Study Protocol

Protocol for

Establishment and Application of an Evaluation System for Precision Excision of Bowel Endometriosis

Project alias:

Efficacy and Safety of Intra-operative Dual Laparoscopy and Neo-rectoscopy (IDLnR) versus Conventional Laparoscopic Surgery (CL) for Bowel Endometriosis: A Multicenter, Open-Label, Randomized Controlled Trial (LUMEN-01)

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This trial protocol has been provided by the authors to give readers additional information about the work.

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Summary

Title	Efficacy and Safety of Intra-operative Dual Laparoscopy and Neo-rectoscopy (IDLnR) versus Conventional Laparoscopic Surgery (CL) for Bowel Endometriosis A Multicenter, Open-Label, Randomized Controlled Trial (LUMEN-01)
Version	1.1
Sponsor	Xiaofang Yi
Investigational Site	Obstetrics and Gynecology Hospital of Fudan University, Shanghai, China
Indications	Bowel Endometriosis (BE)
Study Objective	To investigate the efficacy and safety of intra-operative Dual Laparoscopy and Neo-rectoscopy (IDLnR) in the treatment of bowel endometriosis compared with conventional laparoscopy.
Study Design	Multicenter, prospective, open-label, randomized controlled trial (RCT)
Case Grouping	**Intervention Group:** Novel combined colonoscopy and laparoscopy (IDLnR) **Control Group:** Conventional laparoscopy (CL) **Eligible patients with bowel endometriosis (BE) will be randomly assigned in a 1:1 ratio using a central randomization system to receive either intra-operative Dual Laparoscopy and Neo-rectoscopy (IDLnR) or conventional laparoscopic surgery (CL).**
Sample Size Justification	The primary efficacy endpoint of this study is the improvement rate of the **Low Anterior Resection Syndrome (LARS)** score grade at 6 months postoperatively. A significance level α of 0.05 and a power of 80% were set. Based on retrospective study data, the improvement rates were 75% in the experimental group and 55% in the control group, respectively. Calculation using Power Analysis and Sample Size (PASS) software showed that at least 86 patients should be enrolled in each group. Considering an anticipated dropout rate of 10%, the final required enrollment was determined to be at least 96 patients per group, with a total sample size of 192 patients.

Inclusion Criteria	● Premenopausal women aged 18 to 55 years. ● Preoperative pelvic contrast-enhanced magnetic resonance imaging (MRI) and/or transrectal endosonography confirmed bowel endometriosis (BE) lesions involving the muscular layer of the intestinal wall, located in the rectum and/or sigmoid colon. Postoperative pathological diagnosis serves as the gold standard. ● Pre-treatment LARS score > 20. ● Eligible for laparoscopic surgery. ● Voluntarily participated in this study and signed written informed consent.
Exclusion Criteria	● Pregnancy or lactation. ● Presence of active inflammatory bowel disease, irritable bowel syndrome, or other similar conditions with disease flare-ups within the past 1 year. ● Acute or severe infectious disease within 4 weeks prior to surgery. ● History of malignant tumor, or highly suspected gynecological/gastrointestinal malignancy based on preoperative imaging or tumor marker tests. ● American Society of Anesthesiologists (ASA) physical status classification ≥ Grade Ⅲ, or severe cardiac, pulmonary, hepatic, renal, or coagulation dysfunction that precludes general anesthesia and elective laparoscopic surgery. ● Undergoing robot-assisted laparoscopic surgery or open laparotomy. ● Currently participating in other clinical trials that may affect the outcome assessment of this study. ● Previous participation in other interventional clinical trials that may affect the outcome assessment of this study. ● History of colorectal resection and anastomosis or stoma surgery. ● History of pelvic radiotherapy.
Withdrawal Criteria	● Intraoperative observation that the lesion does not involve the intestinal muscularis propria, or the lesion is located >28 cm from the anal verge. ● Intraoperative or postoperative pathological diagnosis of malignant tumor. ● Withdrawal of informed consent by the patient.
	Primary Outcome Measures Rate of improvement in the LARS (Low Anterior Resection Syndrome) score category at 6 months postoperatively. **Improvement is defined as:**

Study Endpoints	A shift from severe LARS to mild LARS or no LARS, or from mild LARS to no LARS at 6 months after surgery. **Secondary Outcome Measures** **1. Efficacy Evaluation:** **(1) Bowel Function Evaluation:** ① LARS cure rate (LARS category improved to no LARS at 12 months postoperatively) ② LARS improvement rate (decrease in LARS category at 3 and 12 months postoperatively compared with baseline) ③ Change in LARS score (changes at 3, 6, and 12 months postoperatively compared with baseline) ④ Change in Colorectal Anal Distress Inventory-8 (CRADI-8) score (change at 6 months postoperatively compared with baseline) ⑤ Change in Wexner constipation score (change at 12 months postoperatively compared with baseline) **(2) Quality of Life Evaluation:** ① Change in the Gastrointestinal Quality of Life Index (GIQLI) score at 6 and 12 months postoperatively compared with baseline. ② Change in the Endometriosis Health Profile-30 (EHP-30) score at 6 and 12 months postoperatively compared with baseline. **(3) Pain Evaluation:** Change in Visual Analogue Scale (VAS) score at 6 months postoperatively compared with baseline. **Safety Evaluation:** ① Incidence of severe complications such as intestinal perforation, intestinal bleeding, and anastomotic leakage/fistula within 30 days postoperatively (defined as events with Clavien-Dindo classification ≥ Grade III). ② Antibiotic use intensity for therapeutic purposes within 7 days postoperatively (measured in Defined Daily Doses (DDDs)). ③ Proportion of patients with postoperative hospital stay > 7 days.
	• Baseline data will be analyzed based on the Full Analysis Set (FAS). The primary endpoint will be analyzed based on FAS, Per-Protocol Set (PPS), and Actual Treatment Set, with the FAS result as the primary outcome, and PPS and Actual Treatment Set as sensitivity analyses. Secondary efficacy

Statistical Strategy	endpoints will be analyzed based on FAS. Safety endpoints will be analyzed based on the Safety Set (SS). ● All statistical analyses will be performed using Statistical Analysis System (SAS) 9.4. All statistical tests will be two-sided, and a P-value ≤ 0.05 will be considered statistically significant. A 95% confidence interval (CI) will be used. ● Baseline characteristics analysis: Continuous data will be presented as mean ± standard deviation or median (P25, P75). Categorical data will be summarized as frequency (percentage). Student' s t-test / rank-sum test / chi-square test / Fisher' s exact test will be used to compare demographic and baseline characteristics to assess between-group balance. ● Primary endpoint analysis: The improvement rate of LARS grade will be compared between groups using the chi-square test. The confidence interval for the single-group improvement rate will be estimated using the Clopper-Pearson method, and the confidence interval for between-group differences using the Newcombe method. ● Secondary endpoints analysis: The statistical methods for LARS cure rate at 12 months, LARS improvement rate at 3 and 12 months, and change in VAS pain score will be consistent with the primary endpoint. Between-group comparisons of changes in LARS score, CRADI-8 score, Wexner constipation score, and quality of life scores will be performed using analysis of covariance (ANCOVA), adjusted for baseline scores. ● Subgroup analysis: Prespecified subgroup analyses of the primary endpoint will be performed according to stratification factors: study center, desire for uterus preservation (yes/no), and baseline LARS grade (mild/severe). ● The final statistical analysis strategy will be based on the Statistical Analysis Plan (SAP) finalized before database lock.

1. Research Background

Endometriosis (EMs) is an estrogen-dependent chronic inflammatory disease caused by the growth of endometrial tissue outside the uterine cavity. It is a common gynecological disorder that severely affects fertility, physical and mental health in women of reproductive age, with a global prevalence of approximately 10%–15% among this population [1].

