ORIGINAL ARTICLE

DOI: 10.52054/FVVO.2025.39
Facts Views Vis Obgyn

The role of pre-operative gonadotrophin-releasing hormone agonists (GnRHa) on pain, bowel and bladder symptoms in rectovaginal/colorectal endometriosis surgery: a multicenter cohort study

Munazzah Rafique[1], Christian Becker[1,2], Jonathan Lewin[3,4], Arvind Vashisht[3,4], Ertan Sarıdoğan[3,4], Martin Hirsch[1,2]

[1]Department of Obstetrics and Gynaecology, John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom
[2]Oxford Endometriosis CaRe Centre, Nuffield Department of Women's & Reproductive Health, University of Oxford, Oxford, United Kingdom
[3]Department of Gynaecology, University College London Hospitals NHS Foundation Trust, London, United Kingdom
[4]EGA Institute for Women's Health, University College London Hospital NHS Foundation Trust, London, United Kingdom

ABSTRACT

Background: The efficacy of medical and surgical treatment of endometriosis-associated pain is a source of ongoing controversy. There is a lack of evidence about gonadotropin-releasing hormone agonists (GnRHa) use on long-term pain control, bladder and bowel symptoms for patients having surgery for deep rectovaginal/colorectal endometriosis.

Objectives: To assess the effect of preoperative GnRHa (pre-GnRHa) use on pain, bowel and bladder symptoms for patients undergoing surgery for deep rectovaginal/colorectal endometriosis.

Methods: The study evaluated data from the British Society for Gynaecological Endoscopy database, a large international multicentre prospective cohort of patients who underwent deep rectovaginal/colorectal endometriosis surgery between 2009-2021. We included 9433 patients from 101 accredited endometriosis centres. Multivariable logistic regression analysis was used to evaluate the association between pre-GnRHa use and postoperative pain, bowel and bladder symptoms at different time points, controlling for confounders like patient age, body mass index, smoking status, and hysterectomy.

Main Outcome Measures: Rate of cyclical and non-cyclical pelvic and menstrual pain, bowel and bladder symptoms.

Results: The mean age of the patients was 36 years (18-55). Pre-GnRHa use was associated with significant postoperative improvement in premenstrual pain [odds ratio (OR): 0.30, 95% confidence interval (CI): -0.57 – -0.034, *P*=0.02*], menstrual pain (OR: 0.41/10, 95% CI: -0.7 – -0.13, *P*=<0.001*), non-cyclical pain (OR: 0.27/10, 95% CI: -0.5 – -0.04, *P*=0.021*) and lower backache (OR: 0.30, 95% CI: -0.532 – -0.087, *P*=0.006*) up to 12 months postoperatively. Moreover, bladder pain was significantly reduced in the pre-GnRHa group at 12 months (OR: 0.24, 95% CI: -0.451 – -0.039, *P*=0.01*). Significant improvements were observed in bowel symptoms including frequent bowel movements (OR: 0.10, 95% CI: -0.194 – -0.012, *P*=0.02*), incomplete emptying sensation (OR: 0.10, 95% CI: -0.196 – -0.023, *P*=0.01*), cyclical dyschezia (OR: 0.43, 95% CI: -0.724 – -0.142, *P*=0.003*) and non-cyclical dyschezia (OR: 0.28, 95% CI: -0.504 – -0.075, *P*=0.008*) up to 12 months.

Corresponding Author: Munazzah Rafique, MD, Department of Obstetrics and Gynaecology, John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom
E-mail: munazzahr@yahoo.com **ORCID ID:** orcid.org/0000-0002-1751-6287
Received: 21.01.2025 **Accepted:** 03.08.2025 **Epub:** 23.09.2025

Cite this article as: Rafique M, Becker C, Lewin J, Vashisht A, Sarıdoğan E, Hirsch M. The role of pre-operative gonadotrophin-releasing hormone agonists (GnRHa) on pain, bowel and bladder symptoms in rectovaginal/colorectal endometriosis surgery: a multicenter cohort study. Facts Views Vis Obgyn. [Epub Ahead of Print].

ABSTRACT

Conclusions: Pre-GnRHa use is associated with a significant reduction in postoperative menstrual pain and non-menstrual pain as well as improved bowel and bladder symptoms lasting up to two years. It is also valuable to improve the quality of life for patients undergoing surgery for deep rectovaginal/colorectal endometriosis.

What is New? This is the largest prospective international study evaluating pre-GnRHa use in deep rectovaginal/colorectal endometriosis surgery. It provides evidence supporting the role of pre-GnRHa as an adjuvant to surgical treatment, to reduce postoperative pain and improve bowel and bladder function.

Keywords: Endometriosis, rectovaginal, colorectal, GnRHa, pain, bowel, bladder pain

Introduction

Bowel endometriosis affects between 3.8% and 37% of women with endometriosis.[1] Gonadotrophin releasing hormone analogue (GnRHa) are effective in relieving pain symptoms and reducing the extent of endometriotic implants.[2-4] In particular, GnRHa significantly improve pain and intestinal symptoms in patients with bowel stenosis less than 60% and who do not wish to conceive.[1] However, GnRHa induce a pseudomenopausal state and have side effects, such as hot flashes, genital atrophy and bone density loss that can be relieved by "add-back" therapy.[3] Despite its benefits, there are limitations of GnRHa use due to relapse of pain on discontinuation and side effects associated with the transitory pharmacologic menopause condition.[5] Moreover, there is evidence of the recurrence of the lesions to their original size after discontinuation of GnRHa treatment.[6] The safe duration of GnRHa treatment, its role in prevention of the progression of bowel endometriosis and association with recurrence rate remain unclear.[1,3,4]

