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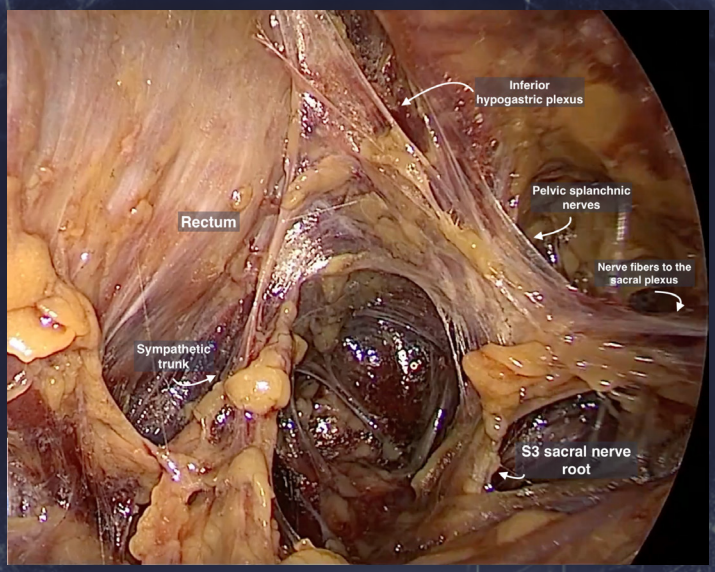

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EDITORIAL

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Facts Views Vis Obgyn 2025;17(3):216-217

The scientific gap

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Keywords: Endometriosis, ultrasound, laparoscopic surgery, GnRHa

In daily life, there is often a gap between what we know and what we actually do. Failure to implement newfound knowledge is also pervasive in medical practice with unacceptable delays between publication of new insights and the conversion of this information into daily clinical practice. For example, the IDEA consensus on the systematic use of transvaginal ultrasound in the detection of pelvic deep endometriosis was published in 2016.[1] It contained a comprehensive, clear description about how to scan and describe the different anatomical structures of the female pelvis and presence of endometriotic lesions. However, it seems only now, several years later, we are beginning to routinely adopt and apply this knowledge into the care of women with endometriosis. How can this time gap be explained? What does this mean for the quality of our clinical practice and the outcomes of our patients?

An important driver of this scientific gap between knowledge and implementation is a failure to evaluate and absorb knowledge. For scientific publications, ask yourself: do you read the full articles or just the abstracts, or do you even just go peruse the conclusions? You might think that an article that has been published in a peer reviewed scientific journal is unimpeachable fact. However, this belief would be naive. Many of us are time poor and so we swipe from one article's abstract conclusions to the next, in line with the modern way of consuming information rapidly from social media channels without time for due consideration or reflection. But what about the strengths of a study? And, even more importantly, what about the limitations? These aspects of a study's validity are usually presented in the discussion section of correction requiring some time to read the full article. Many articles are now available as open access, allowing immediate download of the full text to read on a quiet Sunday morning.

In the current issue of Facts, Views and Vision in ObGyn, Rafique et al.[2] conducted a retrospective, multi-centre cohort study evaluating the role of pre-operative gonadotropin-releasing hormone agonists (GnRHa) on pain, bowel and bladder symptoms in rectovaginal/colorectal endometriosis surgery. The authors conclude that the preoperative use of GnRH analogues is beneficial for post-surgical symptom control. Only reading the conclusion might lead you to routinely use GnRHa pre-treatment in your deep endometriosis patients awaiting surgical excision. However, taking the time to scrutinise the

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paper more thoroughly and read the discussion section highlights limitations in their methodology that may make one pause before liberally prescribing GnRHa before surgical excision of deep endometriosis. For example, key information is missing about the extent of the disease (classification), the indication for use and pre-treatment duration. Moreover, the cohort has a very high rate of shaving of rectal disease as opposed to bowel resection, an overly conservative approach that could suggest incomplete resection of disease and a higher risk of symptom persistence. Despite these deficiencies (inherent in retrospective studies), the data set is large and provides some valuable data to help guide practice. The authors wisely call for a randomised controlled trial on the subject although the feasibility of successfully running such a trial is questionable.

Our focus should be to ensure new, validated and relevant evidence is placed in the "fast lane" of the scientific highway. We need to take the time to evaluate the relevance and validity of published papers more thoroughly. However, such scrutiny should not delay action; our patients deserve rapid implementation of evidence-based interventions. We need high-quality research, responsible publishing and timely implementation into guidelines, quality standards, and medical education curricula. In this way we can close the current scientific gap.

Conflicts of Interest: The authors have no conflict of interest to declare.

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OPINION PAPER

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Dual operating in gynaecological endoscopy: towards a culture of shared learning and safer surgery

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ABSTRACT

Dual operating is increasingly recognised as a valuable strategy in complex gynaecological surgery. Models include supervising (trainer–trainee), buddy (comparable proficiency within a specialty), and inter-specialty (collaboration across specialities). Each approach offers unique benefits for patient safety, surgical training, and surgeon wellbeing. Buddy operating in particular promotes peer-to-peer learning, shared responsibility, and enhances decision-making. As minimally invasive gynaecology evolves, embedding these models into practice may strengthen training, and improve outcomes and workforce resilience. Further evidence is needed to evaluate long-term benefits and cost-effectiveness in different clinical contexts.

Keywords: Buddy operating, supervision, inter-specialty surgery, gynaecological endoscopy, surgical training, patient safety

Introduction

Minimally invasive gynaecological surgery has transformed patient care by reducing postoperative pain, hospital stay, and recovery times compared to laparotomy.[1,2] However, the increasing complexity of procedures such as laparoscopic excision of deep endometriosis and hysterectomy in the frozen pelvis has amplified demands on surgeons. Such operations are technically challenging, ergonomically tiring, and often prolonged. Operating in tandem with another equally competent colleague may help overcome these obstacles.

However, it is not just surgical complexity that drives the need for dual operating. Consultants (or equivalent where this term is not used) are being appointed to posts without the requisite level of surgical skill, such that there is a need for supervision and training by other surgical colleagues. In addition, as technologies and research expand the surgical repertoire at pace, senior surgeons may require training to expand their skill set.

Different models of dual operating can be categorised according to the relative expertise of the participating surgeons (Table 1). Each model carries distinct implications for training, efficiency, and patient outcomes, and the choice of approach should be tailored to the complexity of the case and the expertise available.

The *supervising model* is the most traditional form of dual operating and typically manifests as the consultant–trainee dynamic. The trainee is usually of junior status but as highlighted above, we must also recognise that a "trainee" may be a peer colleague, typically one who has been promoted but lacks the

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craft skills necessary for the post or a colleague who wishes to retrain/develop the range of their skills. It should also be recognised that in contrast to dual operating with a similarly proficient colleague, dual operating with a less proficient colleague, whether trainee or peer, may be more stressful for the supervising surgeon. When the trainee is a peer colleague supervision may be potentially more problematic due to skewed, less clear "trainer-trainee" dynamics. The supervising surgeon conventionally retains overall responsibility for patient safety while allowing the less experienced surgeon to undertake progressive components of the procedure under direct observation and guidance. However, when supervising operating with peers or even more senior colleagues, the boundries ofs responsibility may become blurred.

The supervision model, whether junior, peer or senior colleague, remains essential for surgical education, albeit challenges persist e.g., lengthening operative times. Furthermore, balancing patient safety with meaningful hands-on training requires skill and experience from the supervisor. Arguably supervising trainees in laparoscopic surgery is more difficult and time consuming than conventional open surgery. This is because the subtle movements involved in laparoscopic surgery from expert surgeons/trainers may not always be appreciated and as a result not taught. In contrast, open, laparotomic surgery allows for immediate, tactile, "hands-on" direction. In contrast others may argue that the visualisation and exposure is better in endoscopic surgery compared with open surgery facilitating training.

The *buddy model* involves two surgeons of comparable proficiency operating collaboratively within the same specialty with both surgeons sharing technical tasks, intraoperative decision-making, and responsibility for outcomes. This facilitates shared responsibility for complex cases.

The *inter-specialty model* brings together surgeons from different specialities to address complex cases. In gynaecology, this is most relevant in advanced endometriosis involving the bowel, bladder, or ureters, where colorectal or urological expertise is required. While logistical challenges such as scheduling across departments can be significant, the inter-specialty model represents the most collaborative form of dual operating, and its value in complex gynaecological surgery is self-evident.

Why Dual Operating Matters

Three trends make dual operating particularly relevant:

1. Increasing Surgical Complexity

Deep endometriosis excision, challenging myomectomies because of location, size or multiplicity and anatomical distortion due to adhesions e.g., a frozen pelvis results in prolonged operating times, requiring advanced anatomical dissection and enhanced levels of concentration. Fatigue and cognitive overload are genuine risks that dual operating can help mitigate.[3]

2. Constraints on Training

The European Working Time Directive and rising service pressures limit exposure to surgery whether straight forward "major" cases or complex cases necessitating advanced surgical skills.[4] Dual operating maximises learning opportunities—whether through the supervising model for junior or peer trainees or the buddy model for peer-to-peer learning.

3. Surgeon Wellbeing

Musculoskeletal strain, burnout, and psychological burden are increasingly reported among gynaecological surgeons.[5] Sharing responsibility distributes workload and fosters a culture of mutual support.

Benefits for Patients

For patients, dual operating may translate into shorter operative times, reduced complication rates, and improved outcomes. Evidence from colorectal and hepatobiliary surgery shows that paired consultant operating can lower complication rates and optimise resection margins.[6] Inter-specialty collaboration in endometriosis specialist centres in the UK is particularly

Table 1. Clark models of dual operating.

Level	Definition
Supervising	One surgeon less proficient than the other in the same specialty
Buddy	Both surgeons of comparable proficiency
Inter-specialty[1]	Surgeons with proficiency in different surgical specialties

[1]Complex procedures where urological, colorectal, cardiothoracic or vascular input may be required.

valuable to reduce complication risk especially where single-specialty expertise may be insufficient.[7]

Benefits for Surgeons

For surgeons, dual operating supports skill acquisition and professional growth. In the supervising model, trainers provide direct feedback during live operating. The buddy model allows experienced surgeons to learn from each other—observing subtle variations in technique and decision-making. Inter-specialty collaboration (e.g., with colorectal or urological surgeons) exposes surgeons to complementary surgical approaches, broadening anatomical understanding. Beyond technical learning, dual operating reduces the isolation often experienced in complex procedures. The emergence of dual console systems in robotic surgery provides a useful parallel to buddy operating in conventional laparoscopy.[7] This facilitates structured training, immediate feedback, and shared responsibility for complex steps.[8]

Workforce Sustainability

Sustainability of the surgical workforce is a growing concern. High case complexity, limited training opportunities, and surgeon attrition threaten the delivery of advanced endoscopic care. Dual operating may contribute to sustainability by:

- Preventing musculoskeletal injury through shared workload,
- Reducing burnout by fostering a supportive culture,
- Creating more resilient training pathways and embedding teamwork.

Challenges and Limitations

Despite its benefits, challenges remain. Allocating two consultants to a single procedure may appear inefficient in resource-constrained health systems. Moreover, the supervisory model if involving a fellow peer, make take away training opportunities from colleagues in junior grades adversely impacting their progression. Whilst peer colleagues may want to acquire new skills, the time, effort and resource to achieve this via direct supervision should be in keeping with a department's strategic goals.

Not all procedures require dual operating, and overuse could reduce service capacity. Hierarchy may also hinder implementation: the buddy model relies on equality, which can be difficult to achieve in cultures dominated by senior–junior structures. Finally, robust evidence is limited, with most reports being observational. High-quality prospective studies and health-economic analyses are needed to build the case for widespread adoption.

Future Directions

Professional societies such as the European Society for Gynaecological Endoscopy (ESGE) can play a central role in defining when dual operating should be encouraged. Consensus statements, prospective registries, and training frameworks would strengthen the evidence base. Dual operating could be embedded into fellowship programmes, particularly for advanced endometriosis surgery and complex laparoscopic hysterectomy. Interdisciplinary training pathways may also evolve, with joint gynaecology–colorectal or gynaecology–urology fellowships formalising inter-specialty dual operating.

Conclusion

Dual operating is more than a technical arrangement; it represents a cultural shift towards collaborative, safe and sustainable surgery. In gynaecological endoscopy, where complexity is increasing and surgeon wellbeing is under pressure, dual operating has the potential to enhance patient outcomes, improve training, and protect the workforce. The challenge now lies in moving away from the isolated surgeon towards working in teams, sharing expertise, and promoting sustainable practice with the ESGE ideally positioned to lead this shift.

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ORIGINAL ARTICLE

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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

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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.

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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 criteria, 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 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 Whitney U test. 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 non-cyclical pelvic pain 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.

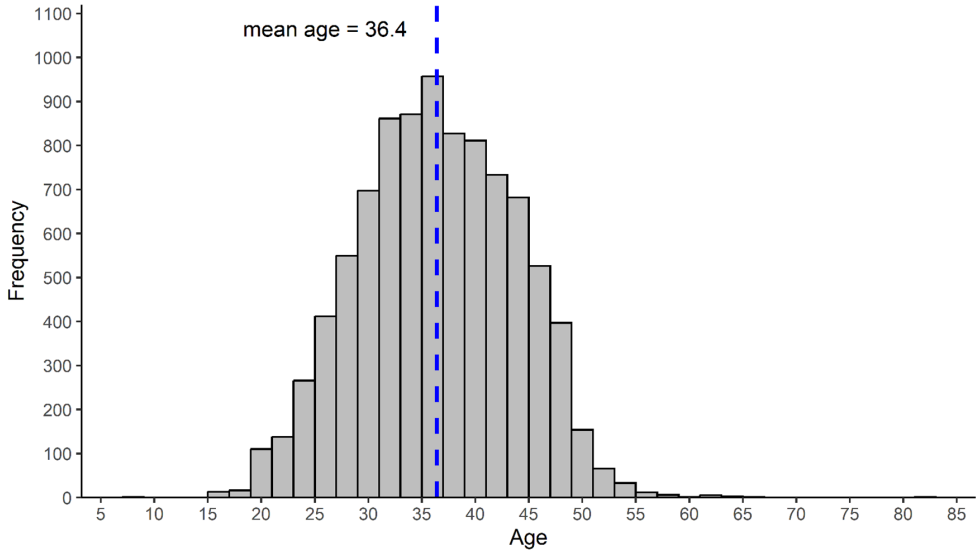

Figure 1. Age histogram.

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.

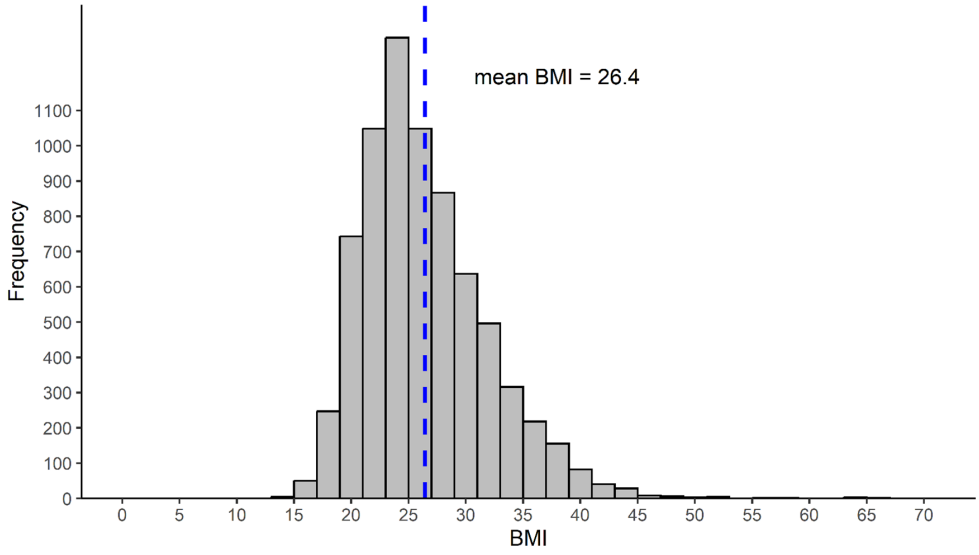

Figure 2. BMI histogram.

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 and 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.

