Minimally-invasive multidisciplinary treatment of deep endometriosis: 103 cases

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Background: Endometriosis is a multifactorial disease which can cause severe pelvic pain that can impact everyday life. In addition, the complex of pain, inflammation, altered pelvic anatomy, adhesions, disrupted ovarian reserve/function, and compromised endometrial receptivity is a common cause of infertility. The treatment of this disease should be individualized according to the clinical situation and to the level of impairment. This study aims to define the role of surgery in the treatment of deep endometriosis with intestinal localization, particularly whether surgery is capable or not to improve painful symptoms, disease recurrence, and fertility.

Methods: In this retrospective clinical single-arm study, from March 2017 to March 2022, we included all patients who underwent to surgical intervention involving bowel resection for deep endometriosis. To analyze the effects of surgery in improving symptoms a standardized questionnaire, based on the verbal rating scale (VRS) [0–4], was given pre-operatively on the first gynecological visit and post-operatively at least 6 months from intervention. In addition, each patient seeking a pregnancy before surgery was contacted at the end of the follow-up to find out whether she had a full-term pregnancy or not.

Results: A total of 103 patients undergoing surgery for deep endometriosis involving the intestinal tract were included in the present study. The indication for surgery was given based on the severity of the symptoms, the desire for pregnancy, or a combination of the two. The 28.9% of the patients became completely asymptomatic after intervention and reported a clear decrease in the intensity of the painful symptomatology. The average pre-operative VRS score was 1.37, in the post-operative period, the average VRS score was 0.4, a difference that was statistically significant. About fertility, we observed a 20% increase after surgery.

Conclusions: Deep endometriosis is an aggressive form of endometriosis which has a great impact in patients' quality of life. Medical therapy control symptoms without a real resolution of them. This study emphasizes as surgical minimally invasive treatment represents the gold standard for the cure of deep endometriosis with excellent results on infertility and symptoms improvement.

Keywords: Deep endometriosis; infertility; pregnancy; bowel resection; minimally invasive surgery

Introduction

Endometriosis is an estrogen-dependent chronic condition characterized by the ectopic implantation of functional tissue lining the uterus outside of the uterine cavity. Under the effect of hormones, the endometrial tissue implanted in an abnormal location undergoes the same changes as the normal endometrium and therefore bleeding which involves an inflammatory involvement of the surrounding tissues, with the consequent formation of scar tissue.

Most frequently, endometrial tissue is found in ovaries, resulting in the formation of "chocolate cysts", but it can also be found in the fallopian tubes, uterosacral ligaments, the gastrointestinal tract, and less often in the pleura, pericardium, or the central nervous system. Three main clinical presentations have been described: peritoneal endometriosis, ovarian endometrioma, and deep infiltrating endometriosis (DIE). The latter is the most aggressive presentation, the nodules deepen more than 5 mm into the tissues. It mostly affects the uterosacral ligaments, the rectovaginal septum and/or the vagina, the recto-sigma, the ovarian fossa, the pelvic peritoneum, the ureters, and the bladders. At the level of the rectouterine pouch (of Douglas), which appears to be the most frequently affected site, we recognize two types of DIE: rectovaginal with infiltration of the rectovaginal septum and retrocervical endometriosis (1).

It is estimated that more than 176 million women worldwide suffer from endometriosis; this pathology occurs in women of childbearing age, with an incidence ranging from 6% to 10%, and is usually diagnosed in the third decade, mostly between the ages of 25 and 30 years (2,3). Approximately 20% of patients with endometriosis are affected by DIE.

There are some characteristics that characterize patients affected by DIE: positive family history for endometriosis, greater absenteeism from school during the menstrual period, the use of the contraceptive pill is more frequent and longer-lasting, high incidence of use of the contraceptive pill before the age of 18 years due to strong dysmenorrhea, patients with a history of surgery for endometriosis show a higher prevalence of DIE.

Endometriosis seems to be an estrogen-dependent disease, it is rare before menarche and tends to be less common after menopause. It seems that estrogens play a role of primary importance in the growth and maintenance of endometriotic lesions. This hypothesis is supported by the fact that the onset of menopause or the blockage of menstrual cycles through hormone therapy determines the regression of the disease (4).

Endometriosis mainly affects both reproductive organs and non-reproductive, this latter condition is called "extragenital endometriosis" (5). The extragenital sites most frequently affected are the gastrointestinal tract and the urinary tract. It is estimated that about 3.8–37% of women with endometriosis are affected by bowel endometriosis (6,7). In 90% of cases, the rectum and the distal part of the sigmoid are involved, followed by the ileum (12%), the appendix (8%), and the cecum (6%) (5,8). Although in literature have been reported rare cases of involvement of the transverse colon (9), stomach (10), gallbladder, Meckel's diverticulum, and some endometriotic cysts of the pancreas and liver (11).

Bowel endometriotic lesions can have variable dimensions and depth of infiltration of the wall and therefore can cause various symptoms, such as: dyschezia, constipation, feeling of abdominal swelling, finding of blood in the feces during the menstrual cycle, diarrhea during the menses, stranguria during the cycle, irradiation of pain to the perineum (12). The pain associated with endometriosis most often takes the form of painful menstruation. It precedes the appearance of bleeding; over time it intensifies, and its location concerns the lower abdomen and deeper pelvic areas. Pain can radiate to the sacral region; it can extend beyond the bleeding period and be present throughout the menstrual cycle. Intraperitoneal adhesions or overgrowth of the fallopian gouges are the most common causes of the problem with the treatment of endometriosis. Sometimes foci of endometriosis produce antibodies to the ectopic

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Highlight box

Key findings
- Minimally invasive surgery is the gold standard in the treatment of deep endometriosis with intestinal involvement with excellent results both in terms of fertility and improvement of painful symptoms.

What is known and what is new?
- Medical treatment of deep endometriosis is not curative and it's often associated with side effects.
- Surgical treatment of deep endometriosis increase the number of post-surgical pregnancies and improve gastrointestinal symptoms.

What is the implication, and what should change now?
- Limited to the surgical skills of the operator, minimally invasive surgery is the preferred approach in the treatment of deep endometriosis.

endometrium, which can induce poor embryo implantation or spontaneous abortions (3).

Infertility is another typical manifestation of endometriosis: 3% of patients with endometriosis are infertile and 30–40% of infertile women are affected by endometriosis (2). Ectopic implantations of endometrial cells cause intraperitoneal bleeding which determines an inflammatory state with biochemical alterations of the peritoneal fluid which would appear to be responsible for poor oocyte quality, reduced sperm mobility, and altered interaction between oocyte and sperm (13). Another factor to consider in severe cases of deep endometriosis is the fibrotic reaction with the consequent formation of adhesions which leads to the distortion of the pelvic anatomy, further compromising the ability to conceive (14,15). Due to the accompanying elements and chronic nature, it is a very important medical, social, and economic problem.