Medical therapy alone is often insufficient to relieve symptoms, necessitating the need of surgical interventions that range from superficial partial thickness excisions to radical colorectal resection and reanastomosis.[7] The patients receiving long-term medical treatment or symptomatic patients with bowel stenosis greater than 60% should consider surgical excision to improve pain, intestinal symptoms and fertility.[1] The postoperative mean pregnancy rate improves from 20%-52% in the patients having surgical treatment for rectovaginal/colorectal endometriosis, however, the efficacy of GnRHa in enhancing assisted reproductive technology outcomes remain inconclusive.[8,9]

Surgery for rectovaginal endometriosis can be technically difficult and requires thorough evaluation of symptomatology, potential medical treatment and expected surgical outcomes.[10] Surgical interventions provide the symptom relief in approximately 70% of cases, improvement in pain related symptoms and enhance the health-related quality of life (QOL) up to six months and at 12 months.[7,11]

The efficacy of both medical and surgical treatments for endometriosis-associated pain is a source of ongoing debate. In this study, we analysed British Society for Gynaecological Endoscopy (BSGE) database to assess the impact of GnRHa on various pain symptoms including menstrual pain, non-menstrual pain, chronic pelvic pain, bladder and bowel related symptoms. We compared these symptoms between the patients who receive GnRHa and those who did not. Furthermore, we evaluated the differences in pain-related, bladder and bowel at different time points up to 6 months, 12 months and 24 months between these two groups.

Methods

Data Collection

The data was obtained from the BSGE database, which comprises a multicenter cohort of patients undergoing endometriosis surgery. All patients provided written informed consent for the storage of their data in the BSGE database and its subsequent use for scientific research and publication. The data collection process adhered to standardized protocols to ensure consistency and reliability across participating centers. The database is managed in compliance with the data protection act, with all patient data encrypted, and securely hosted by a third-party provider contracted by the BSGE.

The BSGE database is collected by clinicians. The preoperative GnRH analogues (pre-GnRHa) usage varied among different endometriosis centers influenced by differences in clinical practice, patient preference, institutional protocols and documentation standards, potentially leading to discrepancies in recorded GnRHa usage. The details of the exact dose and duration of pre-GnRHa use were unspecified. However, according to

current clinical practice, all participating endometriosis centers are expected to use GnRHa within the licensed guidelines, typically for a duration of 3 to 6 months as recommended by National Institute for Health and Care Excellence.[12] The study received ethical approval from the BSGE, Scientific Advisory Group in October 2024. The collected data includes demographic, use of GnRHa, surgical findings, pain symptoms, bladder and bowel symptoms reported at 6, 12, and 24 months post-surgery.

Patient Population

All patients from 2009 to 2021, who fulfill the inclusion/exclusion criteia, were included in this study. The inclusion criteria required patients who underwent surgery for severe rectovaginal/colorectal endometriosis and had para-rectal space dissection as part of their surgical procedure that include shaving, segmental excision or disc resection. All the patients have histological confirmation of the endometriosis post-surgery. High surgical complexity was defined as cases involving bladder nodule excision, ureteric nodule excision or bowel resection (either disc or segmental). The patients were divided into two groups for the analysis according to whether they had pre-GnRHa. The patients who received GnRHa before surgery are referred as "pre-GnRHa" whereas the patients who did not receive pre-GnRHa are referred as "nPre-GnRHa" in this study. For QOL analysis, patients were included if they had one pre-operative and at least one post-operative questionnaire response.

Statistical Analysis

R version 4.2.3 for Windows was used for all data processing, graph creation, and statistical analysis in R Studio (Copyright 2023, the R Foundation for Statistical Computing). Chi-squared test of proportions and independent samples t-tests were used to compare the demographic differences between the groups. Throughout, *P*-values less than 0.05 were regarded as statistically significant. The differences in postoperative pain perception between patients who received pre-operative GnRHa and those who did not, were examined using odds ratios (OR). When the group size was fewer than five, the Fisher's exact test, the chi squared test, or the difference of proportions test were used to determine the statistical significance of the differences. For multivariate analysis, logistic regression was used to model the odds of pain, bladder and bowel symptoms adjusting for patient age, body mass index (BMI), smoking status, hysterectomy status, history of prior endometriosis surgery, and surgical complexity. These outcomes were then compared between pre-GnRHa and nPre-GnRHa groups.

We used mixed-effects linear regression to assess the impact of treatment on QOL. The difference in outcomes were measured using the time x multiplied by treatment group interaction term. This effect was additionally controlled for by different timepoint interactions, since symptom improvement was predicted by type of intestinal surgery conducted and time period after the surgery.

Although the big data studies report demographic as mean, standard deviation using t-tests, we opted for more informative measure of central tendency, using median, interquartile range (IQR) and non-parametric tests including Mann-Whiney U. For pain, bowel and bladder symptoms a latent interval scale was assumed, and the patient responses were analysed using mixed effects linear regression fitted by restricted maximum likelihood using the "nlme" R package version 3.1-162. Moreover, to assess changes in pain and bowel symptom, three sequential models were applied. Model 1 was adjusted for age, BMI, smoking status, surgical approach (laparoscopy vs. open surgery), type of bowel surgery (shave, disc, segment) and hysterectomy +/- oophorectomy, with random effect for each endometriosis centre. Model 2 was as first, and further controlled for post-operative GnRHa use. Model 3 was, the first and second, and further controlled for post-operative GnRH analogues, combined oral contraceptive pill, progestogens and Mirena coil (all hormonal therapies).

