of patients underwent segmental resection with anastomosis only. The radicality of surgery should be limited to the segment affected by endometriosis and surrounding fibrotic tissue. It is important to bear in mind that radical oncologic surgery is not necessary in these patients and may increase morbidity. Ileocecal valve preservation was possible in eight of the patients in this cohort. Preservation of the ileocecal valve is not always possible and depends on the extension of the disease. Laparotomy was performed in 10 patients, 5 due to conversion, in this cohort. Although there are no reports com-

paring laparotomy vs. laparoscopy for ileal resection, minimally invasive surgery appears to be preferable. Morbidity related to deep endometriosis surgery is not negligible. In ileocecal endometriosis perioperative morbidity is framed in extensive and complex surgeries for endometriosis with mayor surgical procedures associated. The percentage of severe complications (Clavien-Dindo >III) was 9.5% in accordance with data published previously ranged 12.5-18 % [6,7].

During the follow-up period, 7 (33.3%) patients presented nonspecific digestive symptoms. No case of intestinal obstruction was recorded. Sixteen patients were evaluated radiologically during follow-up. Seven enterograms were performed (4 CT and 3 MR) and no lesions suggestive of ileocecal recurrence were observed. Three patients underwent reoperation for other reasons and no ileocecal endometriosis recurrence was detected. None of the patients presented recurrence of ileocecal endometriosis during the follow-up period of 21.4 months based on imaging studies and visual inspection in the three reoperated patients.

The limitations of our study include the retrospective design and a relatively small sample size given the rarity of involvement of the ileocecal region.

In conclusion, infiltrating ileocecal endometriosis should be considered in premenopausal women presenting with symptoms of intestinal obstruction. Surgical resection is an effective treatment. Rectosigmoid involvement is present in almost one third of patients with ileocecal endometriosis.

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