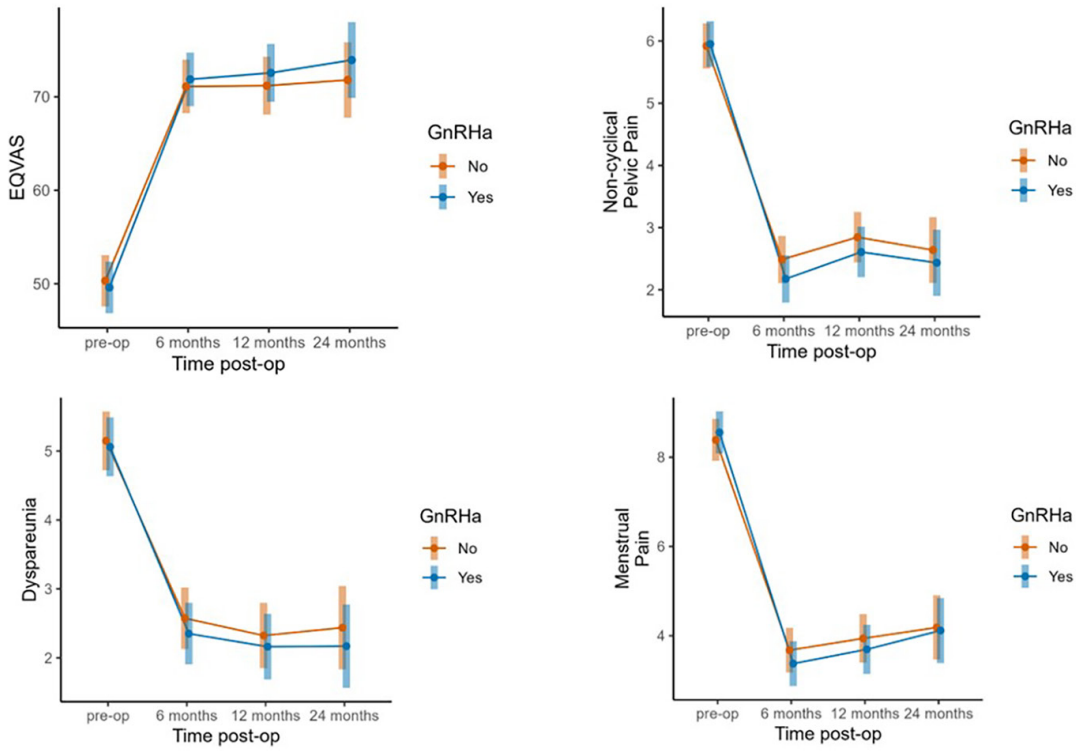

Figure 3. EQVAS and pain scoring.

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 analysis. 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.

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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 analysis. 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 discrepancy from study as planned.

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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.

ORIGINAL ARTICLE

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Menopausal symptoms after hysterectomy with opportunistic salpingectomy: a pilot study

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ABSTRACT

Background: Opportunistic salpingectomy during hysterectomy with ovarian preservation may reduce the risk of ovarian cancer, but concerns remain that adding salpingectomy to hysterectomy could affect ovarian vascularisation and subsequent function.

Objectives: To assess the feasibility of a full-scale trial to evaluate changes in menopausal symptoms based on the menopause rating scale (MRS) six months following hysterectomy, with and without opportunistic salpingectomy.

Methods: A prospective observational pilot study of premenopausal women age 40 to 55 years scheduled for hysterectomy with ovarian preservation was conducted, where participants were counselled and given the option of concomitant salpingectomy or not.

Main Outcome Measures: Forty-six out of 50 women chose opportunistic salpingectomy. It took 17 months to recruit 50 patients. Complete follow-up data was achieved in 43 of the 50 participants.

Results: The median MRS score remained unchanged in the opportunistic salpingectomy group at 9 [interquartile range (IQR): 3–14], both before surgery and six months afterwards (n=39). In contrast, the group of women who did not undergo opportunistic salpingectomy had a median MRS score of 11 (IQR: 3–16) preoperatively, which increased to 25 (IQR: 6–32) six months postoperatively (n=4).

Conclusions: The majority of patients in our cohort opted for opportunistic salpingectomy. However, no deterioration in menopausal symptoms was observed in this group after six months. A randomised controlled trial comparing hysterectomy with and without opportunistic salpingectomy in this patient population may not be feasible, given the strong patient preference for salpingectomy and slow recruitment.

What is New? The development of subjective menopausal symptoms is evaluated after hysterectomy with opportunistic salpingectomy.

Keywords: Hysterectomy, opportunistic salpingectomy, menopause, menopause rating scale, MRS

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Introduction

High-grade serous carcinoma is now understood to originate from serous tubal intraepithelial carcinoma, a precursor lesion found in the fimbriae of the fallopian tube.[1,2] Opportunistic salpingectomy in post-reproductive women (removal of the salpinges bilaterally in women that are scheduled for surgery in the pelvis) has been associated with a 49%-65% reduction in ovarian cancer risk.[3,4] Given its apparent cost-effectiveness, the International Federation of Gynaecology and Obstetrics' position statement supports opportunistic salpingectomy as a preventive strategy for ovarian cancer.[5,6]

Hysterectomy alone may accelerate ovarian failure [hazard ratio (HR): 1.92], possibly due to the disruption of uterine artery branches supplying the ovary.[7] There is concern that adding bilateral salpingectomy could further compromise ovarian vascularisation, potentially exerting a greater impact on ovarian function.

The impact of opportunistic salpingectomy on ovarian function has been studied using menopause markers such as oestradiol, anti-Müllerian hormone (AMH), follicle-stimulating hormone and luteinising hormone levels, as well as ultrasound changes in the ovary or antral follicle count. The 2019 Cochrane Review has concluded that there was no significant difference in postoperative hormonal status and no clinically relevant reduction in AMH. However, the review highlighted a notable lack of studies evaluating objective menopausal symptoms.[8]

A population-based Canadian cohort study of 40,000 women confirmed that women who underwent hysterectomy with opportunistic salpingectomy did not consult earlier with menopausal complaints than those without opportunistic salpingectomy [adjusted HR: 0.98; 95% confidence interval (CI): 0.88-1.09]. Similarly, there was no significant difference in the time from surgery to the prescription of hormone replacement therapy between the two groups (adjusted HR: 0.82; 95% CI: 0.72-0.92).[9]

Conversely, a retrospective observational cohort study of 23000 women reported an increase in menopausal symptoms one year after surgery [relative risk (RR): 1.29; CI: 1.04-1.60], particularly in the subgroup of women between the ages of 44 and 69 years (RR: 1.53; CI: 1.06-2.20).[10]

The Hysterectomy and Opportunistic Salpingectomy (HOPPSA) trial, a multicentre randomised clinical trial evaluating the safety and effectiveness of performing opportunistic salpingectomy at hysterectomy to reduce the risk of epithelial ovarian cancer, is in progress and is collecting data on menopausal symptoms using the menopause rating scale (MRS).[11] We had previously planned to conduct a pilot study to assess the feasibility of a full-scale trial to evaluate changes in menopausal symptoms using the MRS as a primary outcome, six months following hysterectomy, with and without opportunistic salpingectomy.

Methods

We conducted a multicentre prospective pilot cohort study across three centres: Ghent University Hospital, Antwerp University Hospital, and ZAS Middelheim Hospital in Antwerp, Belgium. This study was approved by the independent Medical Ethics Committee of all three participating clinics (permission of the Ethics Committee of the Middelheim Hospital was obtained on the 11th of March 2020, reference number: B009202043074. Permission of the Ethics Committee of the Ghent University Hospital was obtained on the 4th December 2020, decision no: BC-08426. Permission of the Ethics Committee of the Antwerp University Hospital was obtained on 18th November 2020, decision no: 5334).

As part of standard clinical care and shared decision making, patients were counselled by their gynaecologists on hysterectomy and the potential advantages and disadvantages of opting for or declining from opportunistic salpingectomy. Written informed consent was obtained from all study participants. The study information sheets contained information about the evidence of opportunistic salpingectomy in 2020, namely: "researchers showed that the risk of developing ovarian cancer could be reduced by removing the fallopian tubes. The fallopian tubes do not produce hormones and transport oocytes to the uterus to become pregnant. The salpinges can be taken away from the female pelvis when the desire to have children is complete. If the removal of the fallopian tubes is done during another procedure to prevent cancer, the procedure becomes opportunistic. Opportunistic salpingectomy could mean a 49%-65% risk reduction compared to developing ovarian cancer. To date, however, there are no long-term results (e.g. 30 years later) that have studied survival or reduction of the risk of ovarian cancer after surgery. In theory, removing the fallopian tubes could have a limited impact on the functioning of the ovary. On short-term (up to 1 year later) and long-term effects (3 to 5 years later), no difference was seen in hormonal production

after opportunistic salpingectomy. Yet, in September 2019, a renowned research team (Cochrane) concluded that menopause could develop up to 20 months earlier after opportunistic salpingectomy with hysterectomy. Few studies have been conducted on menopausal symptoms after opportunistic salpingectomy."

Inclusion criteria included premenopausal women aged 40 to 55 years scheduled for hysterectomy for benign disease without oophorectomy. Exclusion criteria included a prior period of amenorrhea lasting six months, use of hormonal replacement therapy or any oral contraceptive method within one month before surgery, previous unilateral or bilateral oophorectomy, a history of a malignancy requiring pelvic radiation or systemic chemotherapy, or a history of acute or chronic pelvic inflammatory disorder.

Menopausal symptoms were assessed using the MRS, a validated health-related quality of life scale for evaluating menopausal complaints. The MRS includes eleven questions about different menopausal subdomains, with a total score ranging from 0 to 44; a higher score indicates more severe subjective menopausal symptoms.[12] The scale is widely recognised for its applicability and reliability in evaluating menopausal symptoms. MRS scores were calculated preoperatively and six months postoperatively.

The primary outcome was to estimate the change in MRS scores from preoperatively to six months postoperatively in both groups using descriptive statistics to compare medians and interquartile ranges (IQR). We also intended to test the feasibility of designing a randomised clinical trial.

Results

Over 17 months (Dec 2020 and Jan 2022), 50 patients were enrolled in the study. Of the 52 patients approached, 50 consented to participate after reviewing the patient information leaflet. Demographic data are presented in Table 1. The mean age at the time of hysterectomy was 45 years (± 4.02). The majority of participants (46 out of 50, or 92%) chose to undergo opportunistic salpingectomy at the time of hysterectomy. Seven patients were lost to follow-up six months post-surgery. All the missing data belonged to patients who underwent hysterectomy with opportunistic salpingectomy.

In the opportunistic salpingectomy group, the median MRS score remained stable at 9 (IQR: 3-14) both before surgery and six months after surgery (n=39). In contrast, the group without opportunistic salpingectomy had a median MRS score of 11 (IQR: 3-16) preoperatively, which increased to 25 (IQR: 6-32) six months postoperatively (n=4).

Discussion

Main Findings

Our study was not powered for statistical analysis between the two groups; however, we observed no

Table 1. Demographics of the study population.

	Overall study population (n=50)	**Patients with opportunistic salpingectomy (n=46)**	**Patients without opportunistic salpingectomy (n=4)**
Age at time of surgery in years Median (IQR)	44.0 (42.0-49.0)	44.0 (41.8-49.0)	47.5 (44.8-49.5)
BMI at the time of surgery Median (IQR)	26.1 (22.7-30.7)	26.1 (22.7-29.5)	27.3 (19.2-36.9)
Family history of breast cancer	9 (18%)	9 (19.6%)	0
Family history of ovarian cancer	1 (2%)	1 (2%)	0
Type of hysterectomy			
• Laparoscopic • Laparotomic • Vaginal • v-NOTES	37 (74%) 10 (20%) 2 (4%) 1 (2%)	35 (76%) 9 (20%) 1 (2%) 1 (2%)	2 (50%) 1 (25%) 1 (25%) 0
Menopause rating scale* pre-surgery Median (IQR)	9.50 (2.9-13.5)	9.0 (2.9-13.5)	11 (2.8-16.35)

*Menopause rating scale is a validated health-related quality of life scale for menopausal complaints with values ranging from 0 to 44. A higher score means that the patient experiences more subjective symptoms. IQR: Interquartile range, BMI: Body mass index, v-NOTES: Vaginally-assisted natural orifice transluminal endoscopic surgery.

deterioration in menopausal symptoms, six months after surgery, in the opportunistic salpingectomy group. Additionally, our results clearly demonstrated a strong patient preference for opportunistic salpingectomy when combined with hysterectomy. As our study employed a non-randomised design, patients were free to choose their preferred treatment. A roundtable discussion among the study team explored possible reasons for the patient' preference for salpingectomy. The investigators felt that most patients prioritised the oncological risk reduction while potentially underestimating the relationship between salpingectomy and premature menopause. Despite thorough counselling, patients do not always fully comprehend that menopause is not solely defined by the cessation of menstrual bleeding and the end of fertility, but also by hormonal and systemic changes.

We speculated that the four women, opting to keep the salpinges, may have already experienced more menopausal complaints from the start and attempted to delay further progression by avoiding salpingectomy. However, this strategy appeared unsuccessful, as their mean MRS scores doubled within six months postoperatively.

When salpingectomy involves resecting a large part of the broad ligament, there may theoretically be an increased risk of damaging smaller vessels between the fallopian tube and ovary. We propose to operate as closely as possible to the fallopian surface to minimise potential additional impact on ovarian vascularisation.

Strengths and Limitations

The MRS was chosen as an outcome parameter because it is a validated instrument that offers a reliable assessment of subjective menopausal symptoms. In the literature, there are limited data on MRS scores following hysterectomy with or without opportunistic salpingectomy. The key advantage of the MRS score is that it relies on patient-reported outcomes rather than requiring hospital visits and blood sampling. Biochemical markers of ovarian reserve are not always a good predictor of subjective complaints.

It remains uncertain whether AMH levels, which are being used most frequently as a marker for ovarian reserve, are an accurate measure to assess the effects of opportunistic salpingectomy. AMH values first show a steep decline postoperatively, to make a recovery several months afterwards.[8] There are no cut-off levels formulated to predict the onset of menopause, and AMH levels are of a fluctuating nature. Furthermore, its predictive utility decreases with advancing age.[13]

Seventeen months were needed to obtain fifty inclusions across three different hospitals. The slow recruitment rate was likely influenced by the coronavirus disease-2019 pandemic. Additionally, the exclusion of patients using hormonal contraception, in order to minimise bias in preoperative MRS score, limited enrollment. Many premenopausal patients were on hormonal therapy for irregular bleeding and/or heavy menstrual bleeding, making them ineligible for inclusion. The number of women excluded for this reason was not recorded. In hindsight, this exclusion may have been unnecessary, as contraception is discontinued immediately after hysterectomy.

A key limitation of this study is the short follow-up period. Six months of follow-up may be insufficient to draw conclusions about menopausal symptoms, given that the average age of menopause in Belgium is approximately 51 years, while the mean age of participants was 45 years.

Due to the small sample size, no statistical comparison between surgical subtypes was performed. It is also worth noting that the surgical approach may influence ovarian vascularisation, with laparotomy potentially having a greater impact than laparoscopic hysterectomy.[14] However, no conclusive data currently exist comparing the impact of different surgical techniques on ovarian vascularisation and function.[15]

Clinical and Policy Implications

Given the limited evidence regarding both the cancer preventive potential of opportunistic salpingectomy and its possible effects on ovarian vascularisation, we recommend providing uniform, standardised information during the counselling process for premenopausal patients scheduled for hysterectomy. Such standardised counselling is crucial, as current recommendations emphasise the importance of discussing the benefits and risks of opportunistic salpingectomy but offer no guidance on their implementation in daily practice, leading to wide variations in current practice among gynaecologists. Ideally, opportunistic salpingectomy should be linked to enable systematic follow-up of patients.

Unanswered Questions and Future Research

Conducting a randomised controlled trial (RCT) comparing hysterectomy with and without opportunistic salpingectomy in our patient population appears less

feasible due to a strong patient preference for concurrent salpingectomy and a slow rate of recruitment. However, an interim analysis conducted during 2021 of the HOPPSA RCT comparing the safety and effectiveness of performing opportunistic salpingectomy at hysterectomy, recommended that the study should continue until the target sample size is reached, suggesting recruitment was feasible.[16] The subject enrollment is estimated to be completed in March 2026, and the menopausal symptoms will be evaluated one year following surgery. The results of this trial are eagerly awaited.

Conclusion

The majority of patients in our cohort opted for opportunistic salpingectomy. However, no deterioration in menopausal symptoms was observed in this group after six months. An RCT comparing hysterectomy with and without opportunistic salpingectomy in this patient population may not be feasible, given the strong patient preference for salpingectomy and the slow rate of recruitment. In the meantime we propose conducting prospective observational studies with longer follow-up, integrating MRS scores with serial hormonal assessments to better understand the long-term impact on menopausal symptoms and ovarian function.

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Data sharing: Data is available on request from the authors.

Transparency: Dr Anne-Sophie Maryns affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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ORIGINAL ARTICLE

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Intrauterine application of Budesonide-hyaluronic acid gel in patients with recurrent implantation failure and total loss of junctional zone differentiation on magnetic resonance imaging

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ABSTRACT

Background: Recurrent implantation failure (RIF) and repeated pregnancy loss remain major challenges in assisted reproductive technology, often without identifiable causes despite high-quality embryo transfers. Emerging evidence suggests that abnormalities in the junctional zone (JZ) of the uterus may impair implantation.

Objectives: To evaluate the efficacy of hysteroscopic (HSC) sub-endometrial exploration combined with intrauterine application of budesonide-enriched crosslinked hyaluronic acid (HA) gel on pregnancy outcomes in women with RIF and complete JZ loss on magnetic resonance imaging (MRI).

Methods: This single-centre observational pilot study included 20 women with RIF and MRI-confirmed loss of JZ differentiation. All patients had excellent cryopreserved blastocysts, either from an egg donation program or derived from their own autologous oocytes (<37 years). Under conscious sedation, patients underwent HSC sub-endometrial exploration with micro-incisions at the lateral walls and fundus, followed by intrauterine instillation of budesonide-enriched HyaRegen® gel. [BioRegen Biomedical (Changzhou) Co., Ltd].

Main Outcome Measures: Clinical pregnancy rate, live birth rate, and maternal/neonatal outcomes.

Results: Eighteen of 20 women (90%) conceived. In the donor group, all 9 pregnancies led to live births. In the autologous group, 8 of 9 pregnancies were successful; one was medically terminated at 20 weeks due to foetal malformation. All 17 neonates were healthy at birth and six-month follow-up.

Conclusions: Preliminary observations of this novel approach suggest that it may contribute to improving implantation and live birth rates in women with unexplained RIF and JZ abnormalities.