Results

Patients' Cohort and Demographics

A total of 101 accredited endometriosis centers across six countries (United Kingdom, United States of America, Sri Lanka, Saudi Arabia, Turkey and Iran) contributed 9433 surgical cases to this research. Pre-operative GnRH analogues were given to 3275 (34.7%) of these patients; 6158 patients did not receive pre-operative GnRHa. The age and BMI were assessed visually for normality. While there were no age restrictions, most of the patients were in the 18-55 age range and an IQR of 31.1-41.8, the median age was 36.3. Similarly, the range for BMI was 14->40, with a median of 26 and an IQR of 22-29 (Figures 1 and 2). Overall, 8399 patients (89.1%) had bowel shaving, followed by segmental resection in 762 cases (8%) and disc resection in 272 cases (2.9%). A hysterectomy was performed on 2461 (26.1%) of these patients. Table

1 shows the variations in the patient demographics between the groups that received and did not receive pre-GnRHa.

Menstrual and Non-Menstrual Pain

Overall, the menstrual pain and dyspareunia were significantly reduced for the patients who received perioperative GnRHa with *P*<0.001. The premenstrual pain and lower backache were also reduced in pre-GnRHa group (*P*=0.03 and *P*=0.01) (Supplementary Table 1). The mean differences in pain at 6 months showed increase odds of pain improvement in non-cyclical pelvic pain [OR: 0.34/10, 95% confidence interval (CI): -0.55 – -0.14, *P*=0.001], menstrual pain (OR: 0.47/10, 95% CI: -0.72 – -0.22, *P*≤0.001), premenstrual pain (OR: -0.25, 95% CI: -0.482 – -0.025, *P*=0.02) and lower back pain (OR: 0.30, 95% CI: -0.496 – -0.106, *P*=0.002). Similarly, at 12 months the odds of pain improvement were non-cyclical pelvic pain (OR: 0.27/10, 95%CI: -0.5 – -0.04, *P*=0.021), menstrual pain (OR: 0.41/10, 95% CI: -0.7 – -0.13, *P*≤0.001), premenstrual pain (OR: 0.30, 95% CI: -0.57 – -0.034, *P*=0.02) and lower back pain (OR: 0.30, 95% CI: -0.532 – -0.087, *P*=0.006). Moreover, at 24 months interval from the surgery only the odds of lower back pain were statistically significant with OR: 0.42, 95% CI: -0.713 – -0.145, *P*=0.003 (Table 2). However, there was no statistically significant impact on pain control for dyspareunia postoperatively and gradual reduction in pain control of non-cyclical pelvic pain, menstrual pain and premenstrual pain after 12 months of surgery.

Bladder Pain Symptom

Compared to the nPre-GnRHa group, the patients in pre-GnRHa having any form of deep rectovaginal/colorectal endometriosis surgery demonstrated significantly greater odds of improvement in bladder pain at 12 months' time (OR: 0.24, 95% CI: -0.451 – -0.039, *P*=0.01). The odds of difficulty in emptying bladder were not statistically significant for the patients who were in pre-GnRHa group compared to nPre-GnRHa group (Supplementary Table 2). When multivariable regression analysis was done to control for confounding factors including age, BMI,

Table 1. Demographic and operative differences in pre-GnRHa vs nPre-GnRHa groups.

Characteristics	Pre-GnRHa group (n=3275)	nPre-GnRHa group (n=6158)
Age	36.9 (SD: 7.31)	36.2 (SD: 7.31)
BMI	26.7 (SD: 5.52)	26.2 (SD: 5.52)
Smoking	308 (9.4%)	584 (9.5%)
Hysterectomy	1061 (32.4%)	1400 (22.7%)
Bowel surgery	3275 (34%)	6158 (65%)
- Shaving	2796 (85.4%)	5603 (91%)
- Disc resection	97 (3%)	175 (2.8%)
- Segmental resection	382 (11.7%)	380 (6.2%)
Surgical complexity	3275 (34%)	6158 (65%)
High	772 (23.6%)	1201 (19.5%)
Low	2503 (76.4%)	4957 (80.5%)

Pre-GnRHa: Pre-operative gonadotrophin-releasing hormone agonists, nPre-GnRHa: No pre-operative gonadotrophin-releasing hormone agonists, BMI: Body mass index, SD: Standard deviation.

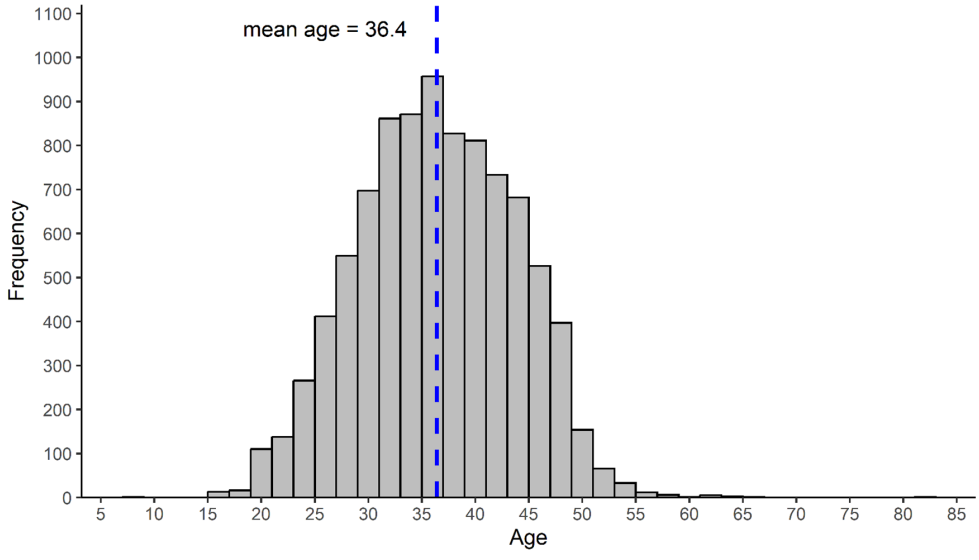

Figure 1. Age histogram.

smoking, hysterectomy, surgical complexity and previous endometriosis surgery, the result showed that the patients in the pre-GnRHa group had similar odds of bladder pain and difficulty in emptying bladder at 6 month, 12 months and 24 month's time between the nPre-GnRHa and the pre-GnRHa groups (Table 3).