Based on the anatomical sites involved, endometriosis is classified into peritoneal endometriosis (PEM), ovarian endometrioma (OMA), deep endometriosis (DE), and other extra-pelvic special types. Among these, bowel endometriosis (BE) [2] is the most common and clinically severe subtype of deep infiltrating endometriosis (DIE). Lesions mainly involve the rectum and sigmoid colon, followed by the cecum, appendix, and other segments.

The prevalence of BE is approximately 3.8%–12% in all patients with endometriosis and accounts for 30%–37% of patients with DIE. In addition to severe dysmenorrhea and chronic pelvic pain, patients with BE often present with bowel-specific symptoms such as anal tenesmus, diarrhea / constipation during menstruation, tenesmus, defecation pain, and even hematochezia. Some patients may develop intestinal stenosis or obstruction, resulting in a heavy disease burden and significantly impaired quality of life.

Current treatments for BE include medical therapy and surgical treatment. Medical therapy only provides short-term relief of some symptoms and cannot reverse organic lesions of the intestinal wall. Moreover, long-term medication is limited by frequent adverse reactions, poor patient compliance, and high symptom recurrence rates after drug withdrawal.

For patients with BE who are unresponsive to medical therapy, have intractable symptoms, or present with intestinal stenosis or gastrointestinal bleeding, laparoscopy-based surgery is the core approach to achieve radical resection of lesions and long-term symptom relief [3]. The primary goal of BE surgery is to completely resect lesions while maximally preserving intestinal wall integrity and physiological function, thereby reducing the risk of surgical complications.

Current mainstream surgical procedures for BE [4] include the Shaving Technique (ST), Disc Resection (DR), and Segmental Resection (SR). However, there is no global consensus on procedure selection [5]. Existing studies suggest that although ST is less invasive, it carries a higher risk of lesion persistence and postoperative recurrence. DR and SR allow more complete lesion resection, but are associated with significantly higher rates of postoperative complications such as bowel dysfunction, anastomotic leakage, and intestinal wall injury; SR carries the highest complication risk.

In clinical practice, procedure selection highly relies on precise evaluation of the depth of lesion infiltration, extent of peri-intestinal involvement, number of lesions, and severity of intestinal stenosis [6]. Accurate full-thickness localization of lesions during surgery is essential for balancing the completeness of resection, preservation of intestinal function, and reduction of complication risks.

Conventional laparoscopy (CL) is the mainstream surgical approach for bowel endometriosis in current clinical practice. However, it has inherent critical limitations: CL only allows evaluation of lesions through visual inspection of the serosal surface and intraoperative

palpation, without direct visualization of the extent and depth of mucosal involvement. This easily leads to two major clinical issues: First, excessive resection of superficially invasive lesions, which upgrades cases eligible for the shaving technique (ST) to disc resection (DR) or segmental resection (SR), unnecessarily disrupting intestinal wall integrity and increasing the risk of postoperative bowel dysfunction and complications. Second, inadequate assessment of deep and multifocal lesions, resulting in residual disease and elevated postoperative symptom recurrence rates. In addition, CL does not enable real-time verification of anastomotic apposition and integrity during surgery, nor can it detect occult intestinal wall injury or anastomotic leakage in a timely manner, further increasing the risk of severe postoperative complications such as anastomotic leakage and intra-abdominal infection.

Improvement in bowel function is a core, specific endpoint for evaluating the safety and efficacy of bowel endometriosis (BE) surgery. Unlike pain symptoms such as dysmenorrhea and chronic pelvic pain—which can be confounded by other pelvic endometriotic lesions, adenomyosis, pelvic inflammatory disease, and other factors and cannot specifically reflect the surgical effect on intestinal lesions—the core pathological change in BE is direct full-thickness invasion of the intestinal wall by ectopic lesions. The resulting bowel dysfunction is directly related to the depth and extent of lesion invasion, making postoperative improvement in bowel function the most specific and objective core indicator for evaluating the efficacy of targeted BE treatment. The Low Anterior Resection Syndrome (LARS) score is an internationally validated Patient- Reported Outcome Measure (PROM) [7, 8] covering core dimensions including stool frequency, urgency, fecal incontinence, and difficult defecation. Initially developed for evaluating bowel function after rectal cancer surgery, it has been validated in numerous studies over the past decade for good reliability and validity in BE patients, and is currently the preferred standardized tool for baseline preoperative bowel function assessment and postoperative efficacy evaluation in BE patients [9, 10]. Studies have shown that approximately 46.4% of BE patients present with varying degrees of LARS preoperatively, of whom 18.6% have severe LARS—a rate significantly higher than in healthy controls. Furthermore, the LARS score reliably reflects long-term postoperative changes in bowel function among BE patients [10] and is directly associated with the extent of lesion resection and surgical approach.

The official classification criteria of the internationally validated LARS scale are as follows: 0–20 = no LARS, 21–29 = mild LARS, and 30–42 = severe LARS. A LARS score ≥ 21 is the cutoff for clinically significant bowel dysfunction, which is directly associated with increased symptom burden and significantly reduced health-related quality of life in patients with bowel endometriosis (BE) [9]**.** This study enrolls only patients with a baseline LARS score ≥ 21 preoperatively, based on three key rationales: First, this criterion precisely targets patients with definite bowel dysfunction, avoiding dilution of the treatment effect by including asymptomatic patients at baseline, thereby ensuring statistical power and reducing the risk of false-negative results. Second, it maximizes baseline homogeneity between groups and eliminates confounding from preoperative bowel function status, allowing the study outcomes to

objectively reflect the true impact of the two surgical approaches on bowel function in BE patients. Third, this inclusion criterion is highly consistent with clinical practice: most BE patients undergoing surgery present with clear bowel dysfunction. Conclusions derived from this population therefore have strong external validity and clinical generalizability.

Available evidence-based medicine confirms that bowel function in patients with BE remains highly unstable within 3 months postoperatively, easily affected by short-term postoperative inflammation, dietary recovery, re-establishment of defecation habits, and perioperative medications. Intestinal function stabilizes by 6 months after surgery, at which point the LARS score reliably and consistently reflects the long-term impact of surgery on bowel function [7, 8, 11]. In addition to the primary bowel function endpoint, complications within 30 days postoperatively (including anastomotic leakage, intestinal injury, intestinal bleeding, etc.) represent core hard safety endpoints and a key prerequisite for clinical adoption of a surgical technique. Indicators such as improvement in pain symptoms, comprehensive gastrointestinal function, and health-related quality of life reflect the overall clinical benefit and align with the patient-centered treatment goal for endometriosis. This study uses a set of validated instruments: the LARS score, Visual Analogue Scale (VAS), Gastrointestinal Quality of Life Index (GIQLI), Endometriosis Health Profile-30 (EHP-30), and Wexner Constipation Score [12], to comprehensively and systematically evaluate the efficacy and safety of the surgical procedures.