Endometriosis should be suspected in all women with chronic pelvic pain, usually more severe during the menstrual cycle or ovulation, in association with dysmenorrhea, dyspareunia, and cyclic intestinal disorders.

The purpose of clinical-instrumental investigations is to document the extension of the disease, plan a multidisciplinary approach, and carry out an adequate counseling with the patient about the type of operation she will undergo and the possible complications. The gynecological examination with inspection of the vagina using a speculum and bimanual examination is the first approach and, in association with an accurate medical history represents a fundamental first step in diagnosis of bowel endometriosis. The pelvic bimanual examination detects 50% of rectovaginal nodules >3 cm in diameter; it is also capable of evaluate whether there are fibrotic nodules affecting the parametrium, the uterosacral ligaments, and the vesicovaginal septum. The pain caused by palpation allows the doctor to have an impression of the extension of endometriosis deep and about the location. The clinical examination must always include an objective examination of the abdomen and a rectal examination which allows us to evaluate the possible dorsal and lateral extension of the disease. The most used radiological investigations are transvaginal ultrasound (TVS) and magnetic resonance imaging (MRI).

The TVS is a widely available and low-cost exam; it represents the first-line imaging technique, providing a detailed image from the pelvis with minimum discomfort for the patient. Ultrasonographically, intestinal endometriosis appears as a linear thickening or hypoechoic nodular of the muscle wall, with irregular borders, with few blood vessels visible on Doppler infiltrating the abdominal wall. During TVS it is possible to evaluate the distance of the intestinal lesion from the anal margin; the uterosacral ligaments are used as landmarks for discriminate endometriotic lesions involving the low or high rectum (16). This exam also allows for defining the number of endometriotic lesions (17,18). Several studies have shown that TVS performed by an experienced gynecologist has a high specificity and sensitivity in diagnosing bowel endometriosis. However, it has poor accuracy in assessing the degree of infiltration of the intestinal wall where transrectal ultrasound (TRUS) plays a better role (19,20).

MRI represents the gold standard in the diagnosis of intestinal endometriosis and has a diagnostic accuracy of 96%. Endometriosis nodules appear hyperintense on T1 and T1, while on T2 sequences they appear faintly hypointense. The use of the contrast media allows the lesion to be better distinguished from the wall healthy intestine. The diagnostic criteria for talking about infiltration of the rectum are the thickening of the wall with adhesion of the rectum to the uterine torus or the irregularity of the parietal thickness in the lower third of the sigmoid colon. MRI allows to better discriminate multifocal lesions and to identify bowel lesions even higher than the rectus sigmoid joint.

TRUS allows to estimate the infiltration of the intestinal wall, especially if there is infiltration of the muscularis own; it also allows to measure the maximum diameter of the lesion and its distance from the anal margin. However, it is not always performed as it is not always available an expert sonographer capable of doing it. Double-contrast barium enema (DCBE) technique shows a narrowing of the intestinal lumen as from extrinsic compression in association with a crenelated appearance of the mucosa. However, this diagnostic investigation does not allow us to directly visualize the lesion and is usually used to assess the degree of stenosis upon suspicion of bowel endometriosis found on MRI or TVS.

Colonoscopy could diagnose only large nodules infiltrating the mucosa and/or causing strictures, its use is therefore limited. It can be useful if the presence of colorectal neoplasia must be excluded.

Exploratory laparoscopy is not recommended only for the possible search for peritoneal endometriosis, especially in adolescents or young adults, since it has not been demonstrated that the treatment of peritoneal endometriosis has some influence on the course of the disease. Finally,

diagnosis of endometriosis is only considered definitive when the presence of endometrial-like tissue outside the uterus is confirmed during surgery (21,22).

Medical treatment, characterized by estrogens, progestogens, and aromatase inhibitors or gonadotropin-releasing hormone (GnRH) analogues, is based on the suppression of symptoms, but it is not curative and is often associated with side effects (23). Surgical treatment is considered for patients with painful, prevent recurrence, and improves fertility; it is also important to prevent the formation of post-operative adhesions (24). About surgery conservative procedures have a lower rate of post-operative urinary/intestinal morbidity and complications compared to radical surgical treatment. However, in some cases, complete removal of the nodule is not achieved following conservative surgery due to the persistence of microscopic disease near the resection margin; this factor would seem to increase the risk of recurrence (25,26). There are different types of surgical treatments regarding bowel endometriosis described with both laparoscopic/robotic, laparotomic, and transvaginal approaches. Considering the greater frequency of involvement of the sigmoid rectal intestinal tract over the years different surgical techniques have been developed: rectal shaving, Rouen technique, discoid resection, and bowel segmental resection. Segmental resections have a better result in terms of improvement of symptoms and fertility. However, they have a higher incidence of complications, especially for lesions of the lower rectum (27).

The aim of this study is to define the role of surgery in the treatment of deep endometriosis with intestinal localization, particularly whether surgery is capable or not to improve painful symptoms, disease recurrence and fertility. We present this article in accordance with the STROBE reporting checklist (available at https://ls.amegroups.com/article/view/10.21037/ls-24-2/rc).

Methods

This study is a single-center and retrospective observational study, conducted at the Complex Structure of General, Emergency, and Oncological Surgery (Director Prof. Roberta Gelmini), in collaboration with the Complex Structure of Gynecology (Director Prof. Fabio Facchinetti) of the University Hospital of Modena. The aim of the study is to investigate the outcomes of surgical treatment of deep endometriosis with intestinal localization in terms of improvement of painful symptoms, disease recurrence, and improvement of fertility. This research involves 103 patients with deep endometriosis who underwent surgery including bowel resection (sigmoid-rectum resection, rectal shaving, discoid resection, ileal resection, strictureplasty) between March 2017—period in which the collaboration between the two units (General Surgery and Gynecology) started—and March 2022 at the Modena Polyclinic. All the patients in the study were examined and diagnostic investigations were performed in our Polyclinic. The data was collected through the analysis of company software and the clinical history of the patients was thus reviewed to obtain demographic data, body mass index (BMI), comorbidities, information on any previous medical or surgical treatments, pre-radiological investigations—intervention and all information regarding the surgical intervention, hospitalization, peri- and post-operative complications and the search for and occurrence or otherwise of pregnancy.

Regarding surgical approaches, we considered rectal shaving for nodules less than 3 cm in diameter infiltrating the intestinal wall less than 7 mm and involving less than 50% of circumference. Discoid resection was considered for single nodule with a diameter less than 3 cm occupying less than a third of intestinal circumference or when rectal shaving was incomplete or has caused an intestinal lesion due to the excessive depth of the nodule. Segmental resection was indicated for multifocal lesions of involvement of more than 50% of the intestinal circumference or for nodules with more than 30 mm of diameter. Stoma packaging was taken into consideration when the anastomosis is low (5 cm or less from the anal margin) or when there is a high risk of anastomotic dehiscence. In case of involvement of the small intestine by multiple endometriosis nodules a stricturoplasty was performed, a longitudinal incision along the affected area by the endometriotic nodule, reaching the healthy tissue on the anti-mesenteric side and then re-suturing the enterotomy.