Bowel Symptoms

The patients in pre-GnRHa had statistically significantly improvement of bowel symptoms including constipation, incomplete emptying sensation and cyclical dyschezia compared to the nPre-GnRHa who were having any form of deep rectovaginal/colorectal endometriosis surgery (Supplementary Table 3). The bowel symptoms at 6 months showed increase odds of improvement in constipation (OR: 0.07, 95% CI: -0.141 – -0.006, *P*=0.03), cyclical dyschezia (OR:-0.44, 95% CI: -0.692 – -0.194, *P*=0.0005), and non-cyclical dyschezia (OR: 0.22, 95% CI: -0.411 – -0.035, *P*=0.01). There were significant odds of improvement in frequent bowel movements (OR: 0.10, 95% CI: -0.194 – -0.012, *P*=0.02), incomplete emptying sensation (OR: 0.10, 95% CI: -0.196 – -0.023, *P*=0.01), cyclical dyschezia (OR: 0.43, 95% CI: -0.724 – -0.142, *P*=0.003), and non-cyclical dyschezia (OR: 0.28, 95% CI: -0.504 – -0.075, *P*=0.008), at 12 months in pre-GnRHa as compared to nPre-GnRHa group. Furthermore, at 24 months interval from the surgery the odds of frequent bowel movements and incomplete emptying sensation were statistically significant with (OR: 0.14, 95% CI: -0.256 – -0.024, *P*=0.01) and OR: 0.20, 95% CI: -0.314 – -0.095, *P*=0.0002) (Table 4). Conversely, there was no statistically significant impact on urgent bowel movements postoperatively among both groups and a gradual reduction in symptom control of constipation, cyclical and non-cyclical dyschezia over 24 months after surgery in patients who were in pre-GnRHa group.

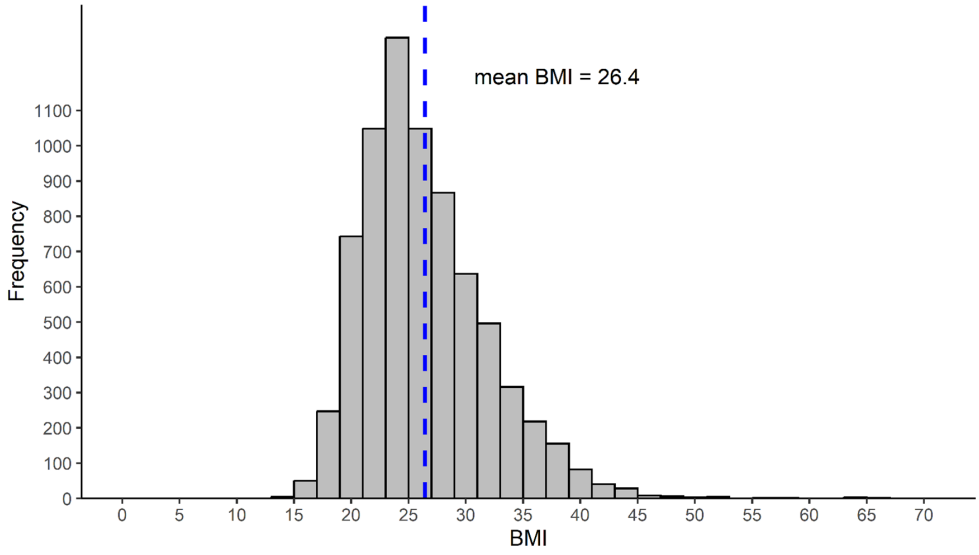

Figure 2. BMI histogram.

BMI: Body mass index.

Table 2. Multivariate analysis of pain and EQVAS scores between pre-GnRHa vs nPre-GnRHa groups.

	6 months (95% CI, *P* value)	**12 months (95% CI, *P* value)**	**24 months (95% CI, *P* value)**
EQVAS	1.48/100 (-0.13-3.1, *P*=0.072)	2.092/100 (0.27-3.92, *P*=0.025)*	2.85/100 (0.55-5.16, *P*=0.015)*
Non-cyclical pelvic pain	0.34/10 (-0.55 – -0.14, *P*=0.001)*	0.27/10 (-0.5 – -0.04, *P*=0.021)*	0.237 (-0.52-0.05, *P*=0.107)
Dyspareunia	0.14/10 (-0.36-0.08, *P*=0.226)	0.08/10 (-0.32-0.17, *P*=0.557)	0.18/10 (-0.5-0.13, *P*=0.257)
Menstrual pain	0.47/10 (-0.72 – -0.22, *P*=<0.001)*	0.41/10 (-0.7– -0.13, *P*=<0.001)*	0.24/10 (-0.6-0.13, *P*=0.204)
Premenstrual pain	-0.25 (-0.482 – -0.025, *P*=0.02)*	0.30 (-0.57 – -0.034, *P*=0.02)*	0.12 (-0.479-0.228, *P*=0.48)*
Lower backache	0.30 (-0.496 – -0.106, *P*=0.002)*	0.30 (-0.532 – -0.087, *P*=0.006)*	0.42 (-0.713 – -0.145, *P*=0.003)*

*Statistically significant *P*<0.05, EQVAS: EuroQol-visual analogue scales, pre-GnRHa: Pre-operative gonadotrophin-releasing hormone agonists, nPre-GnRHa: No pre-operative gonadotrophin-releasing hormone agonists, CI: Confidence interval.