What is New? This study introduces a targeted intrauterine intervention for RIF patients with loss of JZ differentiation, combining HSC exploration and budesonide–HA gel therapy.

Keywords: Recurrent implantation failure, hysteroscopy, budesonide, hyaluronic acid, junctional zone, magnetic resonance imaging

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Introduction

Recurrent implantation failure (RIF) and repeated pregnancy loss (RPL) remain major challenges in assisted reproductive technology (ART). Their prevalence varies depending on maternal age, embryo quality, uterine environment, and ART protocols.[1,2] Globally, miscarriage affects 15–20% of women under 35, rising to 40–50% in those over 40. Up to 75% of embryos fail to implant during ART, with RIF—defined as three or more failed ART transfers with good-quality embryos—affecting 10–15% of women.[1,3,4]

Despite high-quality embryo transfers, many RIF and RPL cases lack a clearly identifiable cause. While much attention is placed on embryo quality, the uterine environment deserves greater focus. Recent evidence highlights the importance of the junctional zone (JZ) or inner myometrium in reproductive success. The JZ regulates uterine peristalsis, implantation, and placentation. Disruptions, such as those seen in adenomyosis, have been linked to implantation failure and recurrent miscarriage.[5,6] Hysteroscopy offers the advantage of exploring the JZ beneath the endometrial surface, allowing for the identification of subtle abnormalities such as adenomyotic cysts or fibrotic lesions that may otherwise go undetected. This targeted assessment is particularly valuable in patients with unexplained implantation failure, where standard imaging may miss functionally relevant pathology.

Magnetic resonance imaging (MRI) has emerged as a superior modality for assessing the JZ, offering structural insights not captured by ultrasound (US) or even histology[7-9] Harmsen et al.[8], demonstrated that MRI, US, and histology evaluate distinct features, and routine histology cannot adequately reflect JZ function. Although the prognostic value of JZ imaging remains under investigation, its relevance in reproductive dysfunction is increasingly recognised.[10,11]

Therapeutic strategies to improve endo-myometrial receptivity are advancing. Hyaluronic acid (HA), a naturally occurring extracellular matrix component with regenerative, anti-adhesive, and anti-inflammatory properties, has demonstrated efficacy in promoting endometrial healing and reducing intrauterine adhesions.[12,13] Corticosteroids such as budesonide modulate the uterine immune environment by suppressing natural killer cell cytotoxicity and cytokine secretion, while promoting human chorionic gonadotropin production and trophoblast proliferation—key processes for successful implantation and early pregnancy maintenance.[14-19]

Study Objective

This pilot study evaluates a novel approach combining hysteroscopic (HSC) sub-endometrial exploration with intrauterine application of budesonide-enriched, crosslinked HA gel in women with RIF and total loss of JZ differentiation on MRI.

Methods

This single-centre observational pilot study was conducted at a specialised ambulatory care unit, the "Life Expert Centre". All participants provided written informed consent. The aim was to evaluate pregnancy and live birth outcomes following HSC sub-endometrial exploration combined with intrauterine application of a budesonide-loaded, crosslinked HA gel (BioRegen Biomedical, Changzhou Co., Ltd, China) in women diagnosed with RIF and total loss of JZ differentiation on MRI.

This study was conducted in accordance with the ethical standards outlined in the Helsinki Declaration and its later amendments and was approved by the Hospital Ethics Committee of CHU Brugmann (le Comité d'Ethique Hospitalier du CHU Brugmann), approval number CE 2024/111, date: 13.08.2024.

Inclusion and Exclusion Criteria

From September 2022, women seeking pregnancy were consecutively enrolled if they met the following criteria:

1. Diagnosis of RIF and/or RPL
2. Presence of excellent embryonic factor, with high-quality blastocyst formation
3. No major pathology seen on "one-stop" uterine assessment, including 2D/3D transvaginal US, ambulatory hysteroscopy, and contrast sonography
4. MRI confirmed total loss of JZ differentiation

Prior to inclusion, all patients had received a minimum of six months of hormonal therapy [gonadotropin-releasing hormone (GnRH) analogues or dienogest], followed by intramuscular platelet-rich plasma (PRP) therapy, and subsequently experienced at least two additional failed embryo transfers using high-quality blastocysts. Patients with chronic endometritis or abnormal HSC findings at the time of assessment were excluded. A minimum of two cryopreserved, excellent-quality embryos was required for inclusion.

Study Groups

Patients were divided into two groups based on oocyte source:

Group 1: 10 women with RIF despite transfer of high-quality embryos in an egg donation program.

Group 2: 10 women under the age of 37 with RIF, using embryos derived from their own healthy oocytes.

A summary of our study protocol is provided in Figure 1.

Imaging Criteria

All patients had no obvious abnormal HSC and/or ultrasonographic uterine findings prior to the occurrence of RIF. The US and HSC criteria used are shown in Figure 2. These include a triangular cavity with no morphological or intrauterine pathological changes. The one-stop procedure includes a transvaginal 2D and 3D US, followed by an ambulatory hysteroscopy and concluded by a contrast sonography.

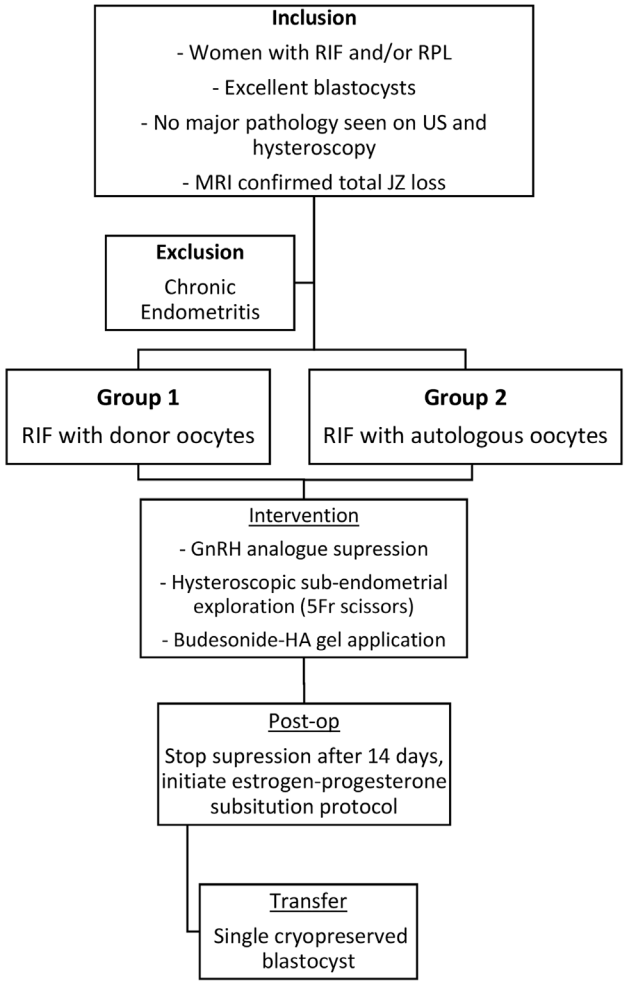

Figure 1. Study protocol.

RIF: Recurrent implantation failure, RPL: Repeated pregnancy loss, US: Ultrasound, MRI: Magnetic resonance imaging, JZ: Junctional zone, GnRH: Gonadotropin-releasing hormone, HA: Hyaluronic acid.

Magnetic Resonance Imaging of Junctional Zone

As shown on MRI, all patients showed a complete loss of JZ differentiation. In some instances, hormonal treatment or operative HSC did partially improve the JZ impairment, yet in all cases, the JZ remained disturbed. Figure 3 exemplifies the MRI of JZ in our study population.

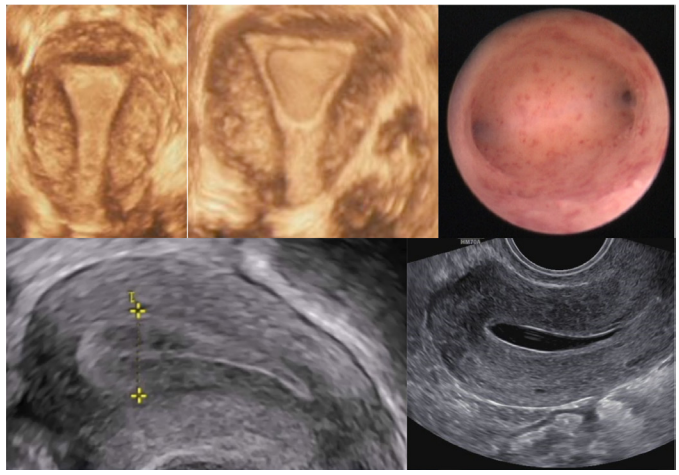

Figure 2. Normal ultrasound and hysteroscopy criteria.

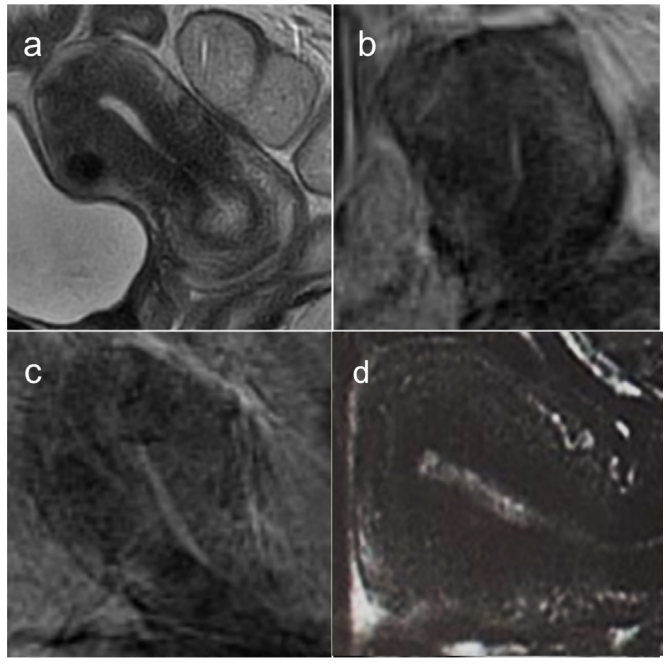

Figure 3. Magnetic resonance imaging reveals complete loss of junctional zone differentiation: junctional zone of a patient from study group 1 (a) and 2 (b); and junctional zone at intake of a patient (c) and after hormonal treatment (d).

Procedure

Under GnRH analogue suppression, HSC endo-myometrial exploration was performed in an ambulatory care setting under conscious sedation. All procedures were performed by a single, highly experienced surgeon (RC). The intervention was conducted using the TrophyScope® XL (Karl Storz, Tuttlingen, Germany), which has an outer diameter of 5.8 mm. Using 5 Fr scissors, micro-incisions were made in the lateral uterine walls and fundus to access the sub-endometrial myometrium. Subtle cystic or solid lesions, if identified, were excised. At the end of the procedure, 8 mL of gel—comprising 1.5 mg/3 mL budesonide pre-mixed with 5 mL of HyaRegen® crosslinked HA gel (final budesonide concentration: 0.19 mg/mL)—was instilled through the outer sheath of the Trophy® hysteroscope (Figure 4).

Fourteen days later, hormonal suppression was discontinued, and patients initiated estrogen–progesterone replacement to prepare for cryopreserved embryo transfer (FET).

Data Collection

Clinical records were reviewed for patient age, parity, history of ART failures and miscarriages, suspected causes of implantation failure, prior gynaecological surgeries, HSC and US findings, JZ-MRI evaluation (Figure 3), date of procedure, embryo transfer date, and pregnancy outcomes. Additional outcomes recorded included delivery mode, birth weight, perinatal complications, and neonatal health. All patients were contacted approximately six months postpartum to gather follow-up information on neonatal health and early development.

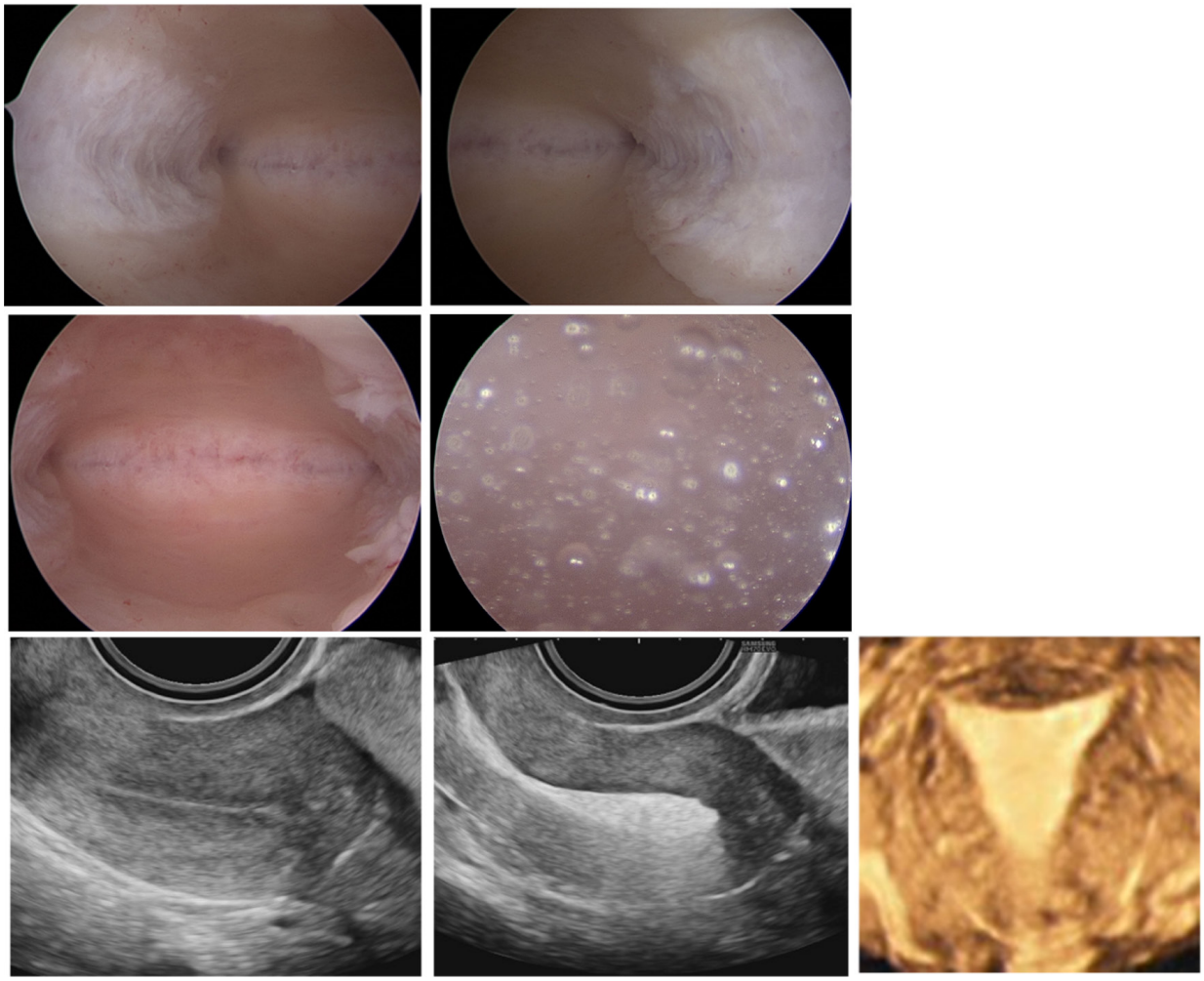

Figure 4. Technique of sub-endometrial exploration and application of budesonide-loaded crosslinked hyaluronic acid gel applied intrauterine.

Results

Demographics and Preoperative Characteristics

Twenty women were included. Study group 1 included 10 women who received ART involving donated oocytes, while study group 2 included 10 women who received embryo or blastocyst transfer involving their own healthy embryos. Patients' demographic data can be found in Table 1.

The mean age was 44.5 and 34.4 years in study groups 1 and 2, respectively. Two patients in group 1 and three patients in group 2 had secondary infertility. Previous gynaecological treatments included (adeno)myomectomy (all laparoscopic apart from 1 per laparotomy), HSC correction of dysmorphic uteri, HSC endo-myometrial exploration, and laparoscopic removal of adhesions.

Pregnancy Outcomes and Live Birth Rate

In both study groups, 9 of 10 women became pregnant after the procedure. In study group 1, which received donated oocytes, all 9 women delivered healthy babies. In study group 2, where the embryological fertility factor could be ensured with one's own oocytes, 8 of 9 pregnancies resulted in live births of healthy babies. One patient needed her pregnancy interrupted at week 20 due to foetal malformation.

Table 1 shows gestational age at delivery, mode of delivery, birth weight, and potential complications at delivery of the 9 and 8 delivered babies in study groups 1 and 2, respectively. All 17 babies were healthy at birth and showed healthy evolution in the first follow-up. The range of gestational age at birth was between 26 weeks and 42 weeks in study group 1 and between 34 weeks and 40 weeks in study group 2. In study group 1, 2 babies were delivered vaginally, and 7 were delivered by C-section. Five babies of women in study group 2 were delivered by C-section, and 3 by vaginal delivery. Birth weight ranged between 1050 g and 4500 g in study group 1 and between 2270 g and 4030 g in study group 2. Six out of 9 deliveries of group 1 were uneventful. However, 3 out of 9 patients (33%) had postpartum complications: one patient required a hysterectomy due to placenta accreta, one patient had placenta praevia, and one woman had postpartum haemorrhage (needing 3 units of blood). Seven out of 8 births in study group 2 were without complications, while one patient had preterm premature rupture of membranes and tested positive for Group B strep bacteria, yet without further complications. Follow-up on neonatal health at approximately six months postpartum revealed no reported complications or concerns.