Post-operative follow-up was conducted through outpatient visits 1 month after surgery and subsequently at 6-month intervals, the outcome of which was extrapolated from company software. In all patients' pre-operative symptoms were evaluated with a value from 0 to 4 according to the verbal rating scale (VRS). Furthermore, each patient was contacted in September 2021 to close the follow-up (three patients were untraceable) asking if they had a full-term pregnancy and asking to always give a value from 0 to 4 according to the VRS to post-operative symptoms.

This research meets ethical guidelines and informed

Table 1 Demographic, clinical, and pre-operative characteristics of patients with intestinal endometriosis

Characteristics	Patients (n=103)	Rate (%)
Age (years), mean [range]	36.55 [23–50]	
BMI (kg/m^2) , mean [range]	24.66 [15.90–33.59]	
Ethnicity		
European	92	89.32
Not European	11	10.68
Familiarity with endometriosis	9	8.74
Smoke	25	24.27
Pre-operative hormon therapy	75	72.82
Time of taking the therapy (months), mean [range]	86.08 [1–264]	
Comorbidity	29	28.16
Previous surgery for endometriosis	35	33.98
Infertility	40	38.83
Pre-operative symptoms	92	89.32
Dyspareunia	74	71.84
Dysmenorrhea	83	80.58
Chronic pelvic pain	64	62.14
Dyschezia	65	63.11
Stranguria	14	13.59
Abdominal distension	56	54.37
Tenesmus	30	29.13
Constipation	61	59.22
Diarrhea	29	28.16
Hematochezia	10	9.71
MRI	88	85.44
Size of the nodule (mm), mean [range]	28.5 [10–81]	

BMI, body mass index; MRI, magnetic resonance imaging.

consent was acquired. The study was approved by the local research ethics committee "Comitato Etico dell'Area Vasta Emilia Nord" (protocol number: 0024582/19) on December 19, 2017, before enrollment, adherent to local and international standards. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).
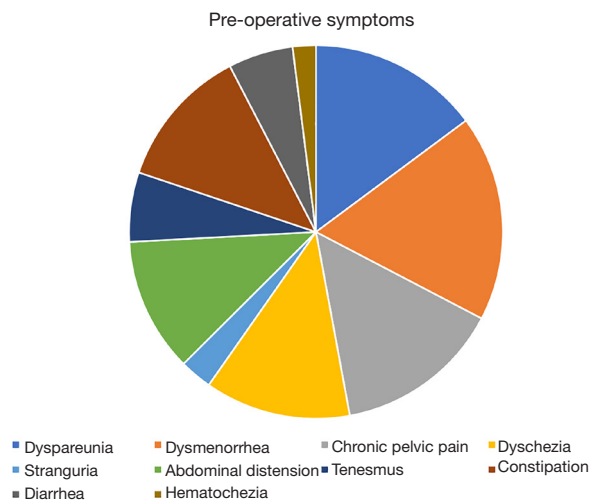
Statistical analysis

In this study, descriptive statistics are reported as proportions or ranged means. Comparisons between patients with and without endometriosis-related pre- and post-operative symptoms, assessment by VRS of the intensity of the numerous symptoms analyzed, and pregnancy or non-pregnancy post-surgery for endometriosis were performed using the test of Pearson's χ^2 for categorical variables. Continuous variables were instead analyzed using Student's t-test. Survivals were estimated using the Kaplan-Meier method, and compared using the log-rank test. The relationship between the various risk factors and survival was studied through Cox regression, both in univariate and, when indicated, multivariate analysis. For this study, a P value <0.05 was used as the significance level. Statistical analysis was conducted using SPSS (Statistical Package for the Social Sciences) version 25.0 software (SPSS Inc., Chicago, IL, USA)

Results

Patient characteristics and pre-operative evaluation

A total of 103 women undergoing surgery for deep endometriosis involving the intestinal tract were included in the present study. The demographic, clinical, and pre-operative characteristics are summarized in *Table 1*. The mean age at the time of surgery was 36.55 years (range, 23–50 years), while the mean BMI was 24.66 kg/m^2 (range, 15.90–33.59 kg/m^2). Of the patients enrolled in the study, 92 were Caucasian (89.32%), 7 were Black (6.8%), 1 was Asian (0.97%), and 3 other (2.91%). Only 9 patients (8.74%) had had a family member affected by endometriosis. Twenty-five patients were smokers (24.27%). Often the 43 diagnosis of endometriosis dates to many years before the operation, so 72.82% of the patients had already taken medical hormonal therapy with an average intake time of 86.08 months, and 35 of them had already undergone previous surgery for endometriosis (33.98%) including unilateral or bilateral ovarian cystectomies and/or removal of peritoneal endometriosis. Since they were mostly young patients, only 29 women reported, in addition to endometriosis, other mild comorbidities such as migraine, fibromyalgia, autoimmune thyroiditis, and interstitial cystitis, except for one woman who had a history of non-Hodgkin's lymphoma. The indication for surgery was given based on the severity of the symptoms, the desire for pregnancy, or a combination of the two. Forty-three

Pre-operative symptoms

- Dyspareunia
- Dysmenorrhea
- Chronic pelvic pain
- Dyschezia
- Stranguria
- Abdominal distension
- Tenesmus
- Constipation
- Diarrhea
- Hematochezia

Figure 1 Graphical representation of pre-operative symptoms.

percent of the patients were found to be infertile at the time of surgery, where infertility means the absence of conception after 1–2 years of intentionally fertile intercourse. Among the symptoms most observed among our patients, shown in *Figure 1*, there are above all dysmenorrhea (80.58%), dyspareunia (71.84%), chronic pelvic pain (62.14%), dyschezia (63.11%), constipation (59.22%), and abdominal distension (54.37%). Following other reported symptoms were tenesmus (29.13%), diarrhea (28.16%), stranguria (13.59%), and hematochezia (9.71%). In the pre-operative work-up, all the patients underwent a gynecological examination with TVS, and 90.29% of them also performed magnetic resonance, to better determine the extent of the endometriotic disease. These diagnostic investigations also made it possible to evaluate the size of the deep intestinal endometriosis nodules, with an average of about 28.5 mm (range, 10–81 mm), in order to plan the most appropriate surgery and correct counseling with the patients. The type of intervention has always been discussed by both the gynecological and surgical teams with a view to obtaining the complete removal of the foci of disease while saving as much healthy tissue as possible, obviously always considering the will of the patient expressed in the informed consent.