Quality of Life EuroQol-visual Analogue Scales Scores

The follow-up rates were 86.7% at 6 months (4832), 60.1% (3351) at 12 months and 33.9% (1891) at 24 months. QOL scores improved statistically significant in the pre-GnRHa group at 12 months (mean difference 2.09/100, 95% CI: 0.27-3.92, *P*=0.025) and 24 months (mean difference 2.85/100, 95% CI: 0.55-5.16, *P*=0.015) (Table 2, Figure 3).

Discussion

Key Findings

The result of our study provides evidence that pre-operative GnRHa use is associated with significant benefit in controlling menstrual and non-menstrual pain, improving bowel function and to a lesser extent alleviating bladder symptoms following surgery for deep rectovaginal/colorectal endometriosis. In particular, pre-operative GnRHa was associated with increased odds of reducing non-cyclical pelvic pain and menstrual pain up to one year after surgery. Premenstrual pain and lower backache showed significant improvement up to two years post-surgery. However, dyspareunia did not show any significant improvement with pre-GnRHa use. Patients receiving pre-GnRHa demonstrated greater improvement in post-operative QOL.

The potential mechanism behind these benefits include reduced inflammation, decreased vascularisation of endometriosis lesions, reduced adhesions and lower risk of recurrence.[13,14] The previous study looking into the pain improvement for patients with GnRHa administration suggested that it can lead to temporary improvement of pain in patients with incomplete surgical treatment which could explain the observed benefits of pre-GnRHa use.[4,5] The surgery of rectovaginal/colorectal endometriosis can be incomplete when the risks associated with extensive disease outweigh the benefits of extensive excision, fertility preservation concerns, or when multidisciplinary team limitations are present.[10,15,16] In such cases, GnRHa may delay symptom recurrence and improve outcomes by suppressing residual disease activity.[14] Over time, the advancement in presurgical imaging like ultrasound and magnetic resonance imaging have contributed to enhanced mapping, surgical planning and potentially improved outcomes.[17,18] Since our study spans over a decade, such evolving surgical and imaging techniques may have influenced the results.

Table 3. Multivariate analysis of bladder symptoms pre-GnRHa vs nPre-GnRHa groups.

Symptom	6 months estimate (95% CI, *P* value)	12 months estimate (95% CI, *P* value)	24 months estimate (95% CI, *P* value)
Bladder pain	0.13 (-0.311-0.049, *P*=0.15)	0.24 (-0.451 – -0.039, *P*=0.01)*	0.16 (-0.429-0.096, *P*=0.21)
Difficulty emptying the bladder	0.14 (-0.308-0.028, *P*=0.10)	-0.14 (-0.335-0.049, *P*=0.14)	0.17 (-0.42-0.07, *P*=0.16)

*Statistically significant *P*<0.05, pre-GnRHa: Pre-operative gonadotrophin-releasing hormone agonists, nPre-GnRHa: No pre-operative gonadotrophin-releasing hormone agonists, CI: Confidence interval.

Table 4. Multivariate analysis of bowel symptoms pre-GnRHa vs nPre-GnRHa groups.

Symptom	6 months estimate (95% CI, *P* value)	12 months estimate (95% CI, *P* value)	24 months estimate (95%CI, *P* value)
Constipation	0.07 (-0.141 – -0.006, *P*=0.03)*	0.06 (-0.142-0.011, *P*=0.09)	0.06 (-0.158-0.037, *P*=0.22)
Frequent bowel movements	0.03 (-0.111-0.049, *P*=0.44)	0.10 (-0.194 – -0.012, *P*=0.02)*	0.14 (-0.25 – -0.024, *P*=0.01)*
Urgent bowel movements	0.03 (-0.106-0.027, *P*=0.24)	0.03 (-0.11-0.041, *P*=0.37)	-0.08 (-0.18-0.012, *P*=0.08)
Incomplete emptying sensation	0.07 (-0.153 – -0.002, *P*=0.04)	0.10 (-0.196 – -0.023, *P*=0.01)*	0.20 (-0.314 – -0.095, *P*=0.0002)*
Cyclical dyschezia	-0.44 (-0.692 – -0.194, *P*=0.0005)*	0.43 (-0.724 – -0.142, *P*=0.003)*	0.28 (-0.663-0.096, *P*=0.14)
Non-cyclical dyschezia	0.22 (-0.411 – -0.035, *P*=0.01)*	0.28 (-0.504 – -0.075, *P*=0.008)*	0.23 (-0.509-0.037, *P*=0.09)

*Statistically significant *P*<0.05, pre-GnRHa: Pre-operative gonadotrophin-releasing hormone agonists, nPre-GnRHa: No pre-operative gonadotrophin-releasing hormone agonists, CI: Confidence interval.