Table 1. Patients' demographic and outcome data.

	Group 1 Donated oocytes n=10	**Group 2 Healthy own oocytes n=10**
Mean age (years)	**44.5 ± 3.7**	34.4 ± 2.5
Parity	P0: 8 P1: 2	P0: 7 P1: 2 P1: 1
Live birth	9	8
Gestational age (weeks)	36.78 ± 4.69	37.5 ± 1.88
Delivery method	C-section: 7 Vaginal: 2	C-section: 5 Vaginal: 3
Birth weight (g)	2807 ± 989	3298 ± 606.76
Complications	Hysterectomy: 1 Placenta praevia: 1 PPH: 1	PPROM, GBS+: 1

± values indicate standard deviation.
PPROM: Preterm premature rupture of membranes, GBS+: Group B strep bacteria, PPH: Post partum haemorrhage.

Discussion

Main Findings

This observational pilot study demonstrates promising outcomes in a cohort of women with RIF and/or RPL, all of whom presented with MRI-confirmed total loss of JZ differentiation and had experienced multiple failed ART cycles despite the transfer of high-quality blastocysts. Following HSC sub-endometrial exploration and intrauterine application of a budesonide-loaded crosslinked HA gel, clinical pregnancy and live birth rates reached 90% in both donor and autologous oocyte groups. This approach appears to improve implantation success and reduce miscarriage rates, without any reported treatment-related complications, suggesting a potential therapeutic benefit of targeting the sub-endometrial environment in this challenging population.

These outcomes align with existing evidence supporting the use of HA in reproductive medicine, particularly its role in enhancing endo-myometrial receptivity and reducing intrauterine adhesions.[19-22] HA provides a scaffold that supports cell proliferation and migration, essential for endo-myometrial regeneration.[23,24] By maintaining a physical barrier in the uterine cavity, HA prevents adhesions and preserves the normal architecture necessary for embryo implantation.[24] However, conventional HA has limitations due to its fluid nature and rapid degradation, which may reduce its efficacy.[25] This study utilised crosslinked HA gel, which has enhanced viscosity and prolonged *in vivo* persistence, allowing for a more sustained effect in reducing postoperative adhesions and improving pregnancy rates following ART.[25-27] The addition of budesonide—a corticosteroid with potent local anti-inflammatory and immunosuppressive effects—likely contributes to the improved uterine microenvironment, promoting trophoblast invasion and successful implantation.[28,29]

Abnormalities in the JZ, such as thickening or loss of differentiation, have been closely associated with impaired implantation, recurrent miscarriage, and other reproductive disorders.[30,31] Research by Brosens et al.[31] emphasises the importance of the JZ in the implantation process and suggests that evaluating the JZ as a distinct entity is crucial for understanding and addressing reproductive failures. Imaging techniques such as high-resolution US and MRI allow for the detailed assessment of the JZ, enabling the identification of structural and functional abnormalities that could contribute to reproductive challenges.[31]

We hypothesise that loss of JZ differentiation on MRI reflects an inflammatory uterine state contributing to unexplained RIF. Targeted HSC delivery of regenerative and anti-inflammatory agents to the endo-myometrial interface may therefore enhance uterine receptivity. This could be of equal importance in other inflammatory diseases such as chronic endometritis and endometriosis.[32]

Remarkably, in study group one, 1/3 patients had post-partum complications, including bleeding and dysfunctional placentation. These events are more likely related to known risk factors such as advanced maternal age and possibly an ageing uterus.

Strengths and Limitations

A notable strength of this study is the homogeneity of the patient population: all participants had experienced multiple failed embryo transfers with confirmed high-quality blastocysts and no major uterine pathology on US or hysteroscopy, yet demonstrated total JZ disruption on MRI. This allowed for a focused investigation of a relatively underexplored anatomical target—namely, the sub-endometrial myometrium—as a potential contributor to implantation failure. Another strength is the integration of a biologically plausible, multimodal strategy: HSC exploration of the sub-endometrial interface, combined with regenerative (HA) and anti-inflammatory (budesonide) therapy. This is supported by recent insights into endometrial and myometrial receptivity and the role of local immune modulation in implantation success.

On the other hand, limitations are present. The sample size is small, and the observational nature of the study precludes causal inference. Without a control group, the independent contributions of sub-endometrial exploration, HA, or budesonide cannot be determined. Additionally, while MRI provides valuable insight into JZ integrity, its interpretation is subjective and not yet standardised across clinical practice. The impact of prior treatments—including hormonal suppression and PRP—on outcomes cannot be excluded. Lastly, while the live birth rate is promising, the generalizability of results to broader ART populations, including those with normal JZ imaging or different endometrial pathologies, remains unknown.

Clinical and Policy Implications

These findings offer preliminary support for a new diagnostic and therapeutic pathway in patients with unexplained RIF or RPL. The presence of JZ abnormalities, as assessed by MRI, may represent an overlooked contributor to implantation failure, especially when standard diagnostic workup appears normal. This calls for more routine consideration of the JZ as a functional and structural entity in reproductive assessments. Therapeutically, the combination of HSC sub-endometrial exploration with targeted intrauterine drug delivery may address local inflammation and architectural disruption that impede implantation. If validated in larger cohorts, this approach could be integrated into ART protocols for selected patients who demonstrate persistent reproductive failure despite optimal embryo quality and hormonal preparation. From a clinical policy perspective, the data underscore the importance of individualised diagnostics in ART. The findings also highlight the need to expand imaging protocols beyond basic ultrasonography to include MRI in certain high-risk or treatment-resistant cases.

Unanswered Questions and Future Research

Several key questions remain. The relative contribution of each intervention component—sub-endometrial exploration, HA, and budesonide—requires clarification. Controlled, randomised studies are needed to determine whether this combination offers superior outcomes compared to standard care or monotherapy approaches.

Understanding the underlying biological mechanisms is essential for optimising this treatment strategy and identifying patient subgroups most likely to benefit. Future studies should investigate how budesonide modulates immune cell populations and cytokine profiles within the endo-myometrial environment, and how HA contributes to tissue remodelling and repair at the level of the JZ. Elucidating these pathways may help refine patient selection and uncover new therapeutic targets for improving endometrial receptivity and implantation success. Additionally, the prognostic value of MRI-detected JZ abnormalities remains to be fully established. Larger studies should examine correlations between different degrees of JZ disruption and reproductive outcomes, as well as potential reversibility following treatment.

Conclusion

To conclude, this pilot study suggests that HSC sub-endometrial exploration with application of budesonide-loaded crosslinked HA gel may be associated with improved pregnancy and live birth outcomes in women with RIF and JZ abnormalities. While the findings are encouraging, the study's observational nature and small sample size limit definitive conclusions. Controlled trials in larger populations are needed to validate these results and to investigate the therapeutic potential and mechanisms of this combined approach in reproductive medicine.

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Data sharing: All data is available to be shared upon request to the corresponding author.

Transparency: The authors affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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ORIGINAL ARTICLE

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Safety and efficacy of relugolix combination therapy in symptomatic uterine fibroids

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ABSTRACT

Background: Relugolix-combination therapy (CT) (oestradiol 1 mg and norethindrone acetate 0.5 mg) is a new gonadotropin-releasing hormone antagonist licensed to treat heavy menstrual bleeding (HMB) associated with uterine fibroids; but little real-world data exists to guide practice.

Objectives: To evaluate the efficacy and safety of relugolix-CT in women with fibroid-associated HMB in two large Italian hospitals.

Methods: A retrospective multicentre study was conducted on 102 women with symptomatic fibroids and HMB, defined as a Pictorial Blood Assessment Chart (PBAC) score >100, who were treated with relugolix-CT for up to 24 months. Women were divided into three groups: group 1 (n=81) receiving only relugolix-CT treatment; group 2 (n=11) receiving at least two months of relugolix-CT prior to hysteroscopic, laparoscopic or open myomectomy; group 3 (n=10) receiving at least two months of pre- and post-myomectomy relugolix-CT.

Main Outcomes Measures: The primary outcome was resolution of HMB, defined as a PBAC score <100. Secondary outcomes included the side effects of treatment.

Results: The population mean age was 43.8 years (±6.06), and the mean baseline PBAC score was 329.9 (± 217 standard deviation). In women treated with relugolix-CT alone, 71 (94.7%) responded after two months. By nine months, only 36 (44.4%) women continued with relugolix-CT. Resolution of HMB was sustained in most women who continued treatment at each follow-up time point. By two months prior to myomectomy, HMB resolved in all women receiving relugolix-CT pre-surgery and nine (90%) women continuing relugolix-CT after myomectomy. No major side effects were reported.

Conclusions: This real-world study supports previous controlled trial data showing relugolix-CT to be a safe, efficacious medical treatment for HMB with fibroids.

What is New? Real-life clinical data support the use of relugolix-CT to treat symptomatic fibroids in isolation or combined with myomectomy.

Keywords: Gonadotropin-releasing hormone antagonist, heavy menstrual bleeding, relugolix, uterine fibroid, myomectomy

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Introduction

Uterine leiomyomas, also referred to as uterine "myomas" or "fibroids", are one of the most common benign, hormone-sensitive, uterine tumours with an estimated prevalence of 70-80% in premenopausal women.[1] When not asymptomatic, they account for symptoms that might severely affect patients' quality of life.[2] Heavy menstrual bleeding (HMB) is the most common symptom associated with fibroids, often leading to anaemia and other symptoms such as dysmenorrhoea, infertility and bulk, pressure effects.[2]

Surgery has long been the treatment of choice in women with fibroid-associated symptoms because medical options for fibroid-related symptoms can often be ineffective.[3] The recent development of oral gonadotropin-releasing hormone (GnRH) antagonists may finally provide an effective, fertility-sparing medical treatment for symptomatic uterine fibroids.[4] Relugolix is a GnRH antagonist, blocking the signalling of endogenous GnRH and thus leading to a fast and reversible suppression of ovarian function and oestradiol and progesterone production.[5] In order to minimise the side effects, mainly bone mineral density loss and vasomotor symptoms, an add-back therapy with oestradiol 1 mg and norethindrone acetate 0.5 mg has been formulated for a once-daily oral administration.[6]

The effectiveness and safety of once-daily relugolix-combination therapy (CT) has already been assessed in high-quality clinical trials.[7-9] However, these trials tend to select "less diseased" populations and, as a consequence, do not fully represent the "real life" context, as stated by Middelkoop et al.[10] in a recent systematic review. Therefore, the purpose of our study was to provide data on the efficacy and safety of relugolix-CT in women with fibroid-associated symptoms in a real-world clinical setting.

Methods

From June 2022 to September 2024, two Italian Hospitals (University of Naples and Public Hospital of Palermo) retrospectively collected data from electronic medical records of premenopausal women aged 18 years or older, diagnosed by ultrasound with at least one uterine fibroid; eligibility was subsequently confirmed through manual chart review according to the study criteria. Demographic and clinical information were entered into a dedicated de-identified database (in compliance with privacy requirements), including details regarding surgical procedures and subsequent follow-up.

Inclusion criteria comprised the presence of at least one uterine fibroid associated with HMB evaluated using the Pictorial Blood Assessment Chart scoring system (PBAC score >100), and a negative pregnancy test at screening. No patient had contraindications to hormonal therapy. All eligible patients received daily relugolix-CT (40 mg of relugolix, 1 mg of oestradiol, and 0.5 mg of norethindrone acetate).

We distinguished three subgroups as follows:

Group 1: Women who underwent only medical therapy.

Group 2: Women who underwent medical therapy before planned myomectomy.

Group 3: Women who received medical therapy before and after planned myomectomy.

All women underwent pelvic ultrasound to characterise fibroids according to the FIGO classification system[11], the Morphological Uterus Sonographic Assessment[12], and Lasmar classification.[13] Menstrual blood loss was assessed using the PBAC score before and during the therapy: a score higher than 100, corresponding to >80 mL of blood loss, was considered diagnostic for HMB, as described in the literature.[14,15] The primary outcome, resolution of HMB, was defined as a PBAC score <100 and further subcategorised: (i) full responder - amenorrhea and spotting only; (ii) bleeding (partial responder). A PBAC ≥100 was categorised as a non-responder. The main secondary outcome was side effects of relugolix-CT.

In Group 1 (relugolix-CT only), patients were followed at standardised intervals (at 1, 2, 3, 6, 9, and 12 months). Scheduled follow-up was conducted either in person or via telemedicine, uniformly across both centres. Additional contacts outside this schedule were arranged only when clinically necessary (e.g., for symptom management or reporting adverse events). In Group 2 (relugolix-CT pre-myomectomy), all patients underwent at least two months of therapy – during which data were collected – prior to undergoing hysteroscopic, laparoscopic, or laparotomic myomectomy, as had already been planned before initiation of therapy. In Group 3 (relugolix-CT pre and post myomectomy), all patients underwent at least two months of therapy – during which data were collected – prior to undergoing hysteroscopic or laparotomic

myomectomy. Due to the presence of a fibromatous uterus and/or additional myomas, and considering their perimenopausal status, medical therapy was continued postoperatively to prevent recurrence of bleeding. Patients were subsequently followed at 3 and 6 months after surgery.

An additional secondary outcome was to evaluate the feasibility of surgery and fibroid characteristics. These were evaluated during the surgical procedure on a numerical scales: fibroid vascularisation was rated from 1 to 5 (1: high, 2: moderate, 3: mild, 4: poor, 5: very poor); the ability to identify the cleavage plane was scored as 0 (easy) or 1 (difficult); fibroid consistency was graded on a scale from 0 (soft) to 10 (hard); and the difficulty of performing the surgical procedure was scored from 0 (very poor) to 10 (excellent), as previously reported.[16]

The study was conducted in accordance with the World Medical Association Declaration of Helsinki. All procedures complied with relevant laws and institutional guidelines and were approved by the Comitato Etico Campania 3 on August 7th, 2024 (report number: 12/24, registration number: 180/2024). Privacy rights of all participants were respected. Selected patients were contacted and signed informed consent forms (study participation and data privacy) prior to enrolment.

Statistical Analysis

In all three groups, given that all patients received at least two full months of relugolix-CT treatment, clinical and symptom-related variables were assessed and compared at baseline and after one and two months of therapy. For Group 1 (medical therapy only), additional assessments were conducted at 3-month intervals up to 24 months, depending on treatment continuation. Patients in Group 3 were re-evaluated at three and six months after surgery.

In the descriptive analysis, the continuous variables were summarised as mean and standard deviation (SD), while categorical variables were reported as absolute numbers and percentages. Statistical analysis was performed using the statistical package JMP Trial (v 17.2.0; JMP Statistical Discovery LLC). Continuous data are expressed as mean±SD.

Results

The final cohort consisted of 102 patients, retrospectively allocated as shown in Figure 1. Enrolled women presented with a mean age of 43.8 years (±6.06), ranging from 25 to 54 years of age, with 96 (94.1%) of Caucasic origin. Thirty-three patients (32.4%) had undergone a previous myomectomy, and 34 (33.3%) of patients had been treated with previous medical therapies. The mean PBAC

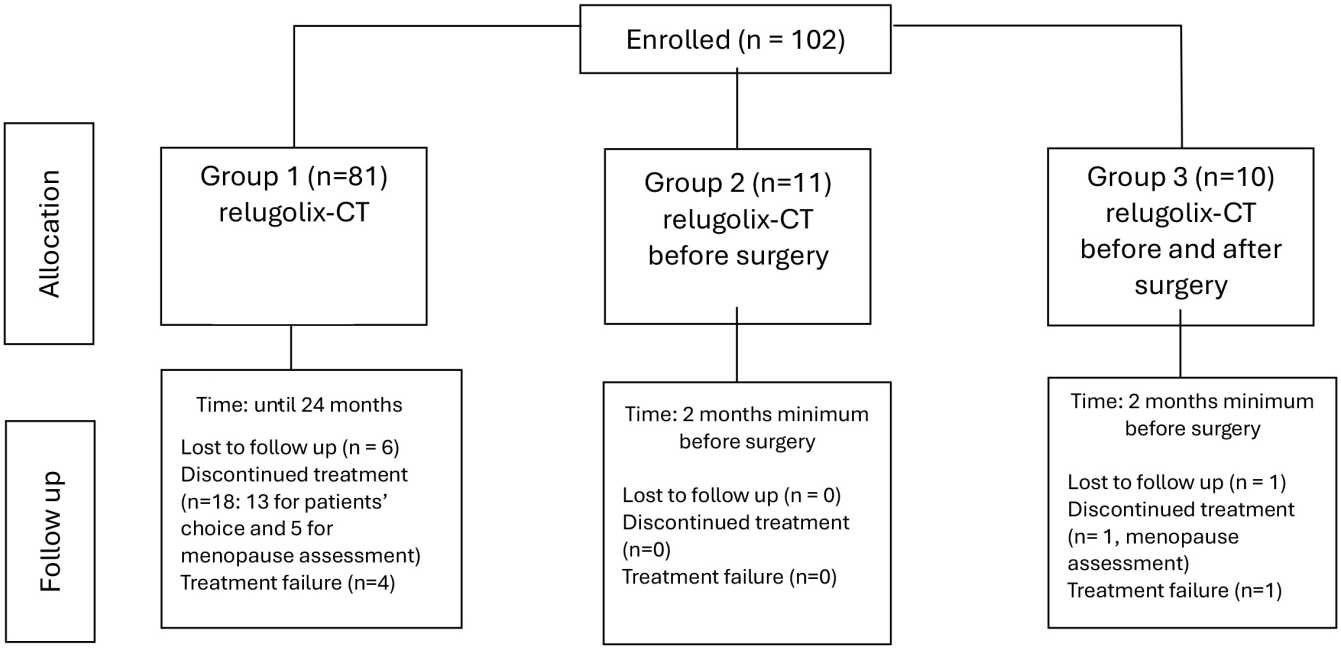

Figure 1. Study flow diagram.
CT: Combination therapy.

score before the introduction of relugolix CT treatment was 329.9 (SD±217; range 120 to 1400). Table 1 details the characteristics of included patients.