The novel Intraoperative Dual Laparoscopy and Neo-rectoscopy (IDLnR) technique [6] provides a new strategy to overcome the key limitations of conventional laparoscopy. Through combined dual-view operation with intraoperative neo-rectoscopy and laparoscopy, IDLnR achieves full-thickness, precise, and real-time localization of BE lesions. On the one hand, neo-rectoscopy allows direct visualization of the intestinal mucosa, accurately determining the depth of lesion invasion, circumferential involvement, and severity of luminal stenosis, providing an objective basis for surgical selection and avoiding excessive resection or residual disease. On the other hand, combined with laparoscopic transillumination of the bowel wall, bidirectional localization of the serosal and mucosal surfaces can be achieved to precisely define the resection margin. Preliminary single - center observational studies conducted by our research team have demonstrated clear clinical advantages of IDLnR in BE surgery: ① The neo - rectoscope has a working length of approximately 28 cm, sufficiently covering the rectum and distal sigmoid colon—the most frequent sites of BE—to meet intraoperative visualization and procedural requirements. ② It enables precise procedure selection based on mucosal lesion appearance: DR or SR is performed directly for lesions protruding into the mucosa, avoiding prolonged surgery from repeated serosal manipulation; ST is prioritized for superficial lesions without obvious mucosal protrusion, maximally preserving intestinal wall integrity and reducing the risk of pelvic contamination from intestinal contents. ③ Continuous low - flow irrigation of the intestinal lumen can be performed intraoperatively to ensure clean anastomotic apposition

during DR or SR, reducing the risk of poor anastomotic healing. ④ Anastomotic integrity can be immediately inspected endoscopically after completion of the anastomosis, allowing prompt repair of occult leaks and significantly reducing the risk of postoperative anastomotic leakage. ⑤ The neo- rector scope features a slim shaft and is autoclavable without requiring specialized endoscopic disinfection equipment. It can be used synchronously under laparoscopic monitoring with a short learning curve, facilitating clinical application in hospitals at all levels. Preliminary follow - up data from our team showed that, compared with conventional laparoscopy, IDLnR significantly improves postoperative bowel function and reduces the incidence of postoperative complications in BE patients, demonstrating promising clinical potential. However, existing evidence is limited to single-center, small-sample observational studies with low levels of evidence. To date, no prospective, multicenter, randomized controlled trial comparing IDLnR versus CL for BE has been conducted worldwide, nor is there high-quality evidence with mid-to-long-term bowel function improvement as the primary endpoint. The long -term efficacy and safety of IDLnR still require validation by high-level clinical studies.

Based on the above background, this project intends to conduct a prospective, multicenter, open-label randomized controlled trial (RCT) enrolling patients with bowel endometriosis (BE) undergoing surgical treatment, to compare the clinical efficacy and safety of the Intra-operative Dual Laparoscopy and Neo-rectoscopy (IDLnR) technique versus conventional laparoscopy (CL). The study uses improvement in bowel function at 6 months postoperatively as the primary endpoint. The selection of this time point is based on comprehensive consideration of evidence-based medicine and clinical practice: First, as mentioned above, 6 months after surgery represents a stable phase for bowel function recovery in BE patients, eliminating transient interference from short-term postoperative stress and inflammation, and more accurately reflecting the long-term therapeutic effect of the surgical approach on intestinal function. Second, this time point is universally adopted as the core endpoint for bowel function evaluation in high-quality RCTs, systematic reviews, and meta-analyses of BE surgery worldwide [8], consistent with international standards, thereby enhancing the comparability and academic recognition of the results. Third, the 6-month follow-up balances scientific rigor and feasibility. Compared with ultra-long follow-up of 1 year or longer, this time point is associated with a lower patient dropout rate and better compliance in multicenter studies, while fully capturing the long-term impact of early complications within 30 days postoperatively on bowel function, ensuring the reliability of outcome data. Fourth, existing studies have confirmed that bowel function status at 6 months postoperatively in BE patients is significantly associated with long-term quality of life, symptom recurrence risk, and reintervention rate [11], giving this endpoint clear clinical predictive value and practical significance. The study also uses the incidence of postoperative complications and severe complications within 30 days. postoperative pain improvement, comprehensive gastrointestinal function, and health-related quality of life as secondary endpoints to systematically evaluate the clinical value of IDLnR in BE surgery. This study will fill the evidence gap in this field, provide high-level evidence for the standardized

clinical application of IDLnR, help optimize the surgical treatment strategy for BE, and ultimately achieve the clinical goals of complete lesion resection, preservation of intestinal physiological function, and improvement of patients' long-term quality of life.

2. Objective

Primary Objective: To evaluate the improvement in bowel function at 6 months postoperatively between the double-scope group (Intra-operative Dual Laparoscopy and Neo-rectoscopy, IDLnR) and the conventional laparoscopy group (CL) in patients with bowel endometriosis.

Secondary Objectives:

(1) To evaluate the incidence of complications and severe complications within 30 days postoperatively in both groups, including anastomotic leakage, intestinal injury, intestinal bleeding, etc.

(2) To evaluate changes in postoperative pain relief, gastrointestinal function, and quality of life between the two groups.

3. Research design

3.1 Study Design

This study is a multicenter, open-label, parallel-group randomized controlled trial (RCT) conducted by three tertiary medical centers: Obstetrics and Gynecology Hospital of Fudan University, International Peace Maternity and Child Health Hospital of Shanghai Jiao Tong University, and Shanghai First Maternity and Infant Hospital. Eligible patients will be randomly assigned in a 1:1 ratio to receive either the double-scope group (Intra-operative Dual Laparoscopy and Neo-rectoscopy, IDLnR) technique or conventional laparoscopy (CL). The primary endpoint is the rate of improvement in the Low Anterior Resection Syndrome (LARS) score category at 6 months after intestinal surgery.

Leading Center for Study Implementation:

Department of Gynecology, Obstetrics and Gynecology Hospital of Fudan University

3.2 Case Grouping

Control group: Underwent localization, observation, and resection of bowel lesions using conventional laparoscopy (CL). The surgery for bowel endometriosis was completed laparoscopically.

Intervention group: Underwent localization, observation, and resection of bowel lesions using intra-operative Dual Laparoscopy and Neo-rectoscopy (IDLnR). The surgery for bowel endometriosis was completed laparoscopically.

3.3 Sample Size Estimation

The primary efficacy outcome was the improvement rate of LARS score grade at 6 months postoperatively. According to retrospective data, the 6-month LARS grade improvement rate was 55% in the control group (conventional laparoscopy for BE) and 75% in the intervention group (IDLnR for BE). With a type I error $\alpha = 0.05$ and power = 80%, the required sample size calculated by PASS was 86 patients per group. After accounting for a 10% dropout rate, at least 96 patients were enrolled per group, with a total sample size of 192.

3.4 Randomization and Blinding

Eligible patients with bowel endometriosis (BE) who met the inclusion and exclusion criteria were randomly assigned in a 1:1 ratio to receive either IDLnR or conventional laparoscopy alone (CL). The grouping procedure is detailed in the figure.

Randomization was performed using a central randomization system provided by the Biostatistics Center of Fudan University. The system is equipped with independent authority management and operational log traceability, which effectively avoids human interference in the grouping process. A dynamic randomization method based on minimization was adopted, with study center, willingness to preserve the uterus (yes/no), and LARS grade (mild/severe) as minimization factors. Dynamic balancing was used to ensure comparability of these key prognostic factors among groups.

The minimization algorithm was pre-specified and sealed by the statistician and unblinded after trial completion. The system calculated the allocation probability in real time according to the distribution of previously enrolled patients to generate the allocation result.

Due to the nature of surgical intervention, blinding of surgeons and patients was not feasible. However, outcome assessors and data analysts remained blinded to group allocation.

4. Study Population

4.1 Inclusion Criteria

- Premenopausal women aged 18–55 years.
- Bowel endometriosis (BE) lesions involving the muscular layer of the bowel wall, located in the rectum and/or sigmoid colon, confirmed preoperatively by pelvic contrast-enhanced MRI and/or transrectal endoluminal ultrasound, with postoperative pathological diagnosis as the gold standard.
- LARS score > 20.
- Eligible for laparoscopic surgery.
- Voluntarily participated in this study and provided written informed consent.

4.2 Exclusion Criteria

- Pregnancy or lactation.
- Complicated with active inflammatory bowel disease, irritable bowel syndrome, etc., with disease flare-up within the past 1 year.
- Acute or severe infectious disease within 4 weeks preoperatively.

- History of malignant tumor, or highly suspected gynecological / gastrointestinal malignancy on preoperative imaging or tumor marker tests.
- American Society of Anesthesiologists (ASA) physical status classification ≥ Grade Ⅲ, or severe cardiac, pulmonary, hepatic, renal, or coagulation dysfunction that precludes general anesthesia and elective laparoscopic surgery.
- Undergoing robot-assisted laparoscopic surgery or open surgery.
- Currently participating in other clinical trials that may affect the outcome assessment of this study.
- Previous participation in other interventional clinical trials that may affect outcome assessment of this study.
- History of colorectal resection, anastomosis, or stoma surgery.
- History of pelvic radiotherapy.