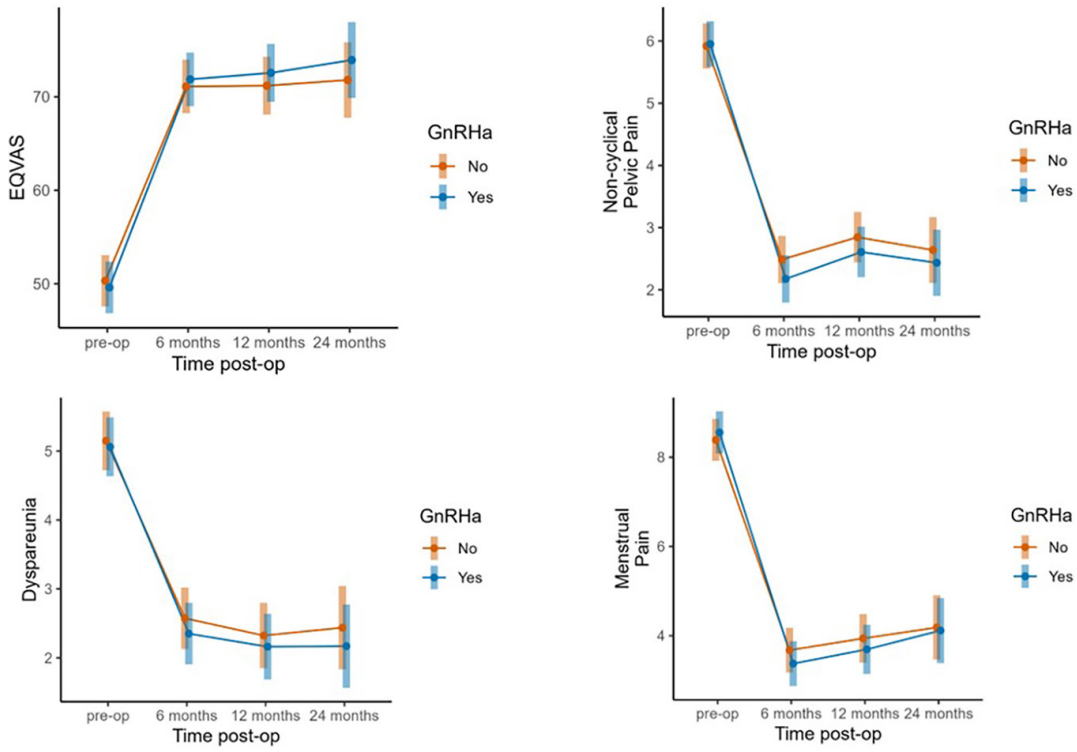

Figure 3. EQVAS and pain scoring.

EQVAS: EuroQol-visual agonistscales, GnRHa: Gonadotropin-releasing hormone agonists.

In our study, the hysterectomy rate was 32.4% in pre-GnRHa group compared to 22.7% in nPre-GnRHa group, which could be a factor for postsurgical pain control. However, we accounted for this as a confounder in multilogistic regression anaylsis. Previous studies suggest that adenomyosis is frequently present in patients with rectovaginal/colorectal endometriosis and influences surgical decisions.[19] In patients with adenomyosis, GnRHa treatment can conceal the disease extent and result in persistence of pain after conservative surgery, leading the decision to hysterectomy.[20,21]

Pre-GnRHa can reduce lesion size and fibrosis, potentially facilitating surgical dissection. However, it may also lead to tissue atrophy and scarring, making it more challenging to identify disease margins and increasing the risk of incomplete resection.[22] Pre-GnRHa use can alter surgical planes by inducing fibrosis, potentially complicating nerve-sparing techniques and increasing postoperative neuropathic pain.[23] Previous study result demonstrated the pre-GnRHa can lead to partial lesion regression, making surgical excision less extensive but increasing the risk of microscopic residual disease, which may contribute to symptom recurrence.[15] GnRHa may improve short-term postoperative pain control by reducing inflammation and residual endometriotic activity, its impact on long-term outcomes remains debated.[20]

Our data showed significant improvement in the bowel symptoms including constipation, cyclical and non-cyclical dyschezia and incomplete emptying sensation in patients who received pre-GnRHa. Most improvements persisted up to one year with more persistent control of frequent bowel movements and incomplete emptying sensation. However, we did not observe significant improvement in urgent bowel movements. Hormonal therapy effectively manages intestinal endometriosis symptoms and better patient satisfaction particularly when the bowel lumen stenosis is less than 60%.[14,24] Therapeutic amenorrhoea can help in complete improvement of cyclic digestive symptoms when is not feasible,[25] although constipation-type symptoms are reported to be less responsive.[14]

The results of our study showed that the bladder pain symptoms were well controlled up to a year for patients receiving GnRHa before surgery but recurrence of urinary symptoms within two years. This is in accordance with the previous study whose result showed that although medical therapy has proved effective in relieving urinary

symptoms, there quick recurrence of irritative urinary symptoms after cessation of therapy.[26]

Strengths and Limitations

The BSGE database, the largest prospective dataset of surgically managed deep rectovaginal/colorectal endometriosis, provided robust sample of 9433 cases for analyse. The large sample size enabled multivariable analysis adjusting for demographic and clinical variations among the groups. This multicentre study minimized bias arising from systemic variation in institutional practice and enabled wide applicability of the results. Moreover, there are annual governance measures required for each endometriosis centre to ensure validity and comparability of data from multiple centres. A key strength of our study is the comprehensive data collection including information on demographics, surgical technique, pain symptoms, bowel symptoms and bladder symptoms over 24 months enabling a detailed evaluation of symptom trajectories and improving patient counselling.

The primary limitation of this research is the lack of randomization. Additionally, we cannot rule out the possibility that the recurrence of symptoms is related to recurrence or persistence of endometriosis in the pre-GnRHa group compared to the nPre-GnRHa group. Moreover, the treatment approaches to the management of rectovaginal/colorectal endometriosis have evolved over these years that may impact on the present analysis.

Clinical Implications and Future Research

Despite its strengths, our study design has limitations, therefore, we recommend future randomized controlled trials (RCT) evaluating preoperative medical management as an adjunct to deep rectovaginal/colorectal endometriosis surgery. Specifically, to determine the relationship with bladder symptoms and GnRHa use. We were able to control for several potential confounding factors, including age, BMI, smoking status, hysterectomy, surgical complexity, and previous endometriosis surgeries. However, there may be other endometriosis related factors that contribute to the clinical heterogeneity such as the severity of adhesions, size of bowel nodule, and presence of bladder or ureteric nodules. We were not able to control non-endometriosis related factors that may influence bowel and bladder symptoms such as irritable bowel syndrome, interstitial cystitis, bladder pain syndrome, etc. that may have contributed to the study limitations.