Women receiving medical therapy alone (Group 1) had their HMB symptoms resolved in 76 (93.8%) of women, with a full symptomatic response - reporting amenorrhea or only spotting - in 63 (77.8%) after one month of treatment. Due to dropouts and losses to follow-up, as well as the fact that patients started therapy at different times, the number of women who reached each specific follow-up time point varied accordingly (Table 1). Resolution rates remained stable from month three to two years for patients who continued treatment (Table 2).

In this relugolix-CT alone group, four women underwent hysterectomy: one was a non-responder (PBAC>100), and one discontinued treatment due to phlebitis-related complications. The remaining two patients achieved a partial therapeutic response (PBAC<100) after one and two months of therapy, respectively, but opted to discontinue daily medical treatment in favour of surgery.

All 11 patients in Group 2 received at least two full months of medical treatment with relugolix-CT before myomectomy. Regarding the HMB evaluation, at the end of the two-month treatment period, all women were full responders (Table 3). Myomectomy was performed by hysteroscopy in five women, by laparoscopy in two and by laparotomy in four women.

In Group 3, comprising 10 women who received relugolix-CT before and after surgery as part of a planned combined medical-surgical treatment approach, nine (90%) women had resolution of HMB, with six (60%) categorised as full responders (Table 2). Among women in this group, myomectomy was performed by hysteroscopy in 5 cases and by laparotomy in the remaining 5.

Regarding the surgical outcomes, in all patients scheduled for surgery (Group 2 and 3), the mean consistency of the fibroids after relugolix-CT pre-treatment was reported as 6.8/10 (SD±1.3), and the mean surgical difficulty was 4.7/10 (SD±1.4). The vascularisation of the fibroids was reported as mild or poor in 9 (42.9%) of women, and the cleavage plane was considered "easy" to identify in the majority of cases (20, 95.2%). No post-operative complications were reported.

In Group 3, which continued medical therapy after myomectomy, the evaluation of HMB at three months showed that three patients were partial responders (30%), while at six months, all patients were responders (100%).

In all women, the most frequent side effects of treatment were mild vasomotor symptoms, mild headache, mood swings, vaginal dryness, weight gain, or a sensation of fluid retention, as reported in previous studies (Table 4).

Table 1. Patients' characteristics at baseline.

PATIENTS' CHARACTERISTICS	
Age years	
mean±SD	43.80±6.06
min-max	25-54
Caucasian ethnicity	96/102 (94.1%)
BMI > 30	6/102 (5.9%)
Nulliparous	49/102 (48.0%)
Infertility	7/102 (6.9%)
Current smokers	18/102 (17.6%)
Previous failed therapy:	
-GnRH agonist	8/102 (7.8%)
-Ulipristal acetate	6/102 (5.9%)
-Combined oral contraceptive	20/102 (19.6%)
-Total	34/102 (33.3%)
Previous myomectomies	33/102 (32.4%)
Iron supplements	67/102 (65.7%)
PBAC score at baseline	
mean±SD	329.9±217
min-max	120-1400

SD: Standard deviation, BMI: Body mass index, GnRH: Gonadotropin-releasing hormone, PBAC: Pictorial blood loss assessment chart.

Discussion

Main Findings

Our data, investigating the efficacy and safety of relugolix-CT in real life, support this new drug as an effective long-term therapeutic resource in women with fibroid-associated symptoms, with a low risk of adverse events and complications. The use of relugolix CT may also help the feasibility of myomectomy, and HMB symptom recurrence is continued post-surgery. Side effects reported by our patients were mild and accounted mainly for vasomotor symptoms and headache, in a proportion which remained stable over the whole follow-up period. Similar records were also obtained by other studies[17], with no serious adverse events registered in our population.

Table 2. Heavy Menstrual Bleeding distribution in patients of Group 1.

Effect of relugolix-CT on heavy menstrual bleeding in women with fibroids receiving exclusive medical therapy (Group 1)									
	1 Month	**2 Months**	**3 Months**	**6 Months**	**9 Months**	**12 Months**	**15 Months**	**18 Months**	**21 Months**	**24 Months**
Relugolix-CT n (%)	81/81 (100)	75/81 (92.6)	64/81 (79.0)	49/81 (60.5)	36/81 (44.4)	26/81 (32.1)	17/81 (21.0)	10/81 (12.3)	6/81 (7.4)	4/81 (4.9)
Full responders (amenorrhea or spotting only) n (%)	63/81 (77.8)	65/75 (86.7)	54/64 (84.4)	40/49 (81.6)	33/36 (91.7)	23/26 (88.5)	15/17 (88.2)	10/10 (100)	6/6 (100)	4/4 (100)
Partial responders (PBAC<100) n (%) PBAC score mean±SD	13/81 (16.0) 81.0 (±8.8)	6/75 (8.0) 79.8 (±7.7)	3/64 (4.7) 88.3 (±3.4)	5/49 (10.2) 72.0 (±7)	3/36 (8.3) 89.0 (±5.2)	3/26 (11.5) 81.8 (±4)	2/17 (11.8) 78.0 (±1.5)	0	0	0
Non-responders (PBAC≥100) n (%) PBAC score mean±SD	5/81 (6.2) 190 (±52.2)	4/75 (5.3) 188.3 (±59.1)	7/64 (10.9) 193.4 (±68.3)	4/49 (8.2) 152.1 (±23.4)	0	0	0	0	0	0

PBAC: Pictorial blood loss assessment chart, SD: Standard deviation, CT: Combination therapy.

Strengths and Limitations

The focus on using relugolix-CT in everyday clinical and surgical needs represents the main strength of our study. We provided follow-up data out to two years and had a low rate of loss to follow-up. Limitations include the uncontrolled, observational and retrospective nature of our study, and the relatively small sample of patients.

Strengths and Limitations Compared to Other Studies

The demographic and clinical characteristics of our study population closely resemble those reported in previous European studies, as the one by Venturella et al.[7]: our patients were mainly non-smokers, non-obese white women in their 40s (43.8 years ± 6.06).

Regarding the history of medical therapy, we notice that most patients had experienced different treatments, but clearly, these could not fulfil women's needs and symptoms.

Compared with the recent publication by Al-Hendy et al.[18] on the treatment of symptomatic UFs with once-daily relugolix-CT, our study shows an even greater and more rapid reduction in HMB in a real-life setting. While the RCT reported a 60% reduction in HMB at one month, our medical-only group showed a reduction of 77.8% at the same time point. Moreover, the long-term effect on bleeding control is consistent with the registration trials.

Within the sample observed, 21 women were already planned for surgery independently of the pharmacological therapy: as recommended recently the choice of the approach should be shared in a common patient and healthcare point of view, considering the whole impact of UF and treatments on women's lives (clinical issues and therapeutic opportunities; women working life, sexual health and fertility).[19-23]

Table 3. Heavy Menstrual Bleeding distribution in patients of Groups 2 and 3.

Effect of preoperative relugolix-CT on heavy menstrual bleeding in women with fibroids undergoing myomectomy (Groups 2 and 3)				
	Group 2 relugolix-CT before surgery		**Group 3 relugolix-CT before and after surgery**	
	1 Month	**2 Months**	**1 Month**	**2 Months**
N. Pts in therapy	11	11	10	10
Full responders (amenorrhea or spotting only) n (%)	11/11 (100)	11/11 (100)	6/10 (60)	6/10 (60)
Partial responders (PBAC<100) n (%) PBAC score mean±SD	0	0	0	3/10 (30) 87.7 (±11)
Non-responders (PBAC ≥100) n (%) PBAC score mean±SD	0	0	4/10 (40) 152.5 (±60)	1/10 (10) 304.0

PBAC: Pictorial blood loss assessment chart, SD: Standard deviation, CT: Combination therapy.

The experience of this real-world retrospective study, where all women treated surgically underwent at least two months of preoperative therapy with relugolix-CT, shows that this medical treatment allows integration and maximisation of the synergy between medical and surgical approaches, supporting the concept that relugolix-CT can serve as an effective pre-operative therapy. This was evident in the clinical benefits observed regarding the evaluation of HMB, where only one non-responder was recorded, thus representing the only therapeutic failure. Moreover, the preoperative use of relugolix-CT improved the vascularisation and consistency of the fibroid, as well as the definition of the cleavage plane and the ease of surgical execution, as recorded by the surgeons, demonstrating that this pharmacological approach does not negatively affect the subsequent surgical procedure.

Few data are available on the surgical outcomes of GnRH antagonists' treatment[8], though they seemed promising to us, as compared to the previously available alternatives. A very recent observational study showed that preoperative GnRH-antagonist therapy may enhance haemoglobin levels, decrease uterine and fibroid size, and alleviate symptoms, potentially enabling safe surgical procedures[22].

Clinical and Policy Implications

Our study provides real-world data. It is well recognised that data from pivotal controlled trials to gain drug approvals may be derived from a "less diseased" population than will receive the treatments in the day-to-day clinical context.[10] Real-world evidence experiences are growing in recent years, providing helpful information that may complement randomised clinical trial findings and may help fill some gaps about the use in the real-world medical settings (larger samples, longer observational periods, more heterogeneous populations).[19] Our real-world evidence provides healthcare decision makers with clinical information about the impact of the drug on everyday life patients, adding beneficial value to public health.[20]

Unanswered Questions and Future Studies

In our record of cases, it was decided in a small percentage of cases to continue medical treatment after surgery to control the symptoms in case of remaining fibroids.

The benefits of continuing relugolix-CT post myomectomy to prevent recurrence of HMB and/or fibroids and future fertility (including outcomes of assisted reproductive techniques) need to be evaluated with further studies, ideally randomised controlled trials.)

Table 4. Side effects of relugolix-CT reported by patients. Values are expressed in numbers (%).

Side effects of relugolix-CT reported by patients										
	Follow-up visits									
	1 month	2 months	3 months	6 months	9 months	12 months	15 months	18 months	21 months	24 months
N. Pts in therapy	102	96	82	62	42	32	21	15	8	4
Side effects: n (%)										
- mild vasomotor symptoms	2 (1.9)	1 (1.0)	34 (41.5)	24 (38.7)	20 (47.6)	15 (46.9)	9 (42.9)	8 (53.3)	3 (37.5)	1 (25.0)
- mild headache	0	0	12 (14.6)	14 (22.6)	10 (23.8)	9 (28.1)	5 (23.4)	5 (33.3)	1 (12.5)	1 (25.0)
- mood swings	1 (0.9)	1 (1.0)	15 (18.3)	6 (9.7)	5 (11.9)	6 (18.8)	4 (19.0)	3 (20.0)	1 (12.5)	0
- vaginal dryness	0	0	11 (13.4)	7 (11.3)	3 (7.1)	2 (6.3)	1 (4.8)	0	0	0
- weight gain/fluid retention feeling	0	0	0	3 (4.8)	6 (14.3)	3 (9.4)	1 (4.8)	1 (6.7)	0	0
	1 (0.9)	0	5 (6.1)	3 (4.8)	3 (7.1)	1 (3.1)	1 (4.8)	1 (6.7)	0	0

CT: Combination therapy.

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Transparency: The Authors affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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ORIGINAL ARTICLE

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Enhancing clinical practice: the Endoscore app for automated surgical data capture and endometriosis scoring

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ABSTRACT

Background: There is a growing unmet need to digitalise the management of clinical data in medicine. Web-based scoring applications for endometriosis align with this trend.

Objectives: This study aimed to evaluate a web-based application that automatically calculates endometriosis staging scores [revised American Society for Reproductive Medicine classification (r-ASRM), the revised Enzian classification (#Enzian), Endometriosis Fertility Index (EFI)] and compare it to manual scoring in a proof-of-concept study.

Methods: 20 endometriosis cases operated on in 2022 were retrospectively selected. Six experienced gynaecologists were randomly allocated to either the conventional paper-based method or the digital application for staging of disease.

Main Outcome Measures: Completion time, score consistency among examiners and methods, and user satisfaction were recorded using a Likert scale and a subjective mental effort questionnaire (SMEQ).

Results: In comparison to the paper-based method, the web-based tool reduced scoring time by 25.1 seconds (128.0 vs. 153.1, $P<0.05$), was perceived as easier to use (higher Likert scale scores), and was associated with low-to-moderate mental effort on the SMEQ. The agreement between electronic and paper forms was rated as very good to excellent for r-ASRM [intraclass correlation coefficient (ICC): 0.93] and #Enzian (ICC: 0.84), while it was moderate for EFI (ICC: 0.67). Interrater agreement utilising the electronic form demonstrated high levels, yielding very good to excellent results for r-ASRM (ICC: 0.93) and EFI (ICC: 0.82) while showing moderate agreement for #Enzian (ICC: 0.63).

Conclusions: The application facilitates sequential data entry for users and automatically calculates r-ASRM, #Enzian, and EFI scores. It decreases scoring duration, strongly aligns with the paper-based method, and enhances user satisfaction.

What is New? This tool can potentially improve clinical efficiency, accuracy, and consistency in the staging of endometriosis.

Keywords: Endometriosis, classification, documentation, application, EFI, rASRM, #Enzian

Introduction

Endometriosis is characterised by the growth, adhesion, and progression of endometrial glands and stroma outside the uterine cavity, and it has significant implications for women of childbearing age.[1] While it affects up to 10% of the general female population, its prevalence can be as high as 50% among infertile women.[2] This chronic inflammatory disease relies on oestrogen for the establishment and proliferation of endometriotic tissue. Although endometriosis often appears benign on histopathologic examination,

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it behaves like a malignant tumour, as lesions exhibit growth, infiltration, and adhesion to adjacent tissues, disrupting physiological processes.[3] Predominantly occurring in women of reproductive age, endometriosis is closely linked with infertility, chronic pelvic pain, and pelvic organ dysfunction.[4]

Much research has focused on defining and classifying the extent of endometriosis. However, there is a poor correlation between clinical symptoms and the extent of endometriotic lesions. The World Endometriosis Society recommends that all women with an endometriosis diagnosis undergoing surgery be staged according to the revised scoring system of the American Society for Reproductive Medicine r-ASRM[5,6]. Additionally, those with deep endometriosis should be staged according to the Enzian classification (#Enzian).[7] Finally, for women concerned about infertility, surgeons should calculate the Endometriosis Fertility Index (EFI) score to estimate their future fertility potential.[8]

Manual paper documentation is time-consuming and lacks automatic saving and cross-checking capabilities. Automatic electronic recording linked to a database is of essential importance in these cases of complicated multiple co-existing scores, especially since they can be traced back easily for statistical and research purposes, as well as patient follow-up optimisation.[9] The accurate documentation of the disease extent and localisation during surgery is one of the core issues of the treatment process of endometriosis for future study purposes.

In this proof-of-concept study, we aimed to evaluate the performance of a web-based application that automatically calculates endometriosis staging scores according to the three currently most used classifications of endometriosis, the r-ASRM, the revised #Enzian classification (#Enzian) and EFI. We also compared the use of this application to classical manual scoring and evaluated its users' acceptance in daily practice.

Methods

The Fribourg Cantonal Hospital (HFR) commissioned an external company to develop the application. Several meetings between the gynaecology and obstetrics department's physicians and the company helped define the required features and user interface as accurately as possible. For this purpose, the core issues of each score were selected and evaluated. Information concerning different scores, if present, was used to calculate multiple scores at a glance. These issues were extrapolated by analysing the original manuscripts presenting the three scores concerned.

Data collected to enable classification and calculation of the three scores were anamnestic and surgical. Anamnestic patients' data included the birth date, which was used to calculate the patient's age, previous pregnancy history, and infertility history of at least 3 years, if present, necessary to calculate the EFI score.

Surgical data included recording the presence of endometriosis and the extension of lesions in terms of larger diameter and total area at the following sites:

- Peritoneum-the sum of the area in cm
- Posterior cul-de-sac-partial or complete obliteration, left and right ovary, the sum of the diameter in cm, respectively, superficial or deep
- Ovarian and fallopian tubes (left and right) - enclosure through adhesions, respectively, filmy or dense
- Fallopian tube patency (left and right)-positive or negative, if tested
- Rectovaginal space or retro-cervical area-in cm
- Utero-sacral ligaments (left and right)-in cm
- Recto-sigmoid-in cm
- Least adnexal function (left and right) according to the EFI score
- Further localisations-presence of adenomyosis; infiltration of the bladder, the ureters, intestine (other than recto-sigmoid)

We then conducted a proof-of-concept study concerning the use of the application compared to the classic analogic paper-based classification and scoring system. For this scope, we retrospectively assessed endometriosis scoring and classification using the two methods, which were performed on a subset of patients randomly chosen from those diagnosed with endometriosis and operated on in 2022. A group of six surgeons from the service of gynaecology at the HFR, with at least two years of experience in the field of endometriosis, were selected. They were randomly assigned to either the classic analogic classification or the digital group.