Operative technique

In total 99 patients (96.1%) underwent laparoscopic surgery, only 4 (3.9%) underwent direct laparotomic surgery due to severe pelvic adhesions, due to the disease itself or the

previous surgeries, and in the case of a condition of pelvic obstruction determined by the volume of the uterine bowel. The laparotomy conversion rate was 0% and we never encountered any intraoperative complications. In 17 cases the localization of endometriosis in the intestine was multiple, so that in 16.5% of cases the patients underwent more than one resection of the digestive tract. In total, we performed: 64 rectal sigmoid resections (62.14%), 29 appendectomies (28.2%), 17 rectal shavings (16.5%), 7 ileal segmental resections (6.80%), 4 discoid resections (3.9%), and 3 ileal strictureplasties (2.9%). It was necessary to perform an ileostomy in 18 patients (17.5%), three of them with the ghost technique. In all patient's endometriosis affected not only the intestine but also the other pelvic organs, so a gynecological operation was always performed in the same operating session. The mean length of hospital stay was 7.1 days (range, 2–21 days). These results are shown in *Table 2*.

Surgical outcomes and histopathological findings

The main surgical outcomes are summarized in *Table 3*. We observed a total of 11 complications within 30 days of surgery (10.68%). Among the most feared complications we had only one case of anastomotic leak (0.97%) treated conservatively with antibiotic therapy and keeping the abdominal drainage in place, one case of rectovaginal fistula (0.97%) treated first endoscopically (by the positioning of an Ovesco) and subsequently, due to failure to solve the problem, by means of surgery. It was observed one case of paravaginal hemorrhagic collection (0.97%) which made it necessary to perform a new laparoscopic surgery for the drainage of the collection, with complete resolution; in another case, we observed the presence of a pelvic abscess (0.97%) treated only with antibiotic therapy. Among the complications considered as minor, there was a case of acute pancreatitis (0.97%) treated by medical therapy with anti-secretory drugs, a case of anemia (0.97%) subjected to transfusion of concentrated red blood cells, a case of infection of wound treated with antibiotic therapy (0.97%) and two cases of post-operative hyperpyrexia (1.9%) treated conservatively with empiric antibiotic therapy with resolution of the clinic. According to the Clavien-Dindo classification, we had type IIIb complications in 3.23% of cases and type II complications in 8.60% of cases. Post-operative complications beyond 30 days of surgery occurred in only three cases, both after 12 months: one patient, previously subjected to rectal resection, following difficult

Table 2 Perioperative results

Characteristics	Patients (n=103)	Rate (%)
Operative techniques		
Rectal sigmoid resections	64	62.14
Rectal shavings	17	16.5
Discoid resections	4	3.9
Ileal segmental resections	7	6.80
Appendicectomies	29	28.2
Ileal strictureplasties	3	2.9
Multiple abdominal operations	18	17.48
Rectal resection + appendicectomy	11	10.68
Rectal resection + ileal segmental resection + appendicectomy	2	1.94
Rectal resection + appendicectomy + strictureplasties	1	0.97
Rectal resection + ileal segmental resection	2	1.94
Rectal shavings + appendicectomy	1	0.97
Rectal shavings + appendicectomy + strictureplasties	1	0.97
Simultaneous gynecological interventions	96	93.20
Laparoscopic	101	98.06
Laparotomic	4	3.88
Laparotomic conversion	0	0
Intraoperative complications	0	0
Hospital stay (days), mean [range]	7.1 [2–21]	
Ileostomy	18	17.5
Ghost ileostomy	3	2.91

evacuation associated with myofascial pain, performed a colonoscopy which showed stenosis of the colorectal anastomosis, treated conservatively with endoscopic dilations. Another patient, previously subjected to ileal segmental resection, complained of stubborn constipation for which magnetic resonance and colonoscopy were performed which only showed a picture of non-specific ileitis and colon rigidity as in adhesion syndrome, treated with conservative therapy. As far as the histological analysis is concerned, all the data have been collected in *Table 4*. For those patients who underwent multiple operations, the deepest nodule was taken into consideration. Analyzing the histological examinations, in most cases the muscular tunic was involved (61.17%), in 23.30% of the cases the mucosa, in 6.8% of the cases the submucosa, and in 9.71% the subserosa. The resection margins were free from residual disease in 98.06% of cases. In 1 patient (0.97%) who underwent multiple resection (right adnexectomy, right lateral parametrectomy, right ovarian dimple peritoneal nodule removal, left ureteral and retrocervical nodule removal, adenomyosis removal, sigmoid resection, appendectomy), we found a poorly differentiated adenocarcinoma of the endometrioid type infiltrating the right ovary, also associated with a microfoci of endometrioid adenocarcinoma on the sigmoid, for which the patient subsequently underwent reoperation for adhesiolysis, hysterectomy and adnexectomy left. Another incidental finding was T1b adenocarcinoma of the uterus in a patient who underwent adhesiolysis, bilateral ureterolysis, excision of the peritoneum of the right ovarian fossa, removal of the nodule of the left lateral parametrium, total hysterectomy, bilateral adnexectomy, segmental resection of the rectum

Table 3 Peri- and post-operative complications

Complications	Patients	Rate (%)
Peri-operative complications within 30 days (n=103)	11	10.68
Anastomotic leak	1	0.97
Rectovaginal fistula	1	0.97
Pelvic abscess	1	0.97
Hemorrhagic collection	1	0.97
Acute pancreatitis	1	0.97
Anemia	1	0.97
Wound infection	1	0.97
Hyperpyrexia	2	1.9
Clavien-Dindo classification (n=93)		
I	0	0
II	8	8.60
IIIa	0	0
IIIb	3	3.23
IV	0	0
Complication's tratment (n=103)		
Medical therapy/antibiotic	7	6.80
Reintervention	3	2.9
Transfusion	1	0.97
Post-operative complications over 30 days which required treatment or exams (n=103)		
Anastomotic stricture	1	0.97
Stubborn constipation	1	0.97

Table 4 Histopatological findings

Characteristics	Patients (n=103)	Rate (%)
Vertical infiltration		
Serosa	0	0
Subserosa	10	9.71
Muscular	63	61.17
Submucosa	7	6.8
Mucosa	24	23.30
Free resection margins	101	98.06
Cancerization	1	0.97

and protective ileostomy. The patient was therefore hooked up to the Modenese Oncological Center and first underwent adjuvant radiotherapy; 6 months after the operation, due to the control computed tomography (CT) scan of pelvic lymphadenopathy, she started chemotherapy treatment.

Follow-up

The average pre-operative VRS score was 1.37. In the post-operative period, a clear decrease in the VRS score was observed with an average of 0.4, a difference that was statistically significant (*Table 5*). We also analyzed each

Table 5 Student's *t*-test analysis of mean presence/absence of symptoms and mean pre- and post-surgery yes/no pregnancy for deep endometriosis with intestinal involvement

Variables	Pre-operative	Post-operative	P	95% CI
Painful symptoms	0.98±0.147	0.71±0.456	<0.001	0.167–0.367
Pregnance	0.44±0.499	0.18±0.390	<0.001	0.102–0.414

Data are presented as mean ± SD, unless otherwise specified. CI, confidence interval; SD, standard deviation.