A prospective trial with comparable groups and more controlled confounding factors like hysterectomy rate may show different result, as surgery alone could provide significant symptom relief. Prospective RCT would provide greater clarity on the role of GnRHa, particularly in bowel and bladder symptom control.

Conclusion

The pre-GnRHa use is associated with significant improvement in menstrual pain, premenstrual pain, and lower backache over 1-2 years. Moreover, the patients receiving pre-GnRHa showed notable improvement in bowel symptoms, including constipation, incomplete emptying sensation, cyclical dyschezia, non-cyclical dyschezia, and frequent bowel movements along with improvement in bladder pain for up to 12 months.

Overall, our findings support the use of pre-GnRHa in improving pain, bowel, and bladder symptoms, which can help in patient counselling before surgery for rectovaginal/colorectal endometriosis. Pre-GnRHa use, may enhance symptom control in short and midterm however, it is important to acknowledge that recurrence or persistence of endometriosis may influence long-term symptom outcomes, highlighting the need for further research to optimize the treatment strategies.

Acknowledgements: The authors would like to thank BSGE to let us use their data base for our study.

Contributors: Surgical and Medical Practices: M.R., C.B., J.L., A.V., E.S., M.H., Concept: M.R., C.B., J.L., A.V., E.S., M.H., Design: M.R., J.L., M.H., Data Collection or Processing: J.L., M.H., Analysis or Interpretation: M.R., J.L., M.H., Literature Search: M.R., M.H., Writing: M.R., M.H.

Funding: The authors declared that this study received no financial support.

Competing interests: No conflict of interest was declared by the authors.

Ethical approval: It obtained approval from the BSGE Scientific Advisory Group for research use of the database, who then provided the data in anonymised form.

Informed consent: All patients gave written consent to the collection of data from their questionnaires and surgical data from their operations to be stored in the BSGE database and used subsequently for research and publication. The data is stored in an encrypted form and hosted by a paid third party.

Data sharing: The datasets used for this study are not available publicly due to legal and confidentiality reasons. However the data anslysis can be requested from author.

Transparency: I affirm that the manuscript is an honest, accurate and transparent account of the study and no impostrant aspects have been omitted. There are no discripensy from study as planned.

References

1. Ferrero S, Camerini G, Leone Roberti Maggiore U, Venturini PL, Biscaldi E, Remorgida V. Bowel endometriosis: recent insights and unsolved problems. World J Gastrointest Surg. 2011;3:31-8.
2. Fedele L, Berlanda N. Emerging drugs for endometriosis. Expert Opin Emerg Drugs. 2004;9:167-77.
3. Rodgers AK, Falcone T. Treatment strategies for endometriosis. Expert Opin Pharmacother. 2008;9:243-55.
4. Tosti C, Biscione A, Morgante G, Bifulco G, Luisi S, Petraglia F. Hormonal therapy for endometriosis: from molecular research to bedside. Eur J Obstet Gynecol Reprod Biol. 2017;209:61-6.
5. Angioni S, Pontis A, Dessole M, Surico D, De Cicco Nardone C, Melis I. Pain control and quality of life after laparoscopic en-block resection of deep infiltrating endometriosis (DIE) vs. incomplete surgical treatment with or without GnRHa administration after surgery. Arch Gynecol Obstet. 2015;291:363-70.
6. Kruse C, Seyer-Hansen M, Forman A. Diagnosis and treatment of rectovaginal endometriosis: an overview. Acta Obstet Gynecol Scand. 2012;91:648-57.
7. Moawad NS, Caplin A. Diagnosis, management, and long-term outcomes of rectovaginal endometriosis. Int J Womens Health. 2013;5:753-63.
8. Daniilidis A, Angioni S, Di Michele S, Dinas K, Gkrozou F, D'Alterio MN. Deep endometriosis and infertility: what is the impact of surgery? J Clin Med. 2022;11:6727.
9. Rodríguez-Tárrega E, Monzo AM, Quiroga R, Polo-Sánchez P, Fernández-Colom P, Monterde-Estrada M, et al. Effect of GnRH agonist before IVF on outcomes in infertile endometriosis patients: a randomized controlled trial. Reprod Biomed Online. 2020;41:653-62.
10. Daraï E, Dubernard G, Coutant C, Frey C, Rouzier R, Ballester M. Randomized trial of laparoscopically assisted versus open colorectal resection for endometriosis: morbidity, symptoms, quality of life, and fertility. Ann Surg. 2010;251:1018-23.
11. Bafort C, Beebeejaun Y, Tomassetti C, Bosteels J, Duffy JMN. Laparoscopic surgery for endometriosis. Cochrane Database Syst Rev. 2020;10:CD011031.
12. National Institute for Health and Care Excellence (NICE). Endometriosis: diagnosis and management. NICE guideline [NG73]. London: National Institute for Health and Care Excellence; 2017. Available from: https://www.nice.org.uk/guidance/ng73
13. Streuli I, de Ziegler D, Santulli P, Marcellin L, Borghese B, Batteux F, et al. An update on the pharmacological management of endometriosis. Expert Opin Pharmacother. 2013;14:291-305.
14. Vercellini P, Buggio L, Borghi A, Monti E, Gattei U, Frattaruolo MP. Medical treatment in the management of deep endometriosis infiltrating the proximal rectum and sigmoid colon: a comprehensive literature review. Acta Obstet Gynecol Scand. 2018;97::942-55.
15. Roman H, Bubenheim M, Huet E, Bridoux V, Zacharopoulou C, Daraï E, et al. Conservative surgery versus colorectal resection in deep endometriosis infiltrating the rectum: a randomized trial. Hum Reprod. 2018;33:47-57.
16. De Cicco C, Corona R, Schonman R, Mailova K, Ussia A, Koninckx P. Bowel resection for deep endometriosis: a systematic review. BJOG. 2011;118:285-91.
17. Quesada J, Härmä K, Reid S, Rao T, Lo G, Yang N, et al. Endometriosis: a multimodal imaging review. Eur J Radiol. 2023;158:110610.
18. Payá V, Hidalgo-Mora JJ, Diaz-Garcia C, Pellicer A. Surgical treatment of rectovaginal endometriosis with rectal involvement. Gynecol Surg. 2011;8:269-77.
19. Vercellini P, Consonni D, Barbara G, Buggio L, Frattaruolo MP, Somigliana E. Adenomyosis and reproductive performance after surgery for rectovaginal and colorectal endometriosis: a systematic review and meta-analysis. Reprod Biomed Online. 2014;28:704-13.
20. Donnez J, Stratopoulou CA, Dolmans MM. Endometriosis and adenomyosis: similarities and differences. Best Pract Res Clin Obstet Gynaecol. 2024;92:102432.
21. Kishi Y, Suginami H, Kuramori R, Yabuta M, Suginami R, Taniguchi F. Four subtypes of adenomyosis assessed by magnetic resonance imaging and their specification. Am J Obstet Gynecol. 2012;207:114.e1-7.
22. Rafique M, Becker C, Lewin J, Vashisht A, Sarıdoğan E, Hirsch M. Pre-operative GnRH agonist use and surgical outcomes in rectovaginal/colorectal endometriosis: an international multicentre prospective cohort study. Facts Views Vis Obgyn. 2025;17:101-109.
23. Meuleman C, Tomassetti C, Wolthuis A, Van Cleynenbreugel B, Laenen A, Penninckx F, et al. Clinical outcome after radical excision of moderate-severe endometriosis with or without bowel resection and reanastomosis: a prospective cohort study. Ann Surg. 2014;259:522-31.
24. Roman H, Vassilieff M, Gourcerol G, Savoye G, Leroi AM, Marpeau L, et al. Surgical management of deep infiltrating endometriosis of the rectum: pleading for a symptom-guided approach. Hum Reprod. 2011;26:274-81.
25. Roman H, Saint Ghislain M, Milles M, Marty N, Hennetier C, Moatassim S, et al. Improvement of digestive complaints in women with severe colorectal endometriosis benefiting from continuous amenorrhoea triggered by triptorelin. A prospective pilot study. Gynecol Obstet Fertil. 2015;43:575-81.
26. Donnez J, Spada F, Squifflet J, Nisolle M. Bladder endometriosis must be considered as bladder adenomyosis. Fertil Steril. 2000;74:1175-81.