The selected surgeons examined the operation protocols of the 20 patients and reviewed operation images and histological reports. They were then asked to describe and classify the surgical status by completing the paper format (Appendix 1) or by the digital format, respectively.

They were then asked to perform a subjective evaluation of the application through a brief questionnaire examining accessibility, ease of use, and estimation of clinical impact on daily practice using a Likert-type scale and the Subjective Mental Effort Questionnaire (SMEQ) questionnaire (Appendix 2).[10] The time required to calculate the scores and the robustness in score calculation between examiners and between the two methods were also evaluated. Finally, the intraclass correlation coefficients (ICC) were calculated to assess the measurement's reliability. Usually, it is suggested that ICC values less than 0.5 are indicative of poor reliability, values between 0.5 and 0.75 indicate moderate reliability, values between 0.75 and 0.9 indicate good reliability and values greater than 0.90 indicate excellent reliability.[11]

We calculated a sample size of 16 patients to have an 80% chance of detecting, at a significant level of 5%, a decrease of one standard deviation in the primary outcome measure (time estimated for calculating the three scores). For instance, this could entail a reduction from 5 minutes in the control group (paper-based) to 3 minutes in the experimental group (application-based), assuming a standard deviation of the difference of 2 minutes. An additional 4 patients were included, bringing the total to 20, considering a 20% possibility of missing or non-interpretable results.

Statistical Analysis

Statistical analysis was performed utilising R Studio version 4.4.2. Data were depicted as mean values accompanied by their respective standard deviations or as medians with interquartile ranges. For datasets conforming to a normal distribution, the Student's t-test was employed. The administration of the SMEQ questionnaire was carried out among experts, with median responses computed alongside their interquartile range. A comparative analysis of paper-based versus electronic compilation duration was conducted, with mean values and standard deviations being presented. The concordance between paper and electronic evaluations was evaluated utilising the mean together with a 95% confidence interval (CI), as was the inter-operator concordance for electronic assessments.

This study was accepted by the Cantonal Ethics Committee of Vaud (Commission cantonale d'éthique de la recherche sur l'être humain, CER-VD), Lausanne, Switzerland (CER-VD number 2021-00258). Informed consent (general consent of HFR) was obtained for each patient included in the study.

Results

From a technical standpoint, the application was built using the Next.js framework (based on React), which facilitates the creation of modern, high-performance web applications. The application is responsive and designed to function across various devices, including computers, tablets, and smartphones. It is hosted within HFR and is accessible at https://app.h-fr.ch/endo.

Regarding the user interface, the application uses a stepper system to guide users through the step-by-step entry of patient data. The extent of endometriosis concerning different localisations is entered. Once the data is entered, the software automatically calculates the r-ASRM, #Enzian, and EFI scores at a glance. For this scope, a Logic arbour was generated (Figure 1). This stepper-based approach ensures easy and structured navigation, minimising errors and enhancing the user experience (Figure 2). The entered data is temporarily stored in the browser, allowing for modifications if needed. These data are finally displayed as a summary that can be exported in PDF format.

The Likert scale results provided by the participants showed an advantage in the use of the web-based application in terms of rendering everyday practice easier since navigating and using the interface and the infographic scoring of the application were easier overall than the paper format score (Figure 3a). The SMEQ confirms these results, showing that the use of the web-based application was of low-moderate difficulty for the participants. No members of the surgical panel reported increased difficulty in the use, whereas two rated scores 20 or less on the SMEQ chart, with the median set at 35 (Figure 3b). Regarding time comparison between the two evaluated methods, the web application proved less time-consuming by 25.1 seconds (electronic 128.0 sec (±56.7) vs. paper 153.1 (±73.7), $P<0.05$) (Figure 4a).

Concerning the robustness of the rASRM, #Enzian, and EFI scores calculation, we evaluated the agreement between the electronic and paper forms. Accordingly, to the current interpretation of the ICC values, rASRM, EFI, and #Enzian scores showed very good and excellent results, respectively, with an ICC of 0.93 (95% CI: 0.48-

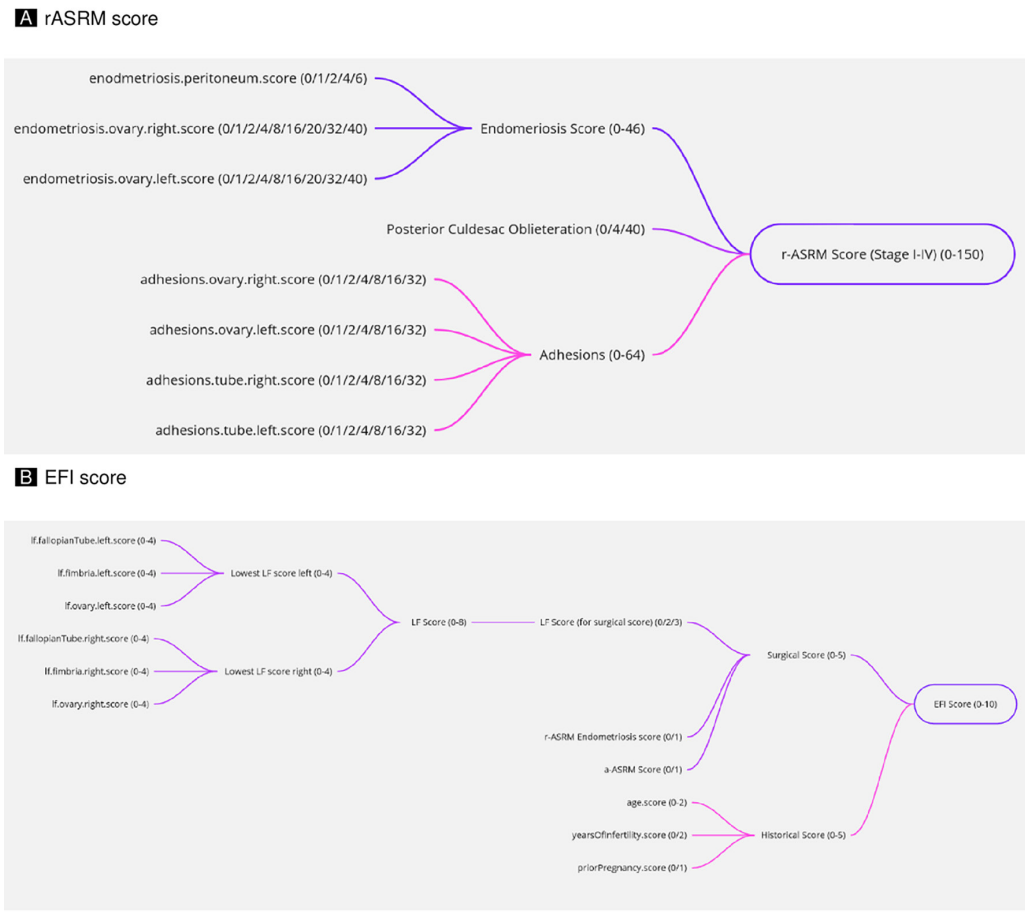

Figure 1. Logic arbour generated to calculate the r-ASRM (Panel A) and the EFI (Panel B) scores.
r-ASRM: Revised American Society for Reproductive Medicine classification, EFI; Endometriosis fertility index.

0.98) for rASRM of 0.96 (95% CI: 0.90-0.98) for EFI, and of 0.84 (95% CI: 0.79-0.88) for the #Enzian score (Figure 4b).

Regarding the agreement between users using the electronic form, the r-ASRM and EFI scores showed very good and excellent results, respectively, with an ICC of 0.93 (95% CI: 0.48-0.98) for r-ASRM and of 0.82 (95% CI: 0.59-0.93) for the EFI score. The #Enzian score showed a moderate concordance, with an ICC value of 0.63 (95% CI: 0.56-0.69) (Figure 4c).

Discussion

Main Findings

There is a growing unmet need to digitalise and, therefore, simplify the management of clinical data in medicine. We successfully developed and tested the feasibility of using a progressive web-based application for endometriosis staging and classification. The comparison of results between analogic and digital evaluations demonstrated high reliability across all three scores: the rASRM, the EFI, and the #Enzian scores. The strong interrater agreement observed in the results for the r-ASRM and EFI scores, and to a lesser extent for the #Enzian score, validates the reliability of the scoring outcomes generated by the web-based application.

Strengths and Limitations

The strengths of this study were the inclusion of six gynaecologists of various degrees of experience, and agreement was found to be unanimously acceptable on their satisfaction and the time saved with the web application. Furthermore, there is the potential to develop further versions of the application, for example, describing the pathology's preoperative extent at the clinical examination or during imaging (ultrasound, magnetic resonance imaging, or others).

Of interest, we tested the application during a national congress of gynaecology and obstetrics. Forty-nine gynaecologists who participated in the congress were asked to test the application on a fictitious case of

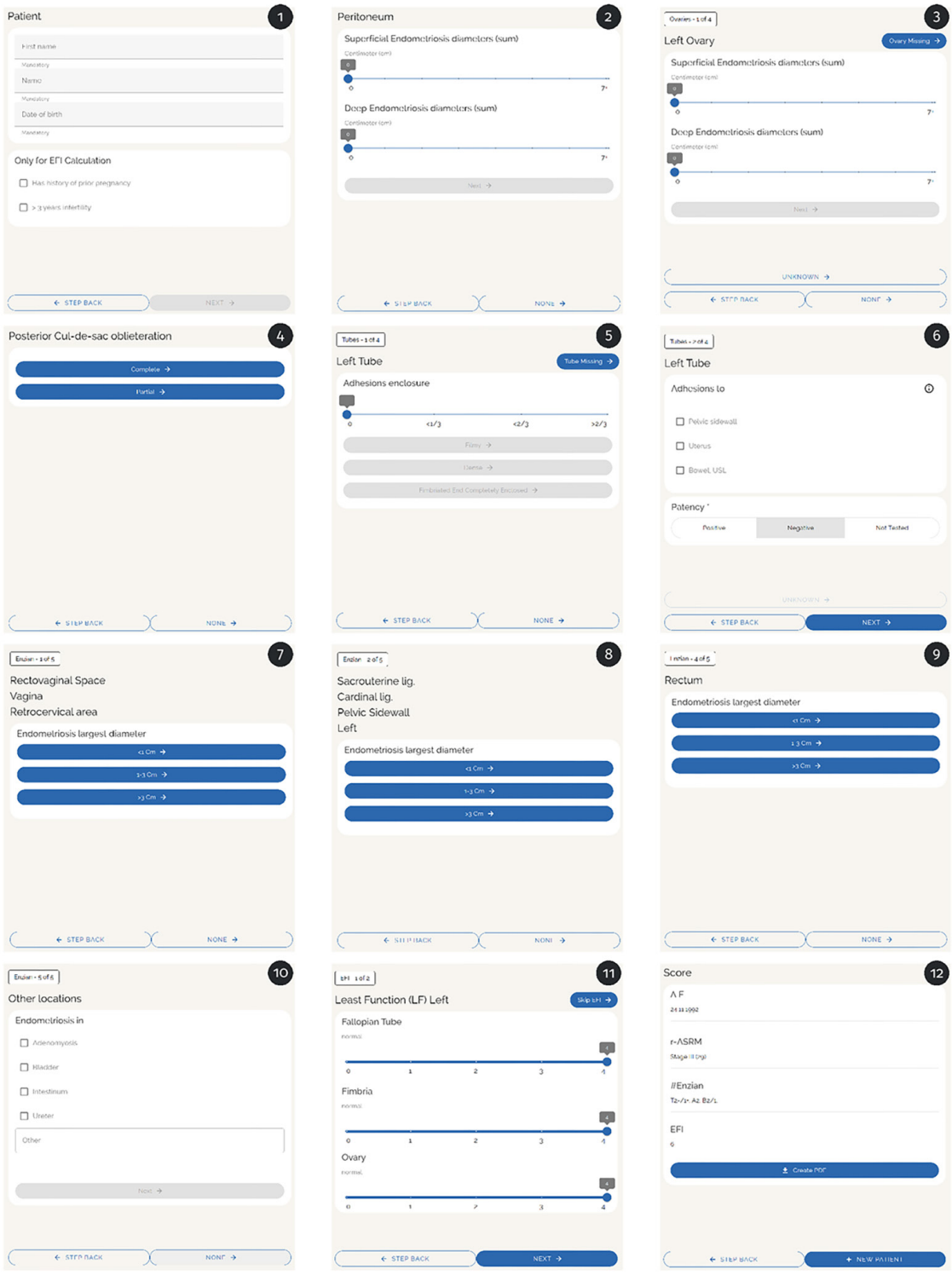

Figure 2. Screenshots of the web-based application user's interface.

Screenshots of the web-based application user's interface for the step-by-step data entry according to localisation and extent of endometriosis lesions and adhesion: 1) Patient's anamnestic data; 2) Peritoneum; 3) Left ovary (right ovary not shown); 4) Posterior cul-de-sac; 5-6) Left tube (right tube not showed); 7-10) Deep infiltration endometriosis of the rectovaginal space and retrocervical area, left sacrouterine ligament and left pelvic sidewall (right sacrouterine ligament and right pelvic sidewall not shown), rectum, as well as other localisations, according to the Enzian (#Enzian) classification; 11) Least function left (right side not shown) according to the EFI classification; 12) A summary of the three scores according to the r-ASRM, #Enzian and EFI classification.

rASRM: Revised American Society for Reproductive Medicine classification, #Enzian: Revised Enzian classification, RFI: Endometriosis Fertility index.

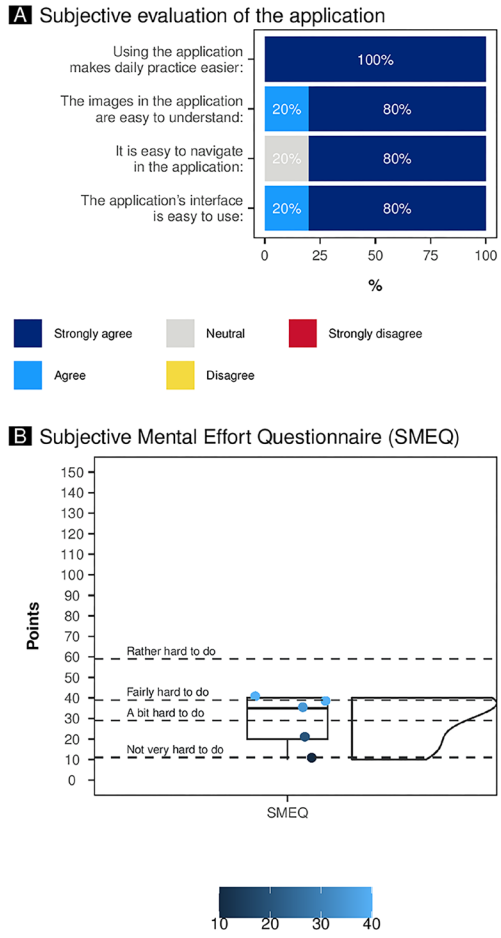

Figure 3. Evaluation of the electronic application utility using: Panel A) a Likert-type scale; Panel B) the Subjective Mental Effort Questionnaire questionnaire.

endometriosis. All were able to complete the scoring via the application within the allocated three minutes, demonstrating excellent compliance and providing very positive feedback regarding its ease of use (data not shown). Even though the extent of time saved in the calculation of the scores ranged only in terms of a few seconds, it was important to test that the application was at least not more time-consuming than the common paper-based form. In addition, although showing little clinical relevance in isolation, this saving can add to significant efficiency gains in high-volume centres or multi-case research settings.

One current limitation of our application is that clinical notes are not saved in a digital format, but only summarised and stored in a PDF format. This is to reduce the constraints linked to personal data management regulation encountered when digital data is stored. An upgraded version of the application will allow the automated integration of data in a patient database. This will also be greatly useful for internal quality checks and research purposes. Another limitation of our results is the retrospective design of the proof-of-concept study. Also, the relatively small number of unselected patients included cannot permit generalisation of the results we presented. A prospective external evaluation and a prospective multicentric study should be performed to further test the clinical relevance of our results in everyday practice.

Strengths and Limitations Compared to Other Studies

Metzemaekers et al.[12] proposed the use of an application in alignment with these efforts to provide uniform surgical registration and classification of endometriosis. The Endometriosis Quality and Grading Instrument for Surgical Performance was the first recorded attempt that used infographics and presented an applicable digital scoring system with immediate use in clinical practice. The study was performed on a group of experts in the

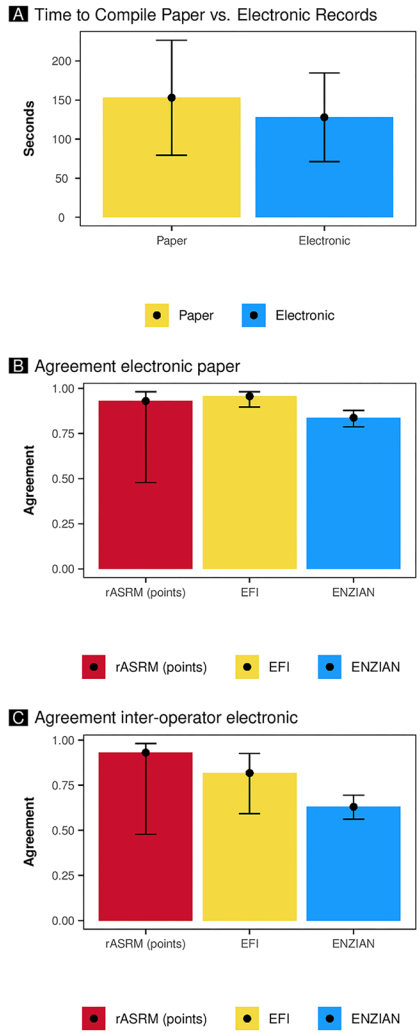

Figure 4. Completion time for calculating endometriosis staging scores using the r-ASRM, #Enzian and EFI classification systems. Panel A) Average time (± standard deviation) needed to compile case records using paper compared to electronic methods; Panel B) Agreement (95% CI) between electronic and paper scoring systems; (Panel C) Inter-operator agreement (95% CI) for electronic scoring of each classification system.

rASRM: Revised American Society for Reproductive Medicine classification, #Enzian: Revised Enzian classification, RFI: Endometriosis Fertility index, CI: Confidence interval.

field of endometriosis, randomly assigned to stage a fictive case of severe endometriosis either in a classical way or using web-based software. The result showed that the digital application was superior in the correct evaluation of the r-ASRM numerical score and stage, as well as the #Enzian score. Also, the application's usability, measured with the system usability scale and the SMEQ, was found to favour the digital evaluation.[12] However, this application does not allow the digital calculation of the revised version of the #Enzian and of the EFI score, as our application does.