Table 6 Analysis according to the Student's *t*-test between the means of evaluation of the VRS of pre- and post-intervention symptoms for deep endometriosis with intestinal involvement

Symptoms	VRS score pre-operative	VRS score post-operative	P	95% CI
Dysmenorrhea	3.08±1.393	0.36±0.869	<0.001	2.377–3.056
Dyspareunia	2.19±1.646	0.54±1.062	<0.001	1.236–2.049
Chronic pelvic pain	1.89±1.524	0.24±0.641	<0.001	1.302–1.989
Dyschezia	1.77±1.627	0.37±0.942	<0.001	1.013–1.793
Stranguria	0.37±1.007	0.08±0.430	<0.01	0.068–0.523
Abdominal distension	1.55±1.500	0.89±1.194	<0.001	0.263–1.058
Tenesmus	0.70±1.234	0.29±0.838	<0.009	0.105–0.724
Constipation	1.51±1.448	1.06±1.409	<0.04	0.031–0.869
Diarrhea	0.57±1.045	0.19±0.685	<0.004	0.123–0.642
Hematochezia	0.15±0.556	0.04±0.207	<0.08	0.014–0.233

Data are presented as mean ± SD, unless otherwise specified. VRS, verbal rating scale; CI, confidence interval; SD, standard deviation.

Table 7 Follow-up

| Outcomes	Patients (n=103)	Rate (%)
Follow-up time (months), mean [range]	27.52 [1–54]	
Pelvic endometriosis recurrence	8	7.77
Complete remission of symptoms (n=100)[†]	30	30
Pre-operative symptoms (n=100)[†]		
Dyspareunia	35	35
Dysmenorrhea	28	28
Chronic pelvic pain	23	23
Dyschezia	18	18
Stranguria	3	3
Abdominal distension	40	40
Tenesmus	13	13
Constipation	57	57
Diarrhea	13	13
Hematochezia	5	5
Pregnancy (n=40)	8	20

[†], three patients lost to follow-up, did not respond to the telephone questionnaire.

symptom individually and in almost all cases a statistically significant post-surgical improvement was obtained except for hematochezia (*Table 6*). As far as fertility is concerned, we had a 20% increase after surgery, which is also a statistically significant result (*Table 5*).

Follow-up data are summarized in *Table 7*. The mean follow-up time was 27.52 months (range, 1–54 months). Organic recurrence of pelvic endometriosis was observed in 8 patients (7.77%), all asymptomatic. We analyzed the possible correlation between the presence of surgical resection margins infiltrated by disease and organic recurrence, but there was no finding statistically 40 significant (P<0.088) (*Figure 2*). During the study period, no patient required any other surgery. As far as symptoms are concerned, 29% of the patients became completely asymptomatic and, in the remainder, a clear decrease in the intensity of the painful symptomatology was observed, as can be seen from *Figures 3,4* and *Tables 8,9*.
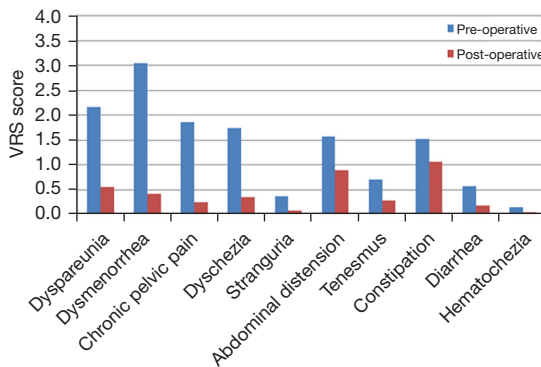
Discussion

Endometriosis is defined as a benign disease, however it has
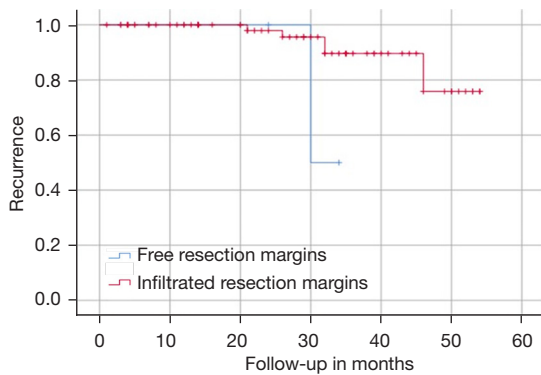
Figure 2 Kaplan-Meier analysis for comparison of endometriosis recurrence in relation to infiltration of the resection margins.
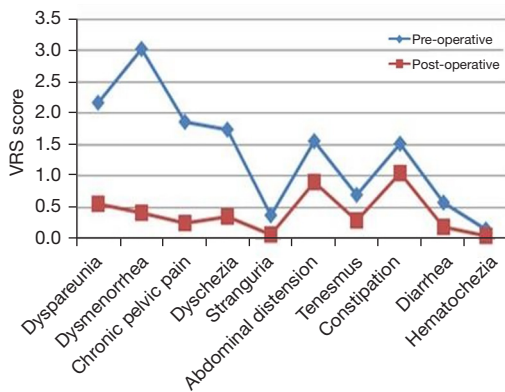
Figure 3 Comparison of pre- and post-operative symptoms according to the VRS—graphic representation. VRS, verbal rating scale.

Figure 4 Comparison of pre- and post-operative symptoms according to the VRS—histogram. VRS, verbal rating scale.

a profound impact on women's lives as it is often associated with disabling chronic pelvic pain, infertility and a reduced quality of life that affects daily life, interpersonal relationships, and work. Although hormonal medical treatments are widely used in the treatment of endometriosis, there is no general evidence to support the beneficial effects of these drugs in the treatment of deep endometriosis (28,29). In the present study, 66 of the 93 patients (70.97%) took hormone therapy pre-operatively, some even for very long periods of time (the maximum time recorded was 264 months), yet it does not appear that they benefited from it, given the subsequent need for surgery. To obtain better long-term results in terms of painful symptoms, fertility and recurrence, surgery represents the treatment of first choice in patients with deep endometriosis (30), especially when this also affects the intestinal tract (6). The minimally invasive approach represents the gold standard in the surgical treatment of endometriosis as it reduces post-operative stress, the risk of infection, the risk of incisional hernia and post-operative adhesions, allows a 44 shorter and a better aesthetic result, an aspect not to be underestimated given the young age of the patients. In our study, the indication to perform surgery in most cases was given due to painful symptoms that did not respond to medical treatment; 91 patients (97.85%) complained of disabling pain symptoms before surgery and only two completely asymptomatic patients underwent surgical treatment for infertility. The pre-operative mean VRS score was 1.37. In the post-operative period, a clear decrease in the VRS score was observed with an average of 0.4, which was statistically significant, and we also analyzed each symptom individually, for which in almost all cases a statistically significant post-surgical improvement was obtained except for hematochezia, where however the persistence of the symptom in the post-operative period was not better investigated with a proctological visit to exclude anorectal pathologies such as fissures or hemorrhoidal pathology. Furthermore, this symptom is not the main sign of the presence of the disease. In the literature, other Authors have also demonstrated the importance of surgery for the purposes of pain control and/or improvement: Remorgida *et al.* (31) demonstrated that in women affected by intestinal endometriosis, the removal of the disease foci is associated with a significant improvement in gastrointestinal symptoms one year after surgery; in the same way Seracchioli and colleagues (32) demonstrated a significant reduction in the severity of gastrointestinal symptoms three years after surgery for deep endometriosis. Although it is difficult to clarify what the impact of intestinal endometriosis alone is