Supplementary Table 1. Pain and EQVAS score pre-GnRHa and nPre-GnRHa group (controlled for all confounders).

	Pre-GnRHa (mean)	nPre-GnRHa (mean)	*P* value
EQVAS	53.5	53.9	0.4
Non-cyclical pelvic pain	5.48	5.50	0.8
Dyspareunia	4.97	5.18	<0.001*
Menstrual pain	8.39	8.18	<0.001*
Premenstrual pain	7.55	8.00	0.03*
Lower back pain	7.04	6.86	0.01*

*Statistically significant *P*<0.05, EQVAS: EuroQol-visual analogue scales, pre-GnRHa: Pre-operative gonadotrophin-releasing hormone agonists, nPre-GnRHa: No pre-operative gonadotrophin-releasing hormone agonists.

Supplementary Table 2. Bladder symptoms (pre-GnRHa and nPre-GnRHa group-controlled for all confounders).

Symptoms	pre-GnRHa mean (SD)	pre-GnRHa median (IQR)	nPre-GnRHa mean (SD)	nPre-GnRHa median (IQR)	t-test *P* value	MWU *P* value
Bladder pain	3.44 (3.09)	1 (1-6)	3.45 (3.13)	1 (1-6)	0.91	0.85
Difficulty emptying the bladder	2.72 (2.87)	1 (1-4)	2.68 (2.83)	1 (1-4)	0.56	0.81

SD: Standard deviation, IQR: Interquartile range, EQVAS: EuroQol-visual analogue scale, pre-GnRHa: Pre-operative gonadotrophin-releasing hormone agonists, nPre-GnRHa: No pre-operative gonadotrophin-releasing hormone agonists, MWU: Mann-Whitney U test.

Supplementary Table 3. Bowel symptoms (pre-GnRHa and nPre-GnRHa group-controlled for all confounders).

Symptom	pre-GnRHa mean (SD)	pre-GnRHa median (IQR)	nPre-GnRHa mean (SD)	nPre-GnRHa median (IQR)	t-test *P* value	MWU *P* value
Constipation	1.62 (1.12)	2 (1-2)	1.57(1.12)	2 (1-2)	0.08	0.03*
Frequent bowel movements	2.09 (1.27)	2 (1-3)	2.10(1.27)	2 (1-3)	7.12	2.77
Urgent bowel movements	1.37 (1.09)	1 (0-2)	1.38(1.11)	1 (0-2)	0.78	0.90
Incomplete emptying sensation	1.56 (1.21)	2 (0-2)	1.49(1.21)	2 (0-2)	0.01*	0.01*
Cyclical dyschezia	6.97 (3.50)	8 (5-10)	6.68(3.54)	8 (4-10)	0.01*	0.01*
Non-cyclical dyschezia	4.61 (3.24)	4 (1-7)	4.52(3.29)	4 (1-7)	0.21	0.16

*Statistically significant *P*<0.05, SD: Standard deviation, IQR: Interquartile range, pre-GnRHa: Pre-operative gonadotrophin-releasing hormone agonists, nPre-GnRHa: No pre-operative gonadotrophin-releasing hormone agonists, MWU: Mann-Whitney U test.