4.3 Exclusion Criteria for Withdrawal:

- Intraoperative findings confirmed that the lesions did not involve the muscular layer of the bowel wall, or all lesions were located proximal to the sigmoid colon.
- Intraoperative or postoperative pathological diagnosis was malignant tumor.
- The patient withdrew informed consent.

4.4 Patient Screening

- **Recruitment Source:** Subjects in this study will be recruited from the Gynecology and Colorectal Surgery outpatient clinics of the participating hospitals.
- **Screening Procedure:** All potential subjects must undergo a comprehensive screening visit, including:

① Medical history collection and physical examination.

② Gynecological examination: including rectovaginal examination or digital rectal examination.

③ Imaging examination: pelvic contrast-enhanced magnetic resonance imaging (MRI).

The above examinations are performed to confirm or exclude the diagnosis of bowel endometriosis and to evaluate its anatomical extent and depth of invasion.

- Preliminary Inclusion Criteria: Subjects who meet all of the following criteria may be considered potential candidates for this study: clinical diagnosis or imaging evaluation consistent with bowel endometriosis, and a pre-treatment LARS score > 20.

5. Diagnosis and Enrollment Confirmation Criteria of the Study

(1) Clinical Diagnostic Criteria: The clinical diagnosis of bowel endometriosis requires at least one of the following objective findings:

a. Symptoms and signs highly suggestive of bowel involvement by endometriosis;

b. Palpable fixed, hard, tender nodules in the rectovaginal septum or bowel wall on rectovaginal examination or digital rectal examination;

c. Imaging (pelvic contrast-enhanced MRI) or endoscopy (enteroscopy) suggestive of muscular layer involvement at the rectum or rectosigmoid junction;
d. Previous endoscopic biopsy with histopathologically confirmed bowel endometriosis.
(2) Imaging Confirmation ProcedureIndependent reading: All pelvic contrast-enhanced MRI images used for screening will be reviewed by a senior team of radiologists specializing in gynecologic imaging (at least two experienced radiologists). All MR images will be read independently, blindly, and prospectively by radiologists within the department. The readers will be unaware of the patient's group allocation and treatment plan to ensure objective and standardized diagnosis.
(3) Final Confirmation of Enrollment
Patients with clinically or radiologically confirmed bowel endometriosis and a LARS score > 20 will be formally enrolled in the study and randomized only after a multidisciplinary discussion to determine the final surgical treatment plan.

6. Outcome Measures

6.1 Primary Outcome Measures

The primary outcome measure of this study is the improvement rate of the Low Anterior Resection Syndrome (LARS) score grade at 6 months after bowel surgery. This study adopts an open-label design. However, the panel responsible for assessing the primary efficacy outcome (composed of one anorectal surgeon and one gynecologist) remained blinded to group allocation and conducted outcome assessment independently. In the event of disagreement between the two assessors regarding the LARS score grade, a third qualified senior specialist (anorectal surgery or gynecology) would perform an independent review and make the final judgment. The result of this third review was used as the final basis for analysis of the primary outcome.
Improvement was defined as a change in LARS grade at 6 months postoperatively from severe LARS to mild LARS or no LARS, or from mild LARS to no LARS.
The LARS score was obtained using the LARS questionnaire.
The definitions of each LARS grade are as follows:

LARS grade	**Total score range of the LARS scale**	**Core characteristics**
No LARS	0-20	Normal bowel function with no significant defecation-related distress and no impact on daily life or social activities.
Minor LARS	21-29	Presence of symptoms such as flatus/fecal incontinence, increased stool frequency, or urgency, but mild in severity. Symptoms are largely controllable by dietary modification and bowel habit

		adjustment, with limited impact on quality of life.
Major LARS	30-42	Severe symptoms including frequent fecal incontinence, intractable severe urgency, and cluster defecation, which significantly interfere with daily activities, social life, and psychological status, often requiring professional intervention.

6.2 Secondary Outcome Measures

(1) Efficacy Evaluation:

- **Bowel Function Evaluation:**

① LARS cure rate (LARS grade improved to no LARS at 12 months postoperatively)

② LARS improvement rate (decrease in LARS grade at 3 and 12 months postoperatively)

③ Change in LARS score (changes from baseline at 3, 6, and 12 months postoperatively)

④ Change in Colorectal Anal Distress Inventory-8 (CRADI-8) score (change from baseline at 6 months postoperatively)

⑤ Change in Wexner constipation score (change from baseline at 12 months postoperatively)

- **Quality of Life Evaluation:**

① Change in Gastrointestinal Quality of Life Index (GIQLI) score (changes from baseline at 6 and 12 months postoperatively).

② Change in Endometriosis Health Profile-30 (EHP-30) score (changes from baseline at 6 and 12 months postoperatively).

- **Pain Evaluation:**

Proportion of patients with ≥ 50% reduction in Visual Analogue Scale (VAS) score at 6 months postoperatively compared with baseline.

(2) Safety Evaluation:

① Incidence of severe complications within 30 days postoperatively, including intestinal perforation, intestinal anastomotic leakage/fistula, and intestinal bleeding (defined as events with Clavien-Dindo classification ≥ Grade III).

② Antibiotic Use Intensity within 7 days postoperatively (measured by DDDs).

③ Proportion of patients with postoperative hospital stay > 7 days.

7. End-point indicators and corresponding result evaluation criteria

7.1 Efficacy Outcome Definition and Assessment Criteria

All questionnaire assessments were performed by trained research nurses. If patients had difficulty understanding or completing the questionnaires, non-directive assistance and explanations were provided in accordance with the study protocol.

(1) LARS grade improvement rate (LARS scale)

The LARS scale was used for self-assessment of symptoms associated with low anterior resection syndrome, including fecal incontinence, stool frequency, and tenesmus. The total score ranged from 0 to 42. A score of <21 indicated no or mild LARS, and a score of ≥21 indicated moderate-to-severe LARS. The scale was completed independently by the patient.

Improvement was defined as a shift from severe LARS to moderate LARS or no LARS, or from moderate LARS to no LARS.

LARS grade improvement rate at 6 months postoperatively = (number of patients with improved LARS grade / total enrolled patients) × 100%.

(2) LARS improvement rate (decrease in LARS grade at 3 and 12 months postoperatively)

The LARS scale was used to assess symptoms related to low anterior resection syndrome. The scale content, scoring range, and grading criteria were the same as those described in item (1).

LARS grade improvement rates at 3 and 12 months postoperatively were calculated as follows:

LARS grade improvement rate = (number of patients with improved LARS grade / total enrolled patients) × 100%.

(3) Change in LARS score (LARS scale)

The LARS scale was used to assess symptoms related to low anterior resection syndrome. The scale content, scoring range, and grading criteria were the same as those described in item (1).

Change in LARS score was defined as the difference between the total LARS score at the specified postoperative time points (3, 6, and 12 months) and that at the baseline visit before randomization:

Change = baseline total score − postoperative follow-up total score.

This was a continuous variable; a positive value indicated symptom improvement, and a negative value indicated symptom worsening.

(4) Change in Colorectal Anal Distress Inventory (CRADI-8) score

The CRADI-8 scale was used to assess symptoms related to anorectal dysfunction. The CRADI-8 scale included 8 items covering fecal incontinence, urgency, abnormal stool frequency, and abdominal pain, with a total score ranging from 0 to 100. Higher scores indicated more severe anorectal distress.

Change in CRADI-8 score was defined as the difference between the total score at 6 months postoperatively and that at the baseline visit:

Change = baseline total score − 6-month postoperative total score.

This was a continuous variable; a positive value indicated improvement in anorectal distress, and a negative value indicated worsening.