The application we presented is specifically designed to describe the localisation and extent of endometriosis during and out of surgery. This application is accessible via a browser and available on personal computers and smartphones. It thoroughly guides the gynaecologist step by step in recording the surgical localisation and extent of endometriosis at surgery. The results generate a PDF sheet documenting the scores according to the three most used classification systems: the r-ASRM,, #Enzian, and EFI scores. The file can be added to the patient's record for storage purposes.

The web-based system was selected for various advantages. The system facilitates the concurrent description and computation of the three endometriosis scores through an intuitive slider-based interface. The

solution guarantees total independence from particular platforms and architectures, facilitating straightforward deployment as a Docker container on either local or web farm servers. The platform is compatible with various devices, including x86-based computers, ARM-based computers, smartphones and tablets, Apple Silicon laptops, and emerging RISC-V devices. The application is accessible via any modern browser, thereby negating the necessity for installations, addressing dependency conflicts, and circumventing multiple builds or compatibility layers.

Our results indicate that the slider-based system facilitated the simultaneous description and calculation of the three scores, unlike the traditional paper-based system, which requires separate processing for each classification system. The parameter-driven design utilising structured logic trees facilitates integration with LLM-based decision support systems and other automated pipelines. The digital endometriosis scoring and classification system operates more efficiently and rapidly than the traditional paper-based documentation system. This finding is consistent with existing literature indicating that digital medical documentation and scoring systems provide multiple benefits compared to traditional paper-based methods.[13,14]

Clinical and Policy Implications

The accurate documentation of the disease extent and localisation during surgery is one of the core issues of the clinical management process of endometriosis and is essential for collecting data for study purposes. The documentation of the surgical status according to the three aforementioned classification systems, r-ASRM,, #Enzian, and the EFI has become an integral part of many centres that treat endometriosis, aiming to centralise and uniform staging of this disease.

We have provided an easy-to-use and practical web application for registering localisation and extent of endometriosis, providing at a glance the score of the three different classifications currently mostly used, rASRM, #Enzian, and the EFI. Providing a user-friendly and fast application for this purpose is crucial for hospitals treating complex conditions like endometriosis, as these imply saving time for specialised personnel and standardised patient data storage.

Unanswered Questions and Future Research

The use of digital applications in medicine is increasing but remains a novelty requiring research and development as well as suitable training to allow for their integration into daily practice. Several apps have been developed to evaluate the clinical symptoms of endometriosis.[15] According to this review, there are currently 12 applications used for this scope. Applications have been shown to substantially help patients and physicians in this process, and several international organisations support their use. Nonetheless, this review highlights the scarcity of effective patient and physician-directed apps for managing and treating endometriosis, particularly for the intraoperative description and management of surgical data. This argument demonstrates the considerable potential for developing mobile resources to aid in diagnosing and treating endometriosis.

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Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/disclosure-of-interest/ and declare that they have no relevant financial, personal, political, intellectual or religious interests.

Ethical approval: This study was accepted by the Cantonal Ethics Committee of Vaud (Commission cantonale d'éthique de la recherche sur l'être humain, CER-VD), Lausanne, Switzerland (CER-VD number 2021-00258).

Informed consent: Informed consent (general consent of HFR) was obtained for each patient included in the study.

Data sharing: The data that support the findings of this study are available from the corresponding author, AFr, upon reasonable request.

Transparency: The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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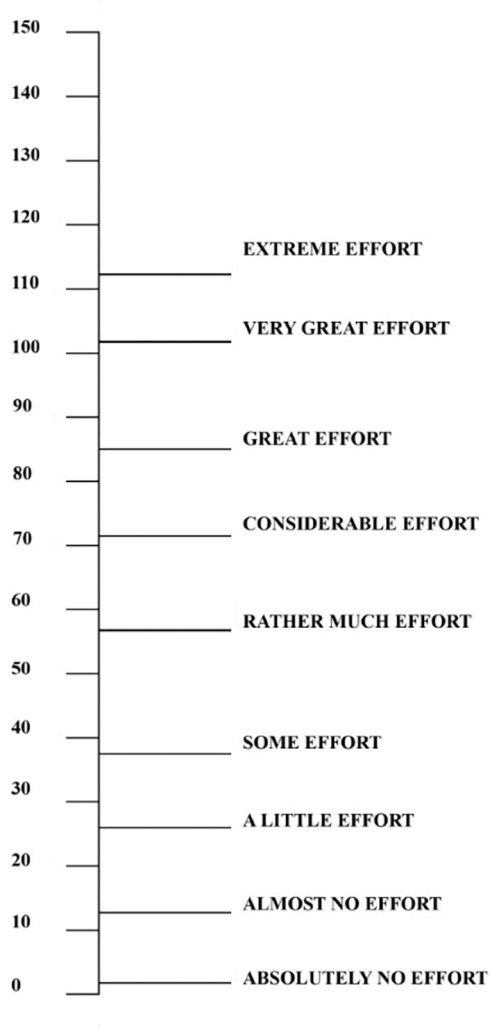
Appendix 1. Assessment of accessibility, usability, and clinical impact using likert scale and SMEQ.

	Statement	5 – Strongly agree	4 – Agree	3 – Neutral	2 – Disagree	1 – Strongly disagree
1	The application's interface is easy to use.	☐	☐	☐	☐	☐
2	It is easy to navigate through the application.	☐	☐	☐	☐	☐
3	The images within the application are easy to understand.	☐	☐	☐	☐	☐
4	Compared to the traditional paper-based method, the application facilitates daily documentation and staging practice.	☐	☐	☐	☐	☐



Appendix 2. The subjective mental effort question (SMEQ).

It is a single-item questionnaire with a rating scale from 0 to 150 with nine verbal labels ranging from "Not at all hard to do" (just above 0) to "Tremendously hard to do" (just above 110).

SYSTEMATIC REVIEW

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Race and ethnicity reporting in endometriosis literature: a systematic review

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ABSTRACT

Background: Accurate reporting of participants' race and ethnicity is essential for assessing the representativeness of study populations and for identifying potential disparities in diagnosis, treatment, and outcomes.

Objectives: To assess the quantity and quality of race and/or ethnicity reporting in the endometriosis literature.

Methods: A systematic review of all human studies reporting data about endometriosis as the primary objective published in 2022. Studies were identified from electronic searches of MEDLINE, Google Scholar, Web of Science, Scopus, ClinicalTrials.gov, and the Cochrane Library databases.

Main Outcomes Measures: The frequency and quality of participants' race and/or ethnicity reporting based on compliance with the guidelines set by the ICMJE. Study characteristics that influenced the reporting of race and/or ethnicity were assessed. Publications from journals that followed ICMJE recommendations were compared with those from journals that did not.

Results: 648/2054 (31.6%) articles met the inclusion criteria. Sixty-five studies (10.0%) reported participants' race and/or ethnicity, and the overall quality of this reporting was poor. The frequency of reporting did not differ between journals adhering to ICMJE guidelines and those that did not (24, 11% vs. 41, 9.5%; P=0.52), between studies involving national versus international populations (60, 92.3% vs. 5, 7.7%; P=0.28), or between male and female authors (33, 50.8% vs. 32, 49.2%; P=0.38) respectively. Race and/or ethnicity were reported more often in prospective than in retrospective studies (37, 56.9% vs. 18, 27.7%; P<0.001), and in multicentre compared to single-centre studies (44, 67.7% vs. 21, 32.3%; P<0.001).

Conclusions: The reporting of race and/or ethnicity in human-based endometriosis research remains both infrequent and inconsistent, including in journals claiming adherence to ICMJE standards. These results highlight the need for improved and uniform documentation of racial and ethnic data in endometriosis research.

What is New? Human-based articles focusing on endometriosis have a low frequency and quality of race and/or ethnicity reporting, even in journals claiming to follow ICMJE recommendations.

Keywords: Epidemiology, demographics, endometriosis, report, disparity

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Introduction

Endometriosis, a gynaecological disorder characterised by the ectopic growth of endometrial-like tissue outside the uterus,[1] has a significant burden on individuals worldwide, manifesting in dysmenorrhoea, chronic pelvic pain, infertility, and various other debilitating symptoms.[2,3]

Studies indicate that endometriosis affects individuals across diverse racial and ethnic backgrounds, albeit with variations in diagnosis, treatment and outcomes.[4-6] In this context, race is commonly understood as a socially constructed categorisation based on perceived physical traits such as skin colour, whereas ethnicity refers to shared cultural identity, including ancestry, language, and traditions.[7,8] Recent research found that Hispanic and Black women were less likely to receive a timely diagnosis of endometriosis, compared to their White counterparts, highlighting disparities in access to care and diagnostic delays.[9,10]

In recent years, there has been a growing recognition of the importance of addressing racial and ethnic disparities in healthcare research. Initiatives such as the National Institutes of Health (NIH) Revitalization Act of 1993 mandated the inclusion of minority individuals in clinical research to ensure that study findings are applicable to diverse populations.[11] Moreover, the International Committee of Medical Journal Editors (ICMJE) developed recommendations for race and/or ethnicity reporting. Specifically, these recommendations encourage researchers to explicitly state the racial and ethnic composition of their study populations and to consider these factors when interpreting study results. This reporting is intended to help identify health disparities and improve the relevance of clinical findings to different demographic groups.[12] Despite these efforts, there is still a lack of clarity regarding the impact of these initiatives on endometriosis literature to adequately represent and consider the experiences of diverse racial and ethnic groups.

This study aimed to assess the quantity and quality of race and/or ethnicity reporting in the endometriosis literature.

Methods

This systematic review adhered to an *a priori* study protocol that outlined the methods for search, strategy, study selection, data extraction and synthesis. The protocol was registered in the International Prospective Register of Systematic Reviews (ID: CRD42023486163). Two authors independently performed all steps, and discrepancies were resolved through discussion among all authors. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 checklist and flowchart[13] were followed to report the whole study.

Eligibility Criteria, Information Sources, Search Strategy

Searches were conducted in six electronic databases (i.e. MEDLINE, Google Scholar, Web of Sciences, Scopus, ClinicalTrials.gov and Cochrane Library) from January to December 2022 using different combinations of the following search terms: "endometriot*"; "endometrios*"; "endometriom*"; "rac*"; "ethni*". Since a cross-sectional analysis of the whole endometriosis literature was not feasible for our aim, we chose the above-mentioned literature screening period (January - December 2022) as a representative sample of the recent endometriosis literature. References from relevant studies were also screened.

Study Selection

We included all peer-reviewed, human-based primary research articles focusing on endometriosis.

A priori defined exclusion criteria were:

- Non–research-focused articles (i.e. editorials, commentaries, and letters to the editor);
- Reviews and meta-analyses;
- Case reports;
- Non-human studies;
- Articles reported in languages other than English.

Data Extraction

We extracted the following data from the included studies analysing the full-text manuscript and tables and figures: demographic information [(age and body mass index (BMI)], race and ethnicity. We recorded how race was categorized (i.e.., "race", "ethnicity", "race and/or ethnicity", "descent", "population", "ancestry", other, or not classified) and the method of classification (i.e. self-report, healthcare professionals' or researchers' perception, parent/caregiver report, national/government ID, personal/parent birth country, or unspecified methods such as clinical database review or institutional electronic medical record review). Additionally, we noted the journal name and whether it adhered to the ICMJE recommendations, the geographical scope

(multi-country or single country), and the geographical region according to World Health Organization (WHO) classifications (Americas, African, European, Eastern Mediterranean, Southeast Asian, Western Pacific). This parameter was based on the research group's country of origin for studies examining national populations, and on the corresponding author's country of origin for international articles. We also recorded study design characteristics (retrospective or prospective, multicentre or single centre) and the corresponding author's gender (male or female).

Risk of Bias Assessment

Due to the inadequacy of standard risk of bias tools for evaluating race and ethnicity reporting, we assessed study quality using recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals as outlined by the ICMJE recommendations.[8] Specifically, we evaluated:

- "Who classified the individuals in terms of race and ethnicity";
- "Why the classification adopted in the study was used";
- "Whether the classification options were defined by the investigator or the participant";
- "Why race and ethnicity were reported in the study";
- "Whether the variable of race was defined in the article".

Statistical Analysis

Data were collected using Microsoft Excel (Version 2021), and descriptive statistics were computed for categorical variables. Chi-squared and Fisher's exact tests were employed to compare the study characteristics and the proportion of race and/or ethnicity reporting as well as differences between ICMJE and non-ICMJE journals. Statistical significance was set at *P*-value <0.05. All analyses were performed using Stata 17 software (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC).

Ethics Statement

The study was exempt from IRB approval due to the study design (systematic review of the literature).

Results

Studies Selection

From January 1, 2022, to December 31, 2022, 2,054 articles were published on endometriosis in indexed journals. At the end of the study selection process, 648 (31.6%) studies were included in our analysis (Figure 1).

Studies, Characteristics and Endpoints

Race and/or Ethnicity Reporting in All Indexed Journals

Among the 648 included articles, only 65 (10.0%) articles reported the race or ethnicity of the study participants (Table 1). Among the articles that reported race and ethnicity, the most common classification used was "ethnicity" (33, 50.8%), followed by "race and/or ethnicity" (43, 25.9%). The modality adopted to classify patients was frequently unspecified (44, 67.7%), followed by self-reporting by study participants (10, 15.4%) and perception of researchers (10, 15.4%).

The adherence to ICMJE recommendations for race and/or ethnicity reporting was notably low. Specifically, "who classified the individuals in terms of race or ethnicity" was reported in 2 studies (3.1%); "why the classification reported in the study was used" was never explained, "whether the classification options were defined by the investigator or the participant" were described in one study (1.5%), "why race was assessed in the study" was explained in 7 studies (10.8%) and "the variable of race within the text article" was defined in 20 studies (30.8%).

Comparisons Between Study Characteristics and Race and/or Ethnicity Reporting (Table 2)

Of the included articles, 149 (23.0%) were prospective studies and 305 (47.0%) were retrospective studies. There was a significantly higher frequency of prospective studies in articles reporting race or ethnicity compared to those that did not (37, 56.9% vs. 112, 19.2% $P<0.001$). Multicentric studies were more common in race-reporting articles than single-centre studies (21, 32.3% vs. 77,13.2%, $P<0.001$). Although the rate of studies examining international populations was higher in race-reporting articles, this difference was not statistically significant (5, 7.7% vs. 27, 4.6%).

WHO America region exhibited the highest consistency in reporting race or ethnicity (29, 44.6% vs. 61, 10.5%, $P<0.001$), with the United States (20, 44.4%) and Brazil (4,18.2%) being the most represented publishing countries. Conversely, the WHO Western Pacific region published the fewest race reporting articles (11, 16.9% vs. 230, 39.5%, $P<0.001$), with China (1, 0.6%) and Australia (6, 21.4%) representing the countries with the least reporting. The difference between the rate of race reporting and

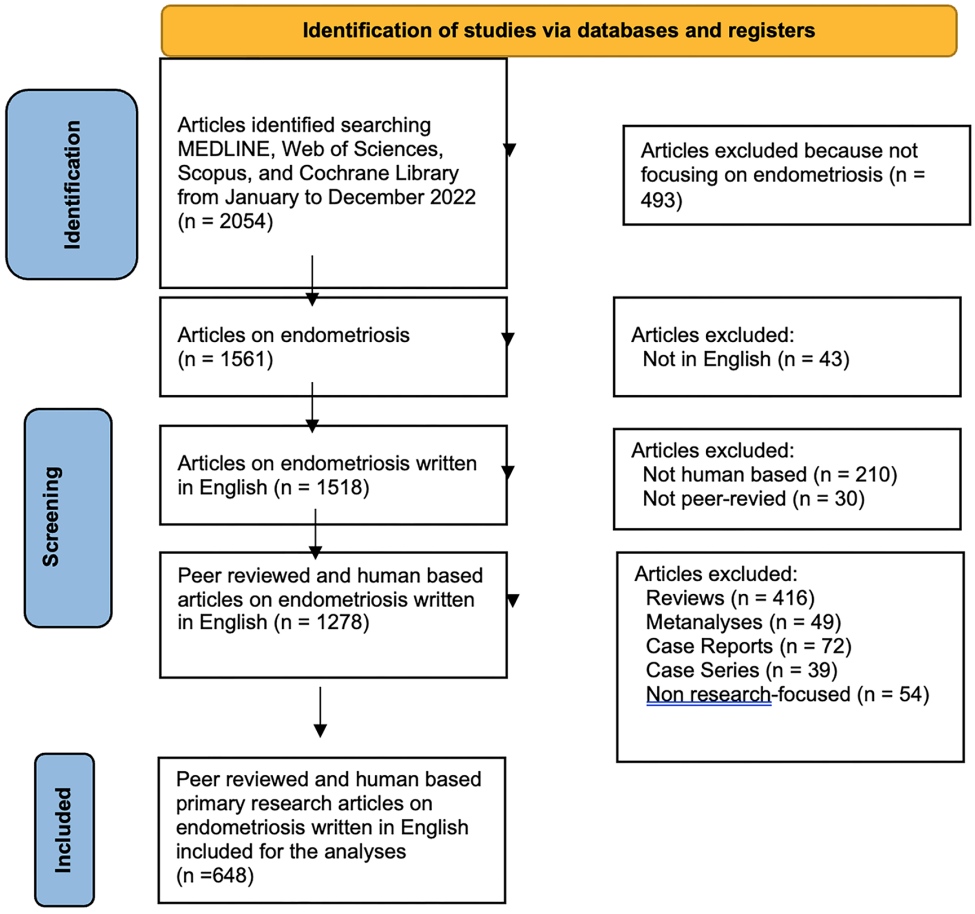

Figure 1. PRISMA 2022 flow diagram for new systematic reviews which included searches of databases and registers only.

race non-reporting articles in other WHO regions was not statistically significant.