Table 8 Pre-operative symptoms according to the VRS (n=103)

Pre-operative symptoms	Pain scale VRS, n (%)				
	0	1	2	3	4
Dyspareunia	29 (28.15)	9 (8.7)	17 (16.50)	13 (12.62)	34 (33.01)
Dysmenorreha	14 (13.59)	3 (2.91)	10 (9.71)	15 (14.56)	48 (46.60)
Chronic pelvic pain	31 (30.10)	16 (15.53)	22 (21.36)	14 (13.59)	20 (19.42)
Dyschezia	41 (39.81)	10 (9.71)	14 (13.59)	16 (15.53)	22 (21.36)
Stranguria	89 (86.41)	5 (4.9)	2 (1.9)	3 (2.9)	4 (3.9)
Abdominal distension	47 (45.63)	10 (9.71)	14 (13.59)	21 (20.39)	11 (10.68)
Tenesmus	73 (70.87)	11 (10.68)	8 (7.77)	5 (4.9)	6 (5.8)
Constipation	42 (40.78)	16 (15.53)	16 (15.53)	20 (19.42)	9 (8.7)
Diarrhea	74 (71.84)	14 (13.59)	5 (4.9)	9 (8.7)	1 (0.97)
Hematochezia	93 (90.3)	7 (6.8)	2 (1.9)	0	1 (0.97)

VRS, verbal rating scale.

Table 9 Post-operative symptoms according to the VRS (n=103)

Post-operative symptoms	Pain scale VRS, n (%)				
	0	1	2	3	4
Dyspareunia	76 (73.8)	11 (10.68)	9 (8.7)	2 (1.9)	4 (3.9)
Dysmenorrhea	81 (78.64)	10 (9.71)	9 (8.7)	2 (1.9)	4 (3.9)
Chronic pelvic pain	86 (83.50)	11 (10.68)	4 (3.9)	0	1 (0.97)
Dyschezia	89 (86.41)	2 (1.9)	5 (4.9)	4 (3.9)	2 (1.9)
Stranguria	99 (96.12)	0	2 (1.9)	1 (0.97)	0
Abdominal distension	62 (60.2)	13 (12.62)	14 (13.59)	11 (10.68)	1 (0.97)
Tenesmus	91 (88.35)	11 (10.68)	14 (13.59)	11 (10.68)	1 (0.97)
Constipation	61 (59.22)	12 (11.65)	10 (9.71)	11 (10.68)	8 (7.77)
Diarrhea	91 (88.35)	6 (5.8)	2 (1.9)	0	2 (1.9)
Hematochezia	97 (94.17)	5 (4.9)	0	0	0

VRS, verbal rating scale.

on infertility, there are numerous studies in the literature which demonstrate how the surgical treatment of pictures of deep endometriosis of medium/severe severity is associated with a 24–57% increase in conceptions after surgery (33,34). In our analysis, in line with these studies, we demonstrate a 20% increase in the number of post-surgical pregnancies, a statistically significant figure compared to the pre-surgical control. There is no common consensus on the most appropriate surgical treatment in the case of intestinal endometriosis and post-operative complications certainly represent a challenge for the surgeon. The types of intervention can be basically divided into conservative (rectal shaving, discoid resection, strictureplasty) and radical (segmental resections) (35). Whether conservative treatment is preferable for intestinal endometriosis is controversial. Some studies have shown that radical surgery substantially improves patients' quality of life (36) but is associated with a greater risk of post-

operative complications, among which the most feared are anastomotic leak, rectovaginal fistula, and pelvic abscess with an incidence ranging from 3% to 20% (37-39). Mohr *et al.* reported the complication rates of rectal shaving, discoid resection, and segmental resection as 6%, 23%, and 38%, respectively (40). Kondo *et al.* (41) and Maytham *et al.* (42) showed similar results. However, Roman *et al.* (43) reported a higher complication rate in the conservative group rather than in the radical treatment group (49% *vs.* 41.6%, respectively), as indeed also Koh *et al.* (44). In our study, the anastomotic leak rate was 1.1%, as was the case for rectovaginal fistula and pelvic abscess; these data were found to be better than the average (39,45). Donnez and colleagues in their review reported anastomotic leakage rates between 0 and 4.8%, and rectovaginal fistula rates between 0 and 10.3% (38). From our univariate risk analyses (not reported), no statistically significant association emerged between the type of surgery (whether conservative or radical) and post-operative complications. Both in rectal resections and in discoid resections we always perform a double leak test, both with methylene blue and by hydropneumatic test. Furthermore, in all resections performed over the last year, whether rectosigmoid or ileal, the indocyanine green test was always performed to evaluate the correct vascularization of the intestinal stumps to be anastomized. It is important to note that some of the complications encountered, such as in the case of the patient with hemorrhagic collection that required re-operation, are related to the combined resection of other pelvic structures such as the ovaries and/or uterus. In our series, 18.28% of the patients performed a temporary ileostomy, of which two ghost ileostomy, and this data is in line with those found in other studies (26,46). The choice of whether create a protective ileostomy or not often depends on the preferences of the surgical team, however it must always be guided by some factors such as the level of the anastomosis, the result 46 intraoperative leak test, the type of surgery, the presence of multiple resections and/or concomitant vaginal resection (47,48). Among the various complications reported in the literature, low anterior resection syndrome (LARS) should also be included, more widely studied in the case of resections performed for colorectal cancer where the mesorectal resection, for the purposes of an oncologically correct treatment, must be as radical as possible (49). In the case of endometriosis, however, since this is a benign pathology, the separation of the mesorectum from the intestinal wall can be performed closer to the latter, where the vessels are smaller and easier to coagulate; the mesentery is dissected no more than 2 cm away from the endometriotic nodule thus maintaining adequate vascularization of the stumps and avoiding injury to the hypogastric nerve plexuses or somatic nerve fibers. In our study, none of the patients complained symptoms, at the time of follow-up, that could lead to low rectal resection syndrome. A limitation of the study is the lack of data on the distance of the rectal nodule from the anal margin, therefore it was not possible to include this evaluation in the statistical analysis of the data. Some authors have stated that the surgeon's experience can influence the development of intra- and post-operative complications. Dubernard *et al.* (50) reported a post-operative complication rate of 15.5%, higher than in other studies; they stated that the surgeon's lack of experience in laparoscopic colorectal resections for endometriosis was a possible cause for this high incidence. Nowadays it is well established that in the treatment of deep endometriosis there must be a multidisciplinary team composed of gynecologists, general surgeons and possibly urologists working in the same hospital (51). The radiological study is also fundamental in planning the therapeutic approach. Another matter of debate between conservative and radical treatment is that some authors believe that conservative treatment increases the risk of recurrence due to the persistence of microscopic disease near the resection margins (52). Fedele *et al.* (53) showed in their study that the risk of endometriosis recurrence requiring further treatment was much higher in patients treated conservatively than in those undergoing segmental resections. However, there are also other studies in the literature which demonstrate the opposite, that is, it doesn't seem to be a correlation between the positivity of the margins and the recurrence rate (54). We did not demonstrate a correlation in our analysis statistically significant between the involvement of the resection margins tout court and the development of organic recurrence. The recurrence rate of endometriosis in our study was found to be 8.6% and in all cases it was asymptomatic forms found exclusively on ultrasound imaging. In the literature, endometriotic recurrence after surgery is found in 4.7–25% of cases during a follow-up >2 years, so our data appear to be in linea with what is present in other studies. Although rare, endometriosis can undergo malignant transformation in less than 1% of cases (55). In our work, the incidence of endometriosis cancer was found to be 1.1%, in agreement with the data found in the literature. The low number of cases of cancer of deep endometriosis does not justify, alone, the indication for surgical treatment, even if the same could have the