(5) Change in Wexner constipation score

The Wexner constipation score was used to evaluate the severity of constipation. The scale included 8 items: stool frequency, straining, incomplete evacuation, abdominal pain, and need for manual assistance, with a total score ranging from 0 to 30. Higher scores indicated more severe constipation.

The change in Wexner constipation score at 12 months postoperatively compared with baseline was calculated. This was a continuous variable; a negative value indicated improvement in constipation, and a positive value indicated worsening.

(6) Change in Gastrointestinal Quality of Life Index (GIQLI) score

The 36-item GIQLI scale was used to assess gastrointestinal-related quality of life, covering gastrointestinal symptoms, physical function, and psychological status. The total score ranged from 0 to 144; higher scores reflected better gastrointestinal quality of life.

Changes in GIQLI score at 6 and 12 months postoperatively compared with baseline were calculated.

(7) Change in Endometriosis Health Profile-30 (EHP-30) score

The core module of the EHP-30 questionnaire was used to assess disease-specific health-related quality of life. The core module contained 30 items covering pain, emotional state, and social function. Domain and total scores were transformed to a 0 – 100 scale according to standard methods; higher scores indicated a more severe negative impact of the disease on quality of life.

Changes in EHP-30 score at 6 and 12 months postoperatively compared with baseline were calculated.

(8) Improvement in Visual Analogue Scale (VAS) score

Pain was assessed using the VAS (0 = no pain, 10 = worst imaginable pain) at baseline and 6 months postoperatively. The proportion of patients with a ≥ 50% reduction in VAS score at 6 months postoperatively compared with baseline was calculated.

7.2 Safety Outcome Definition and Assessment Criteria

(1) Definition of complications within 30 days postoperatively

In this study, a complication was defined as any adverse medical event that occurred within 30 days after the randomly assigned surgery (either combined IDLnR and laparoscopy or conventional laparoscopy) and had a reasonable causal relationship with the surgical intervention. Complications were graded and counted according to the Clavien-Dindo classification system. Severe complications were defined as those occurring within 30 days postoperatively that were related to surgery and required invasive intervention (e.g., reoperation, endoscopy, radiological intervention), resulted in organ failure, or were life- threatening (i.e., Clavien-Dindo Grade III or higher). Severe complication rate = (number of patients with Clavien-Dindo Grade III or higher complications / total enrolled patients) × 100%. The diagnosis of complications was confirmed jointly by a multidisciplinary team (surgery, anesthesiology, radiology).

Assessment of Relatedness to the RCT Intervention

For each complication, the relatedness to the intervention received shall be evaluated by the investigator (typically a gynecologist or surgeon) or an expert committee appointed by the sponsor (e.g., Clinical Endpoint Committee). The relatedness is generally classified into 5 levels as follows:

① Definite relation: The event has a reasonable temporal sequence with the intervention; cannot be reasonably explained by other conditions of the subject; improves after discontinuation or symptomatic treatment; and recurs upon re-exposure.

② Possible relation: The event has a temporal sequence with the intervention; is more likely explained by the surgery, although the influence of other conditions of the subject cannot be completely excluded.

③ Possible unrelated: The event has a temporal sequence with the intervention but is more likely explained by other conditions or concomitant therapies of the subject.

④ Definite unrelated: The event has no reasonable temporal sequence with the intervention; or can be fully explained by other conditions or concomitant therapies of the subject.

⑤ Unassessable: Insufficient information to make a judgment.

Application in This Study

All adverse events (AEs) within 30 days postoperatively shall be documented, and their relatedness to the surgery shall be assessed. AEs assessed as definitely related or possibly related to the intervention are the primary focus for evaluating the safety of the investigational procedures.

Scope of severe complications relevant to this study:

a. Endoscopy-related intestinal perforation

Mechanical intestinal perforation is caused by direct penetration or laceration of the bowel wall by the endoscope or auxiliary instruments, most commonly at bowel loops (e.g., sigmoid colon, splenic flexure) or adherent bowel segments.

Hydrostatic perforation results from a sudden increase in intraluminal pressure due to excessive or rapid water infusion during endoscopy, especially when the bowel wall is weakened by lesions (e.g., endometriotic infiltration) or fragile.

b. Endoscopy-related intestinal hemorrhage

Hemorrhage occurring intraoperatively or within several hours postoperatively, usually associated with intraluminal procedures.

c. Normal bowel wall injury

Mucosal or submucosal laceration, hematoma formation, or non-full-thickness injury that may cause pain, inflammation, or delayed perforation, diagnosed intraoperatively or within 30 days after endoscopy.

d. Anastomotic leakage/fistula

Anastomotic leakage/fistula is defined within 30 days postoperatively by the presence of fever, abdominal pain, turbid feculent-smelling abdominal drainage, combined with abdominal CT showing perianastomotic fluid/gas, extravasation of oral contrast medium from the anastomosis, or confirmation by surgical exploration.

e. Intestinal obstruction

Intestinal obstruction is diagnosed within 30 days postoperatively by abdominal pain, distension, cessation of flatus and defecation, combined with abdominal radiograph/CT showing bowel dilatation and air-fluid levels, after excluding other etiologies (confirmed by surgeons based on imaging findings).

(2) Proportion of patients with postoperative hospital stay > 7 days

Defined as the proportion of cases with a postoperative hospital stay exceeding 7 days due to intestinal surgery-related factors.

Calculation formula:

(Number of eligible cases with postoperative hospital stay > 7 days / Total number of eligible cases included in this indicator analysis) × 100%.

(3) Antibiotic Use Intensity within 7 days postoperatively (measured by DDDs)

Definition and scope: Only therapeutic antibiotics initiated or continued postoperatively due to fever are included. The study period is defined as postoperative days 0–7.

Calculation of therapeutic antibiotic DDDs:

Total DDDs = Σ (Total consumption of each antibiotic in g / WHO-DDD value of that antibiotic in g).

Total consumption of each antibiotic (g) = Single dose (g) × Times per day × Duration of therapy (days).

The WHO-DDD value (g) refers to the Defined Daily Dose established by the WHO Collaborating Centre for Drug Statistics Methodology, available at: https://www.whocc.no/atc_ddd_index/.

Combination therapy: DDDs for each antibiotic are calculated separately and then summed to obtain the total DDDs.

The following shall not be counted in the calculation of therapeutic antibiotic density:

① Preoperative prophylaxis: single-dose antibiotics given before surgical incision (usually within 60 minutes prior to skin incision) in compliance with guidelines.

② Intraoperative supplementary doses: antibiotics added only due to prolonged surgery (e.g., >2 drug half-lives) or massive intraoperative blood loss, with no further use postoperatively.

③ Non-infectious indications: antibiotics used explicitly for non-infectious conditions.

④ Pre-existing infections: antibiotics for treating confirmed preoperative infections (e.g., preoperative pneumonia, acute cholecystitis) shall be deducted from the total postoperative dose.

8. Qualifications of the participating investigators

8.1 Basic Principles of Surgical Qualifications

All patients enrolled in this trial underwent surgery performed by members of the gynecology and intestinal surgery teams. Before the initiation of this study, all participating gynecologists and surgeons had completed standardized technical training on intestinal lesion resection for endometriosis and the intraoperative application of a novel enteroscopy. All participating gynecologic surgeons were required to be qualified for Grade IV laparoscopic surgery. The standardization of surgical procedures was verified using a surgical step checklist and MDT consultation records.