potential benefit of reducing the risk of malignant progression of endometriosis.

Conclusions

Deep endometriosis is considered the most aggressive form of endometriosis as it can involve the entire pelvis, subverting the normal anatomy and function of various organs such as the intestine, with a profound negative impact on the patients' quality of life. Medical therapy can temporarily control the symptoms, which however recur as soon as the patient interrupts the treatment with intent to procreate or due to side effects. Furthermore, hormone therapy does not prevent the progression of the disease. Our study, albeit with some limitations related to its retrospective nature and the small number of patients, highlights how the multidisciplinary minimally invasive approach is the gold standard in the surgical treatment of deep endometriosis with intestinal involvement, with excellent results both in terms of fertility and improvement of painful symptoms, guaranteeing a better quality of life, against a limited surgical risk and a low rate of complications.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://ls.amegroups.com/article/view/10.21037/ls-24-2/rc

Data Sharing Statement: Available at https://ls.amegroups.com/article/view/10.21037/ls-24-2/dss

Peer Review File: Available at https://ls.amegroups.com/article/view/10.21037/ls-24-2/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://ls.amegroups.com/article/view/10.21037/ls-24-2/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any parts of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This research meets ethical guidelines and informed consent was acquired. The study was approved by the local research ethics committee "Comitato Etico dell'Area Vasta Emilia Nord" (protocol number: 0024582/19) on December 19, 2017, before enrollment, adherent to local and international standards.

References

1. Abesadze E, Chiantera V, Sehouli J, et al. Post-operative management and follow-up of surgical treatment in the case of rectovaginal and retrocervical endometriosis. Arch Gynecol Obstet 2020;302:957-67.
2. Giudice LC, Kao LC. Endometriosis. Lancet 2004;364:1789-99.
3. Audebert A, Bäckström T, Barlow DH, et al. Endometriosis 1991: a discussion document. Hum Reprod 1992;7:432-5.
4. Patel BG, Lenk EE, Lebovic DI, et al. Pathogenesis of endometriosis: Interaction between Endocrine and inflammatory pathways. Best Pract Res Clin Obstet Gynaecol 2018;50:50-60.
5. Veeraswamy A, Lewis M, Mann A, et al. Extragenital endometriosis. Clin Obstet Gynecol 2010;53:449-66.
6. Remorgida V, Ferrero S, Fulcheri E, et al. Bowel endometriosis: presentation, diagnosis, and treatment. Obstet Gynecol Surv 2007;62:461-70.
7. Wolthuis AM, Meuleman C, Tomassetti C, et al. Bowel endometriosis: colorectal surgeon's perspective in a multidisciplinary surgical team. World J Gastroenterol 2014;20:15616-23.
8. Redwine DB. Intestinal endometriosis. In: Redwine DB. editor. Surgical management of endometriosis. 1st ed. Boca Raton: CRC Press; 2004:208-233.
9. Hartmann D, Schilling D, Roth SU, et al. Endometriosis of the transverse colon--a rare localization. Dtsch Med

Wochenschr 2002;127:2317-20.

10. Iaroshenko VI, Salokhina MB. Endometriosis of the stomach. Vestn Khir Im I I Grek 1979;123:82-3.

11. Liu K, Zhang W, Liu S, et al. Hepatic endometriosis: a rare case and review of the literature. Eur J Med Res 2015;20:48.

12. Koninckx PR, Ussia A, Adamyan L, et al. Deep endometriosis: definition, diagnosis, and treatment. Fertil Steril 2012;98:564-71.

13. Jørgensen H, Hill AS, Beste MT, et al. Peritoneal fluid cytokines related to endometriosis in patients evaluated for infertility. Fertil Steril 2017;107:1191-1199.e2.

14. Hurst BS, Shimp KE, Elliot M, et al. Molecular evaluation of proliferative-phase endometrium may provide insight about the underlying causes of infertility in women with endometriosis. Arch Gynecol Obstet 2014;289:1119-24.

15. Kissler S, Hamscho N, Zangos S, et al. Diminished pregnancy rates in endometriosis due to impaired uterotubal transport assessed by hysterosalpingoscintigraphy. BJOG 2005;112:1391-6.

16. Habib N, Centini G, Lazzeri L, et al. Bowel Endometriosis: Current Perspectives on Diagnosis and Treatment. Int J Womens Health 2020;12:35-47.

17. Belghiti J, Thomassin-Naggara I, Zacharopoulou C, et al. Contribution of Computed Tomography Enema and Magnetic Resonance Imaging to Diagnose Multifocal and Multicentric Bowel Lesions in Patients With Colorectal Endometriosis. J Minim Invasive Gynecol. 2015;22:776-84.

18. Rossi L, Palazzo L, Yazbeck C, et al. Can rectal endoscopic sonography be used to predict infiltration depth in patients with deep infiltrating endometriosis of the rectum? Ultrasound Obstet Gynecol 2014;43:322-7.

19. Holland TK, Cutner A, Saridogan E, et al. Ultrasound mapping of pelvic endometriosis: does the location and number of lesions affect the diagnostic accuracy? A multicentre diagnostic accuracy study. BMC Womens Health 2013;13:43.

20. Piketty M, Chopin N, Dousset B, et al. Preoperative work-up for patients with deeply infiltrating endometriosis: transvaginal ultrasonography must definitely be the first-line imaging examination. Hum Reprod 2009;24:602-7.