8.2 Standard Operation Procedure (SOP) of IDLnR

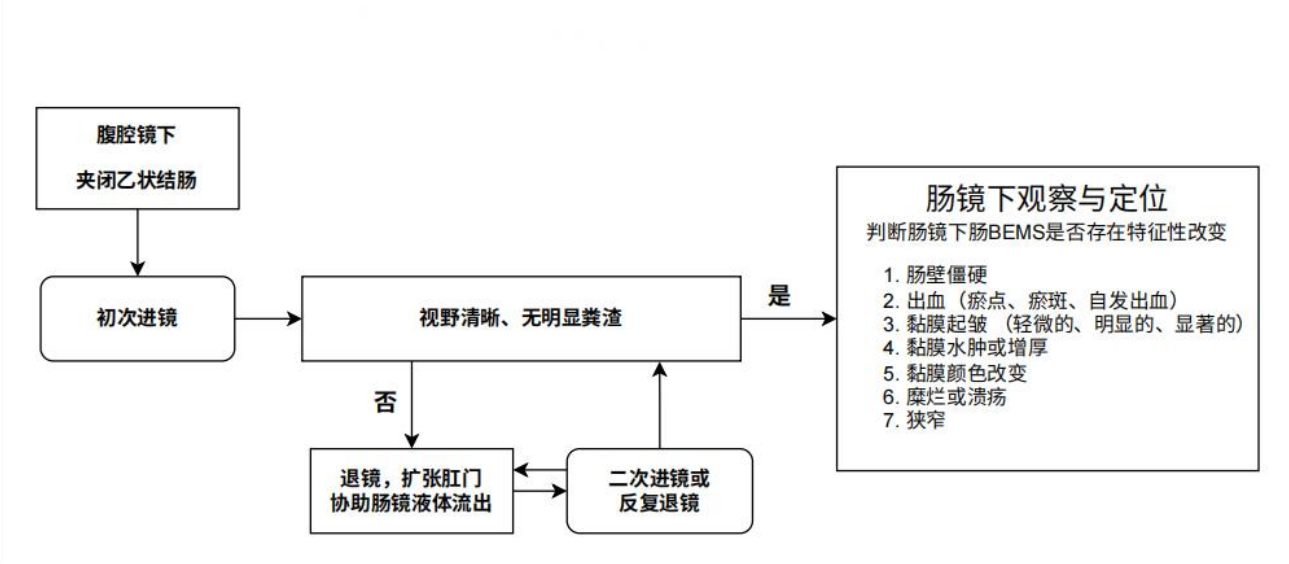


Figure 1. Intra-operative Dual Laparoscopy and Neo-rectoscopy (IDLnR) protocol for bowel endometriosis (BE)

- **Laparoscopic Clamping of the Sigmoid Colon**
- **Initial Neo-rectoscopy Insertion**
- **Clear Visual Field, No Significant Fecal Residue**

If YES: Proceed to **Neo-rectoscopic Observation and Localization**
If NO: Proceed to **Scope Withdrawal, Anal Dilation, and Assisted Drainage of Irrigation Fluid**

- **Scope Withdrawal, Anal Dilation, and Assisted Drainage of Irrigation Fluid ↔ Repeat Scope Insertion or Serial Withdrawals**
- **Repeat Scope Insertion or Serial Withdrawals**→ Return to **Clear Visual Field, No Significant Fecal Residue**
- **Neo-rectoscopic Observation and Localization**

Objective: Evaluate for characteristic endoscopic changes of bowel endometriosis

① Intestinal wall stiffness
② Hemorrhage (petechiae, ecchymosis, spontaneous bleeding)
③ Mucosal folding (mild, obvious, marked)
④ Mucosal edema or thickening
⑤ Mucosal discoloration
⑥ Erosion or ulceration
⑦ Stenosis

Note: BE, bowel endometriosis. The protocol ensures clear visualization of the intestinal mucosa for accurate identification of characteristic endometriotic changes, with standardized troubleshooting for poor visualization.

9. Standard Trial Procedure

9.1 Standard Procedure for Patient Screening

Patients with suspected bowel endometriosis will be recruited from participating centers. All candidates will undergo clinical evaluation (history, pelvic examination) and contrast-enhanced pelvic MRI to confirm the diagnosis. Eligible patients (bowel endometriosis with self-reported LARS score >20) will be evaluated by a multidisciplinary team, and those providing written informed consent will be randomized to either the IDLnR or conventional laparoscopy group within 3 days before surgery, following standard endometriosis management guidelines. The screening process is detailed in Appendix Figure 2.

9.2 Standard Procedure for Trial Operation

Intervention Group: Intra-operative Dual Laparoscopy and Neo-rectoscopy (IDLnR) Procedure

Patients in the experimental group will undergo Intra-operative Dual Laparoscopy and Neo-rectoscopy (IDLnR) for precise localization and resection of intestinal endometriotic lesions, with laparoscopic completion of bowel endometriosis surgery.

Prophylactic antibiotics will be administered in a standardized manner in accordance with routine clinical practice.

IDLnR Procedure Flow

Step 1: Pneumoperitoneum Establishment and Trocar Placement

Establish pneumoperitoneum and insert 4–5 laparoscopic trocars.

Step 2: Pelvic Adhesiolysis and Rectal Realignment (If Indicated)

If the pouch of Douglas is completely obliterated, or if there is rectosigmoid folding or torsion, open the rectouterine pouch laparoscopically using an ultrasonic scalpel, and reduce the torsed, stiff rectal segment to its anatomical position.

Step 3: Laparoscopic Sigmoid Colon Occlusion

During laparoscopic manipulation, the surgeon inserts atraumatic bowel forceps, locates the sigmoid colon or rectosigmoid junction under direct laparoscopic visualization, and gently clamps the bowel to temporarily occlude the bowel lumen.

Step 4: Neo-rectoscopy Insertion and Visualization

During neo-rectoscopy, the assistant continuously infuses water into the colonoscope while gently advancing the scope transanally into the rectal lumen, maintaining an infusion pressure of 10 mmHg. The colonoscope is advanced gradually along the rectal canal.

If excessive fecal residue impairs visualization during insertion, the colonoscope may be withdrawn first, followed by anal dilation to facilitate evacuation of residual feces, then reinserted for observation; this step may be repeated as necessary.

Step 5: Lesion Localization via Transillumination

When the tip of the colonoscope reaches the site of rectal lesion invasion, the laparoscopic surgeon will visualize the transillumination light emitted from the colonoscope tip around the proximal margin of the rectal lesion — a bright spot formed by the colonoscope light source in the dim abdominal cavity.

Step 6: Mucosal Assessment and Lesion Mapping

The surgeon inspects the anterior rectal wall mucosa for abnormal signs, performs repeated scope withdrawal to carefully observe the pathognomonic changes of submucosal or mucosal invasion by endometriosis, precisely localizes the intestinal lesions, estimates the depth of infiltration, and determines the lesion extent and surgical approach.

Step 7: Scope Withdrawal and Bowel Reperfusion

Slowly withdraw the colonoscope, followed by gentle anal dilation with a finger. After complete anal decompression, the laparoscopic surgeon releases the bowel forceps occluding the sigmoid colon laparoscopically to restore intestinal patency.

Step 8: Completion of Laparoscopic Surgery

The surgeon proceeds with the remaining laparoscopic procedures based on the observation results and the primary surgical plan.

Control Group: Conventional Laparoscopy (CL)

Intraoperative localization, inspection, and resection of intestinal lesions were performed using conventional laparoscopy (CL), followed by completion of bowel endometriosis surgery.

Prophylactic antibiotics were administered in a standardized manner according to routine clinical practice.

Control Group (CL) Procedure

Step 1: Establish pneumoperitoneum and insert 4–5 laparoscopic trocars.

Step 2: If the pouch of Douglas is completely obliterated, or if there is rectosigmoid folding or torsion, the rectouterine pouch is dissected laparoscopically using an ultrasonic scalpel, and the torsed, rigid rectal segment is restored to its anatomical position.

Depth of lesion infiltration, extent of disease, and surgical approach were determined solely based on laparoscopic visualization.

Step 3: The surgeon proceeded with the laparoscopic procedure according to the intraoperative findings and primary surgical plan.