21. Kennedy S. Should a diagnosis of endometriosis be sought in all symptomatic women? Fertil Steril 2006;86:1312-3.

22. Wykes CB, Clark TJ, Khan KS. Accuracy of laparoscopy in the diagnosis of endometriosis: a systematic quantitative review. BJOG 2004;111:1204-12.

23. Vercellini P, Crosignani PG, Somigliana E, et al. Medical treatment for rectovaginal endometriosis: what is the evidence? Hum Reprod 2009;24:2504-14.

24. Laganà AS, Vitale SG, Trovato MA, et al. Full-Thickness Excision versus Shaving by Laparoscopy for Intestinal Deep Infiltrating Endometriosis: Rationale and Potential Treatment Options. Biomed Res Int 2016;2016:3617179.

25. Roman H, Hennetier C, Darwish B, et al. Bowel occult microscopic endometriosis in resection margins in deep colorectal endometriosis specimens has no impact on short-term postoperative outcomes. Fertil Steril 2016;105:423-9.e7.

26. Nirgianakis K, McKinnon B, Imboden S, et al. Laparoscopic management of bowel endometriosis: resection margins as a predictor of recurrence. Acta Obstet Gynecol Scand 2014;93:1262-7.

27. Fanfani F, Fagotti A, Gagliardi ML, et al. Discoid or segmental rectosigmoid resection for deep infiltrating endometriosis: a case-control study. Fertil Steril 2010;94:444-9.

28. Dunselman GA, Vermeulen N, Becker C, et al. ESHRE guideline: management of women with endometriosis. Hum Reprod 2014;29:400-12.

29. Laganà AS, Vitale SG, Granese R, et al. Clinical dynamics of Dienogest for the treatment of endometriosis: from bench to bedside. Expert Opin Drug Metab Toxicol 2017;13:593-6.

30. Koh CE, Juszczyk K, Cooper MJ, et al. Management of deeply infiltrating endometriosis involving the rectum. Dis Colon Rectum 2012;55:925-31.

31. Remorgida V, Ragni N, Ferrero S, et al. The involvement of the interstitial Cajal cells and the enteric nervous system in bowel endometriosis. Hum Reprod 2005;20:264-71.

32. Seracchioli R, Poggioli G, Pierangeli F, et al. Surgical outcome and long-term follow up after laparoscopic rectosigmoid resection in women with deep infiltrating endometriosis. BJOG 2007;114:889-95.

33. Duepree HJ, Senagore AJ, Delaney CP, et al. Laparoscopic resection of deep pelvic endometriosis with rectosigmoid involvement. J Am Coll Surg 2002;195:754-8.

34. Minelli L, Fanfani F, Fagotti A, et al. Laparoscopic colorectal resection for bowel endometriosis: feasibility, complications, and clinical outcome. Arch Surg 2009;144:234-9; discussion 239.

35. Stepniewska A, Pomini P, Bruni F, et al. Laparoscopic treatment of bowel endometriosis in infertile women. Hum Reprod 2009;24:1619-25.

36. Dousset B, Leconte M, Borghese B, et al. Complete surgery for low rectal endometriosis: long-term results of a

100-case prospective study. Ann Surg 2010;251:887-95.

37. Redwine DB, Wright JT. Laparoscopic treatment of complete obliteration of the cul-de-sac associated with endometriosis: long-term follow-up of en bloc resection. Fertil Steril 2001;76:358-65.

38. Donnez O, Roman H. Choosing the right surgical technique for deep endometriosis: shaving, disc excision, or bowel resection? Fertil Steril 2017;108:931-42.

39. Fingerhut A, Elhadad A, Hay JM, et al. Infraperitoneal colorectal anastomosis: hand-sewn versus circular staples. A controlled clinical trial. French Associations for Surgical Research. Surgery 1994;116:484-90.

40. Mohr C, Nezhat FR, Nezhat CH, et al. Fertility considerations in laparoscopic treatment of infiltrative bowel endometriosis. JSLS 2005;9:16-24.

41. Kondo W, Bourdel N, Tamburro S, et al. Complications after surgery for deeply infiltrating pelvic endometriosis. BJOG 2011;118:292-8.

42. Maytham GD, Dowson HM, Levy B, et al. Laparoscopic excision of rectovaginal endometriosis: report of a prospective study and review of the literature. Colorectal Dis 2010;12:1105-12.

43. Roman H, Vassilieff M, Tuech JJ, et al. Postoperative digestive function after radical versus conservative surgical philosophy for deep endometriosis infiltrating the rectum. Fertil Steril 2013;99:1695-704.

44. Bertocchi E, Barugola G, Benini M, et al. Colorectal Anastomotic Stenosis: Lessons Learned after 1643 Colorectal Resections for Deep Infiltrating Endometriosis. J Minim Invasive Gynecol 2019;26:100-4.

45. Ruffo G, Sartori A, Crippa S, et al. Laparoscopic rectal resection for severe endometriosis of the mid and low rectum: technique and operative results. Surg Endosc 2012;26:1035-40.

46. Malzoni M, Di Giovanni A, Exacoustos C, et al. Feasibility and Safety of Laparoscopic-Assisted Bowel Segmental Resection for Deep Infiltrating Endometriosis: A Retrospective Cohort Study With Description of Technique. J Minim Invasive Gynecol 2016;23:512-25.

47. Vigueras Smith A, Sumak R, Cabrera R, et al. Bowel anastomosis leakage following endometriosis surgery: an evidence based analysis of risk factors and prevention techniques. Facts Views Vis Obgyn 2020;12:207-25.

48. Nguyen TH, Chokshi RV. Low Anterior Resection Syndrome. Curr Gastroenterol Rep 2020;22:48.

49. Bokor A, Hudelist G, Dobó N, et al. Low anterior resection syndrome following different surgical approaches for low rectal endometriosis: A retrospective multicenter study. Acta Obstet Gynecol Scand 2021;100:860-7.

50. Dubernard G, Piketty M, Rouzier R, et al. Quality of life after laparoscopic colorectal resection for endometriosis. Hum Reprod 2006;21:1243-7.

51. Kennedy S, Bergqvist A, Chapron C, et al. ESHRE guideline for the diagnosis and treatment of endometriosis. Hum Reprod 2005;20:2698-704.

52. D'Hooghe T, Hummelshoj L. Multi-disciplinary centres/networks of excellence for endometriosis management and research: a proposal. Hum Reprod 2006;21:2743-8.

53. Fedele L, Bianchi S, Zanconato G, et al. Is rectovaginal endometriosis a progressive disease? Am J Obstet Gynecol 2004;191:1539-42.

54. Heaps JM, Nieberg RK, Berek JS. Malignant neoplasms arising in endometriosis. Obstet Gynecol 1990;75:1023-8.

55. Zanardi R, Del Frate C, Zuiani C, et al. Staging of pelvic endometriosis based on MRI findings versus laparoscopic classification according to the American Fertility Society. Abdom Imaging 2003;28:733-42.