9.3 Standardized Preoperative Management

All patients (both the experimental group and the control group) received standardized preoperative evaluation, including:

- Comprehensive clinical evaluation: bimanual vaginal-rectal examination or transrectal digital examination, Visual Analog Scale (VAS) for pain assessment, gastrointestinal symptom questionnaire, quality of life assessment, etc.;
- Thromboembolic risk assessment: Perioperative thrombosis prevention was usually initiated preoperatively. According to the assessment grade, mechanical measures such as early ambulation, physical therapy, or compression elastic stockings were routinely adopted;
- Imaging evaluation: Pelvic enhanced magnetic resonance imaging (MRI), focusing on assessing the length and depth of lesions involving the rectum, the distance from the anal dentate line, and the circumferential involvement of the intestinal tract;
- Laboratory examinations: Routine blood tests, liver and kidney function tests, etc.;
- Multidisciplinary Team (MDT) discussion: Including at least experts from gynecology, anorectal surgery, and radiology to evaluate the timing of surgery.

9.4 Standardized surgical quality control system

All patients (both the experimental group and the control group) received standardized surgical quality control and management, which specifically included:

(1) Anastomotic inspection: The blood supply of the rectal serosa was observed under laparoscopy, and the integrity of the anastomosis was evaluated by an air- leak test.

(2) Additional procedures: Concurrent resection of other endometriotic or adenomyosis lesions in the ovaries or pelvic cavity was performed when indicated.

(3) Management and rescue measures for severe adverse events:

① Anastomotic leakage/fistula: Conservative treatment: nil per os, gastrointestinal decompression, broad-spectrum antibiotics, and parenteral nutrition. Surgical repair or enterostomy was performed if necessary.

② Intestinal obstruction: Nil per os, gastrointestinal decompression, and correction of electrolyte disturbances. Surgical exploration was performed if necessary.

③ Intestinal hemorrhage: Transient or minor bleeding was managed conservatively with observation. For active or massive bleeding, colonoscopy was the first choice to identify the bleeding site and attempt endoscopic hemostasis.

④ Intestinal perforation: The primary procedure was terminated immediately. The grade, location, and condition of the intestinal segment were rapidly evaluated. Laparoscopic primary repair, anastomosis, or stoma creation was selected according to the patient's condition.

9.5 Standardized Postoperative Management

All patients (experimental group and control group) received a standardized long-term management protocol for endometriosis, including:

(1) For patients who retained their uterus and had fertility requirements: guidance on conception and pregnancy planning.

(2) For patients who retained their uterus but had no fertility desire: interventions such as insertion of a levonorgestrel-releasing intrauterine system or oral dienogest, with regular follow-up to evaluate efficacy and adverse drug reactions.

(3) For patients who underwent hysterectomy: regular follow-up of ovarian function and status.

(4) For patients who underwent hysterectomy with salpingo-oophorectomy: follow-up of pelvic recovery.

(5) Rehabilitation program: encouragement of early ambulation, gradual dietary adjustment, etc.

Follow-up schedule: Outpatient follow-up was performed at 1, 3, 6, and 12 months postoperatively (and continued every 6 months until the end of the study) to assess symptom relief, complications, intestinal function recovery, and improvement in quality of life.

10. Prohibited concurrent treatments

To ensure the accuracy of efficacy assessments such as pain relief and intestinal function improvement, and to eliminate confounding factors, this study prohibited the long-term preoperative use of the following interventions that may affect efficacy and safety evaluation:

① Drugs that may influence intestinal function and intestinal healing (mucosal/anastomotic repair):

glucocorticoids, immunosuppressants, chemotherapeutic agents, broad-spectrum antibiotics, etc.

② Drugs that may increase the risk of intestinal bleeding:

antiplatelet agents (aspirin, clopidogrel, ticagrelor, prasugrel, etc.), thrombolytic drugs (urokinase, streptokinase, alteplase, etc.).

③ Analgesic interventions that may interfere with pain evaluation:

Except for the standardized postoperative analgesia specified in the study protocol, long-term preoperative use of opioids and other analgesic measures that may confound pain assessment results was prohibited.

11. Data Management

Data management will be performed using a centralized electronic data capture (EDC) system. Data entry will be conducted by trained personnel, and double data entry verification will be adopted to ensure data accuracy. All data will be securely stored with restricted access, and regular data audits will be performed to guarantee data quality.

12. Statistical Analysis

12.1 Statistical Analysis Datasets and Analysis Plan

Study outcomes will be analyzed using the Full Analysis Set (FAS), Per-Protocol Set (PPS), and Safety Set (SS).

Efficacy evaluations will be performed for the FAS and PPS, and safety evaluations will be based primarily on the SS.

- **Full Analysis Set (FAS):**

All randomized patients who underwent surgery will be included. Patients who received prohibited medications or treatments specified in the study protocol will generally be excluded from the Per-Protocol Set (PPS) but retained in the Full Analysis Set (FAS).

- **Per-Protocol Set (PPS):**

A subset of the FAS, including patients who completed surgery, adhered to the protocol for all scheduled follow-ups, did not receive any other medications or treatments that could affect efficacy evaluation during the trial, and had no other major protocol violations.

- **As-Treated Set:**

Patients whose treatment strategy was changed preoperatively will be analyzed according to the surgical procedure actually performed.

- **Safety Set (SS):**

All patients who completed surgery and had available safety data will be included.

- **Statistical analysis principles:**

Baseline data will be analyzed based on the FAS.

The primary endpoint will be analyzed using the FAS, PPS, and As-Treated Set, with the FAS result as the primary analysis and PPS and As-Treated Set as sensitivity analyses.

Secondary endpoints will be analyzed based on the FAS.

Safety endpoints will be analyzed based on the SS.

12.2 Statistical Analysis Methods

All statistical analyses will be performed using SAS version 9.4. All statistical tests will be two-sided, and a P- value ≤ 0.05 will be considered statistically significant. A 95% confidence interval (CI) will be used.

Baseline Characteristics Analysis

Quantitative data will be presented as mean ± standard deviation or median (P25, P75). Categorical data will be summarized as frequencies and proportions.

Student's t- test / rank- sum test / chi- square test / Fisher's exact test will be used to compare demographic and baseline characteristics to verify between- group balance.

Primary Outcome Analysis

The improvement rate of LARS grade will be compared between groups using the chi-square test.

The confidence interval for the single- group improvement rate will be estimated using the Clopper- Pearson method, and the confidence interval for between- group differences will be calculated using the Newcombe method.

Secondary Outcomes Analysis

The statistical methods for the following endpoints are consistent with the primary outcome:

- 12-month LARS cure rate
- 3-month and 12-month LARS improvement rate
- Changes in Visual Analogue Scale (VAS) pain score

Between- group comparisons of changes in LARS score, CRADI- 8 score, Wexner constipation score, and quality- of- life score will be performed using analysis of covariance (ANCOVA), adjusted for baseline scores.

Safety Outcomes Analysis

The incidence of adverse events (AEs) will be compared between groups using the chi-square test or Fisher’ s exact test and summarized in tabular form.

The incidence of serious adverse events (SAEs) of Grade 3 or higher will be compared between groups, and the incidence of each type of AE (adverse reaction) related to the investigational procedure will be evaluated.

The between- group comparison of postoperative therapeutic antibiotic use will be analyzed using Student’ s t- test or nonparametric test.

Dropout Analysis

The overall dropout rate and dropout rate due to AEs will be compared between groups using the chi-square test.

Subgroup Analysis

Prespecified subgroup analyses for the primary endpoint will be performed according to:

- Random stratification factors: study site and whether the uterus was preserved
- Baseline LARS grade (mild vs. severe)

The final statistical analysis strategy will be based on the Statistical Analysis Plan (SAP) finalized before database lock.

13. Ethical approval

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Obstetrics and Gynecology Hospital of Fudan University.

The IRB approved the human subject research on March 2026 (Ethics Approval No.: 2026-33).

All patients provided written informed consent prior to study enrollment.

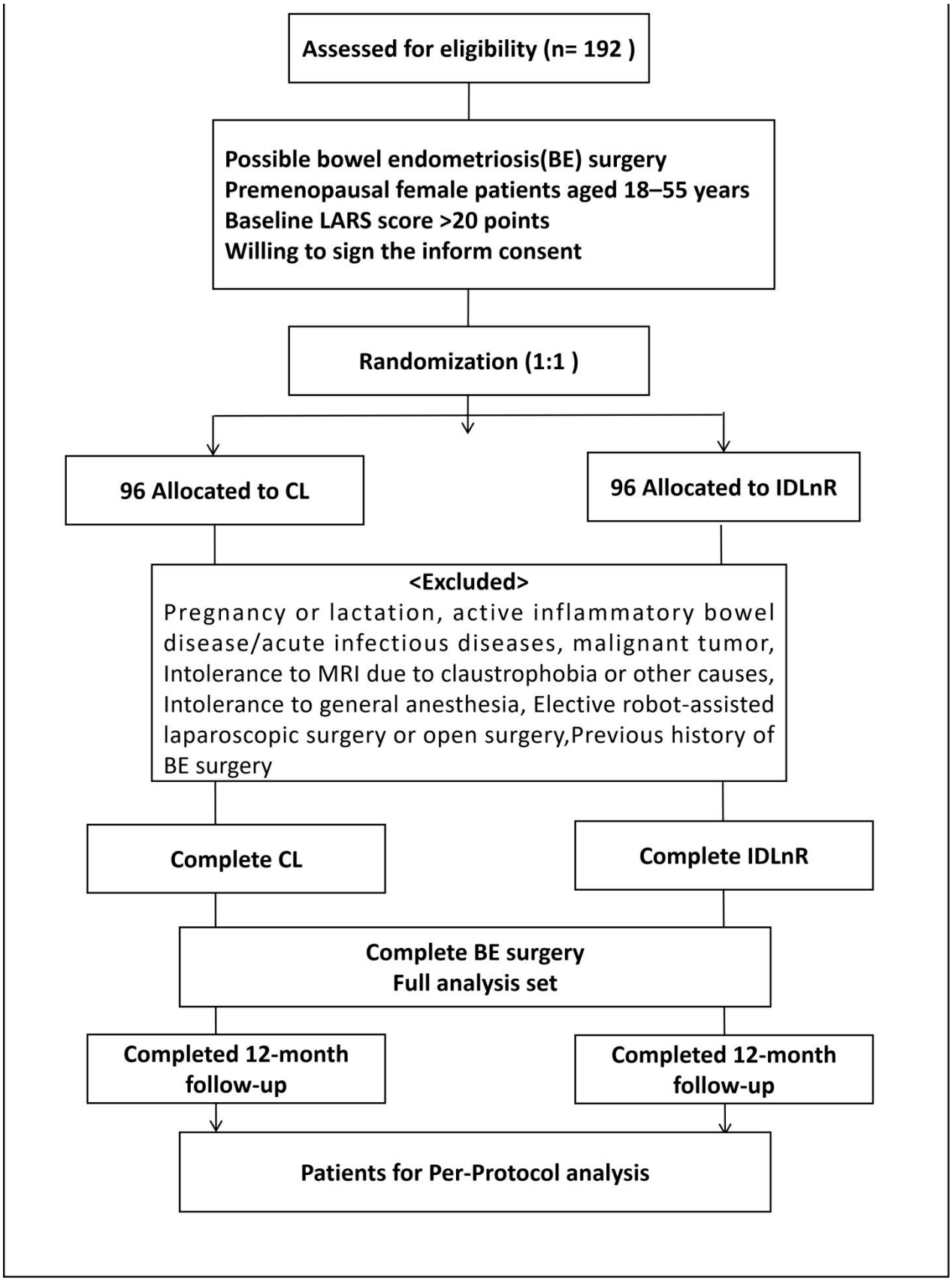
This trial will be registered on ClinicalTrials.gov, with the first registration planned in April 2026.

The results of this study will be submitted for publication in peer-reviewed journals and presented at international conferences.

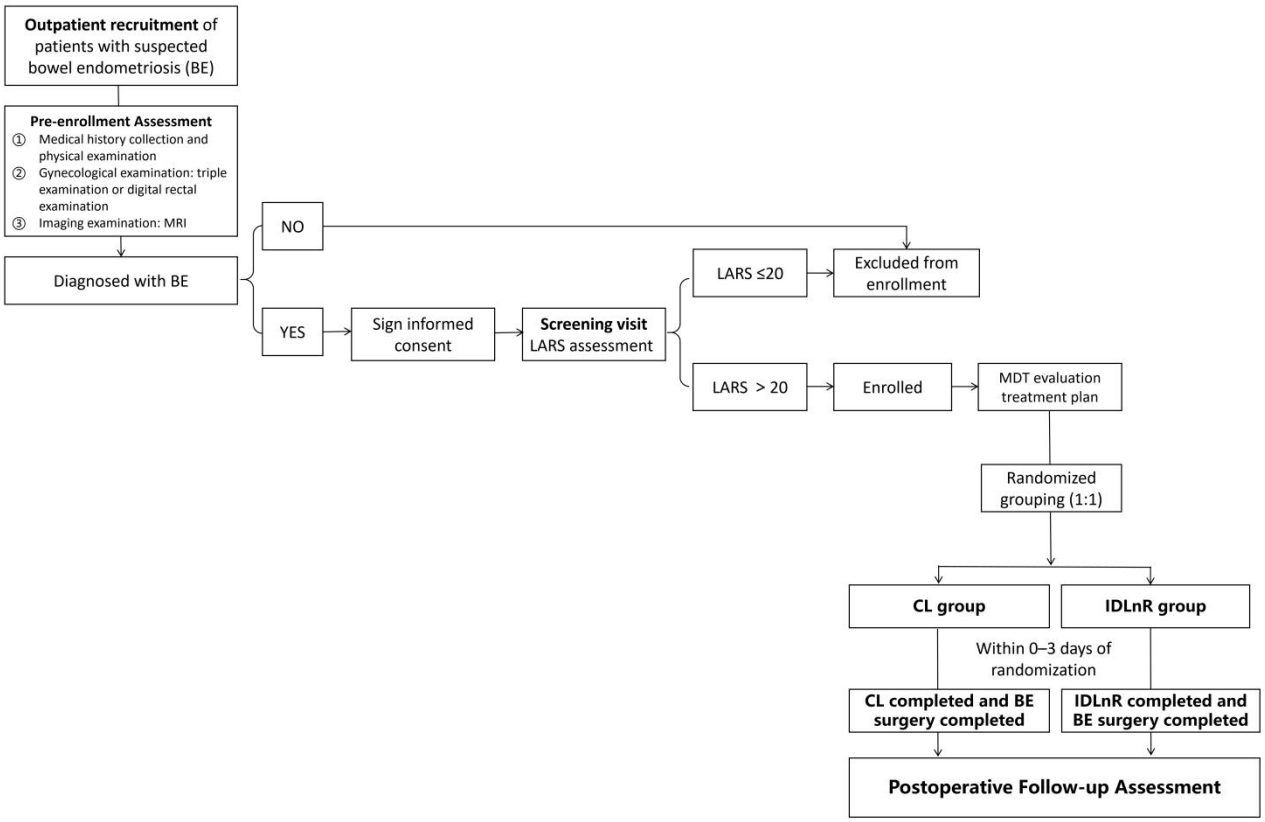
In addition, to meet transparency requirements, study results will be publicly disclosed on ClinicalTrials.gov.

After publication of the trial results, de-identified participant data may be made available upon reasonable request, in compliance with institutional and ethical guidelines.

Appendix 1: Flowchart of RCT LUMEN-01 Study (CL vs IDLnR)



Appendix 2: Screening Flowchart of RCT LUMEN-01 Study



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