Comparison Between Studies from ICMJE and Non-ICMJE Journals (Table 3)

Among the 648 included studies, 216 were published by journals adhering to ICMJE recommendations (33.3%). Demographic characteristics (patients' age and BMI) reporting was significantly higher in articles from ICMJE journals compared to non-ICMJE journals (118, 54.6% vs. 182, 42.1%, *P*=0.003). A minority of the articles, both from ICMJE (62, 20.4%) and non-ICMJE journals (104, 16.1%), reported participants' race or ethnicity; however, there was no statistical difference between the two groups (24, 11.1% vs. 41, 9.5%). The most common classification in both the ICMJE and non-ICMJE journals was "ethnicity" (9, 37.5% and 24, 58.5%, respectively), followed by "race and/or ethnicity" in ICMJE journals (8, 33.3%) and "race" in non-ICMJE journals (6, 14.6%). No statistical difference was observed between the ICMJE and non-ICMJE journals regarding the method of classification. In particular, the method of patients' classification in both the ICMJE and non-ICMJE journals was unspecified in most cases (15, 62.5% and 29, 70.7%, respectively), followed by "perception of healthcare professionals/researchers" in ICMJE articles (5, 20.8%) and "self-report" in non-ICMJE journals (7, 17.1%).

Quality of the Studies

Regarding the quality of race and/or ethnicity reporting, authors in non-ICMJE journals never reported "who classified the individuals in terms of race or ethnicity", while authors in ICMJE journals never reported "why the classification reported in the study was used". "Whether the classification options were defined by the investigator or the participant" was explained in one (4.2%) of the ICJME journals and in one (2.4%) of the non-ICMJE ones. Furthermore, "why race was assessed in the study" was clarified in 16.7% of ICMJE journals and in 7.3% of non-ICMJE journals.

Discussion

Main Findings

Our study showed low rates of race and ethnicity reporting in endometriosis literature, in terms of quantity and quality, regardless of the journal's statement of adherence to ICMJE recommendations.[12]

This finding is consistent with previous research highlighting inadequate reporting of social determinants of health in medical literature, particularly concerning race and ethnicity.[14-16] The underreporting of race and ethnicity in endometriosis studies not only obscures the true burden of the disease but also perpetuates inequalities in healthcare access and outcomes. These findings highlight the need to prioritise and standardise race and ethnicity reporting in endometriosis research.

Concerning adherence to reporting guidelines, such as those provided by the ICMJE, our study reveals poor adherence to recommended practices for race and ethnicity reporting. This finding is consistent with existing literature, which reported equally low rates of race reporting when analysing surgical and endometrial cancer literature.[17,18]

Furthermore, our analysis identifies significant disparities in race and ethnicity reporting based on study characteristics. Prospective studies and multicentric studies were more likely to report race and ethnicity compared to retrospective and single-centre studies, respectively. This result is in line with previous findings of a review focusing on surgical literature.[14,19]

Table 1. Quantitative analyses of included studies.

	All included studies (648/2054, 31.6%)
Demographic characteristics reported (age AND body mass index)	300 (46.3%)
Race/ethnicity reported	**65 (10.0%)**
Classification reported	
Race	10 (15.4%)
Ethnicity	33 (50.8%)
Race/ethnicity	13 (20%)
Population	3 (4.6%)
Ancestry	1 (1.5%)
Not classified	5 (7.7%)
Method of classification	
Self-report	10 (15.4%)
Perception of health care professionals/researchers	10 (15.4%)
National registration identity	1 (1.5%)
Unspecified	44 (67.7%)

Table 2. Rates of race and ethnicity reporting according to characteristics of included studies.

	All articles (648)	**Race reported (65)**	**Race not reported (583)**	***P*-value**
Study design				<0.001
Prospective	149 (23.0%)	37/65 (56.9%)	112/583 (19.2%)	
Retrospective	305 (47.0%)	18/65 (27.7%)	287/583 (94.1%)	
Other	194 (29.9%)	10/65 (15.4%)	184/583 (31.3%)	
Single-centre vs. multicenter study				<0.001
Single centre	550 (84.9%)	44/65 (67.7%)	506/583 (86.8%)	
Multicentre	98 (15.1%)	21/65 (32.3%)	77/583 (13.2%)	
National vs. international study				0.28
National	616 (95.1%)	60/65 (92.3%)	556/583 (95.4%)	
International	32 (4.9%)	5/65 (7.7%)	27/583 (4.6%)	
WHO region				<0.001
African	3 (0.5%)	1/65 (1.5%)	2/583 (0.3%)	0.27
Americas	90 (13.9%)	29/65 (44.6%)	61/583 (10.5%)	<0.001
South-East Asia	15 (2.3%)	0/65 (0%)	15/583 (2.6%)	0.39
European	264 (40.7%)	23/65 (35.4%)	241/583 (41.3%)	0.35
Eastern Mediterranean	35 (5.4%)	1/65 (1.5%)	34/583 (5.8%)	0.15
Western Pacific	241 (37.2%)	11/65 (16.9%)	230/583 (39.5%)	<0.001

WHO: World Health Organization.

Our study also highlights regional disparities in race and ethnicity reporting, with notable variations across WHO regions. These findings are consistent with previous studies, which found that randomised controlled trials enrolling United States patients had more race and/or ethnicity information than those recruiting an international population.[14,19]

Collectively, these findings highlight not only the inconsistency of race/ethnicity reporting but also the importance of examining the reasons why such information is often underreported.

Moreover, our findings also underscore the need for clinicians to recognise disparities in diagnosis and management, for policymakers to promote standardised reporting and inclusive research, and for researchers to integrate social determinants of health and adhere to international guidelines, in order to advance global health equity in endometriosis care and research.

Comparison with Existing Literature

One important explanation for the frequent omission of race and ethnicity data may be the limited representation of minority groups in many studies. Analyses across medical literature have shown that small subgroup sizes often restrict the possibility of meaningful statistical analysis and may discourage authors from reporting these variables.[14,18,19] For instance, Berger et al.[14] highlighted that race/ethnicity analyses in randomised trials were frequently underpowered to detect differences, while Maduka et al.[18] and Mitchell et al.[19] noted that small subgroup numbers reduce interpretability and contribute to inconsistent reporting practices. These findings suggest that the underreporting observed in endometriosis research may partly reflect methodological challenges rather than a lack of relevance. Nevertheless, transparent documentation of race/ethnicity remains important, particularly when guided by a clear hypothesis or when representation is sufficient to support analysis, as this enables the identification of disparities and improves the applicability of findings across populations.

Addressing racial and ethnic disparities in endometriosis research, therefore, appears essential for advancing health equity and improving outcomes for all individuals affected by the disease. By prioritising transparency, accountability, and inclusivity in race and ethnicity reporting, researchers, clinicians, policymakers, and funding agencies can work together to ensure that endometriosis research reflects the diversity of the population and informs strategies to address systemic inequities in healthcare access and outcomes.[20]

It has been demonstrated that endometriosis is less likely to be diagnosed in Black women and in Asian women, when compared with White women.[4] This difference seems to be related to a different clinical presentation among various race/ethnicities, a different socio-economic status or an implicit bias among health care

Table 3. Rates of race and ethnicity reporting among International Committee of Medical Journal Editors (ICMJE) and non-ICMJE journals.

	ICMJE (n=216, 33.3%)	**Non-ICMJE (n=432, 66.7%)**	***P*-value**
Demographic characteristics reported (Age AND body mass index)	118 (54.6%)	182 (42.1%)	0.003
Race and ethnicity reported	24 (11.1%)	41 (9.5%)	0.52
Classification reported			0.37
Race	4 (16.7%)	6 (14.6%)	
Ethnicity	9 (37.5%)	24 (58.5%)	
Race/ethnicity	8 (33.3%)	5 (12.2%)	
Population	1 (4.2%)	2 (5%)	
Ancestry	0	1 (2.4%)	
Not classified	2 (8.3%)	3 (7.3%)	
Method of classification			0.42
Self-report	3 (12.5%)	7 (17.1%)	
Perception of researchers	5 (20.8%)	5 (12.2%)	
National registration identity	1 (4.2%)	0 (0%)	
Unspecified	15 (62.5%)	29 (70.7%)	

providers to consider this diagnosis less likely in Black and Asian women.[5]

In addition to variation in disease prevalence and diagnosis among women of different races/ethnicities, literature reports the potential impact of this trait on the management of endometriosis with equal lesions' distribution.[5,21] According to Movilla et al.[10] study, Black or African American patients had the highest major postoperative complications and the lowest rates of minimally invasive surgery.[22-24] Moreover, a recent study suggests that race and/or ethnicity may influence disease severity, with Asian women being more likely to be diagnosed with stage III/IV endometriosis compared with White women.[25] This may be probably due to societal and economic factors impacting their access to care. Factors such as insurance coverage, referral networks, and access to high-volume surgeons are known to place patients from certain racial and ethnic groups at varying probabilities of accessing high-volume surgeons.[10] These findings support the hypothesis that diagnosing and treating highly prevalent diseases like endometriosis based on studies not reporting race and ethnicity may overlook potentially preventable adverse outcomes.[26,27]

Strengths and Limitations

The main strength of this study is that, to our knowledge, this is the first race-reporting systematic review on human-based peer-reviewed articles about endometriosis. Furthermore, this study employed a thorough search strategy across multiple databases and across various study characteristics, ensuring a comprehensive retrieval of relevant articles on endometriosis and maintaining methodological rigour in the data extraction and analysis process.

However, several limitations should also be acknowledged. First, the main limitation of the present systematic review is that, despite efforts to identify relevant studies, the limited availability of race and ethnicity data in endometriosis literature may have constrained the scope and generalizability of the findings. In particular, it appears unlikely to accurately identify how race and ethnicity were determined in studies based on the perception of researchers, since race is a social construct, not a biological one, but also based on clinical databases (e.g. Surveillance, Epidemiology, and End Results Program; National Cancer Database) and institutional electronic medical record review. Therefore, the method of race classification in most articles was labelled as "unspecified", as it was unclear whether race and/or ethnicity were established by self-reporting or other methods.

Second, in order to ensure a high-quality article review process, we decided to design a single year-focused review (i.e., 2022), with a subsequent potential selection bias. Further studies are needed to evaluate the race-reporting trend in endometriosis literature in other time frames.

Third, excluding studies reported in languages other than English might have created an impact on overall results; despite that, we *a priori* decided to establish this exclusion criterion to avoid the effect of potential mistranslation and lower quality of the included studies.

Another limitation is that our analysis was restricted to the reporting of race/ethnicity as documented in published studies. We could not incorporate broader social determinants—such as socioeconomic status, educational level, or insurance coverage—that interact closely with race and ethnicity and may provide a clearer understanding of disparities in access to care or diagnostic delay. In line with the WHO framework on the social determinants of health, it is important to recognise that health outcomes are the result of complex interactions between social, economic, and environmental conditions. Future investigations should integrate these dimensions and, where possible, apply statistical approaches such as two-way analyses to disentangle the respective contributions of social context and race/ethnicity.

Finally, the assessment of race/ethnicity reporting did not rely on a validated risk of bias tool and therefore cannot capture the underlying reasons why primary authors chose not to report these variables. The quality of race/ethnicity reporting assessment adopted was therefore exploratory and was intended as a descriptive appraisal, rather than a formal risk of bias evaluation, and was aimed at highlighting gaps in compliance with ICMJE recommendations.

Conclusion

Race and ethnicity are infrequently and poorly reported in international literature regarding endometriosis. This finding underscores the critical importance of addressing racial and ethnic disparities in endometriosis research and highlights the urgent need for improved race and ethnicity reporting practices. By identifying disparities, understanding their underlying causes, and proposing evidence-based inclusion of racially and ethnically diverse patient populations in clinical literature, we can

move closer to achieving health equity in endometriosis care and beyond.

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REVIEW ARTICLE

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Bladder dysfunction after advanced pelvic surgeries: neuropelveological strategies for prevention and management

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ABSTRACT

Advanced pelvic surgeries, such as radical hysterectomy, deep endometriosis surgery and sacrocolpopexy, pose risks to autonomic pelvic nerves leading to voiding dysfunction and reduced quality of life. This review article evaluates neuropelveological strategies for preventing and managing bladder dysfunction by exploring pelvic neural anatomy, nerve-sparing techniques, and postoperative rehabilitation approaches. Nerve-sparing approaches can reduce postoperative urinary retention and improve recovery of bladder function. Neuromodulation techniques provide additional support in managing persistent voiding dysfunction in selected cases. A multidisciplinary approach integrating detailed knowledge of pelvic neural anatomy, precise surgical techniques and structured postoperative management can minimise bladder dysfunction and optimise patient outcomes.

Keywords: Bladder dysfunction, neuropelveology, nerve-sparing surgery, neuromodulation, postoperative management

Introduction

In extensive gynaecological disorders, pelvic nerve injury can be related not only to the disease itself but also to complex surgical procedures that demand precise dissection for clear margins.[1] Lack of understanding of the intricate anatomy of pelvic neural structures further exacerbates this risk. Damage to the autonomic nerves can result in bladder, bowel, or sexual dysfunction, severely impacting the patient's

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quality of life, and sometimes leading to irreversible organ dysfunction.[2] Advanced pelvic surgeries, including procedures for deep infiltrating endometriosis, radical surgery for cervical cancer, and sacrocolpopexy for pelvic organ prolapse are at the highest risk for these complications. Studies suggest that bladder dysfunction occurs in approximately 30% to 80% of patients undergoing these surgeries, depending on the type of surgery, emphasising the magnitude of the issue.[3,4]

Managing these pathologies requires a thorough understanding of pelvic anatomy, meticulous preoperative planning, adherence to the principles of neuropelveology, and effective postoperative care.[5] Among the affected organs, the bladder is particularly vulnerable. This article aims to provide an in-depth exploration of neuropelveological strategies to preserve autonomic nerves, with a focus on detailed preventive measures and comprehensive postoperative management tailored to specific surgical interventions.

Pelvic Neuroanatomy and Bladder Innervation

The pelvic autonomic nervous system integrates sympathetic, parasympathetic, and sensory fibres to regulate bladder function and maintain homeostasis of the pelvic organs. Understanding the anatomy and topography of these neural pathways is critical to minimising complications during pelvic surgeries.[6]

The superior hypogastric plexus (SHP) is the origin of sympathetic innervation to the bladder and other pelvic organs. This triangular network is formed by fibres from T11-L2, which converge from the abdominal aortic plexus, lumbar splanchnic nerves, and inferior mesenteric plexus.[7] Situated anterior to the sacral promontory at the L5-S1 level, the SHP is covered by the anterior layer of visceral pelvic fascia. The SHP gives rise to the hypogastric nerves (HNs), which descend bilaterally along the pelvic sidewalls and serve as key conduits for sympathetic fibres (Figure 1). These nerves run medial to the ureters and lateral to the mesorectum, making them vulnerable during rectal and lateral pelvic dissections.[8]

The HNs are critical structures for bladder storage function, as they facilitate detrusor relaxation and internal sphincter contraction.[9] Sensory fibres responsible for transmitting information about bladder fullness, pain, and distension also primarily travel through the HNs.[10] These sensory fibres are crucial for coordinating the storage phase of micturition, enabling the central nervous system to regulate bladder filling.[11] The HNs can be identified transperitoneally along the pelvic sidewalls, medial to the ureters (Figure 2). Due to their close proximity to the uterosacral ligaments and the presacral fascia, the HNs need to be carefully dissected during procedures at higher risk of nerve damage, such as radical hysterectomy, endometriosis excision and sacrocolpopexy.[12,13]

The pelvic splanchnic nerves (PSNs), carrying parasympathetic fibres, originate from S2-S4 spinal segments. These delicate nerves travel through the dorsocaudal pararectal space before merging with the hypogastric nerves to form the inferior hypogastric plexus (IHP) (Figure 3).[2] While their primary role is motor innervation to stimulate detrusor contraction and facilitate bladder emptying, the PSNs also carry visceral afferent fibres that contribute to the sensory pathways of pelvic organs.[15] However, in the context of bladder innervation, sensory signals are predominantly mediated by the hypogastric nerves rather than the parasympathetic system.[9]

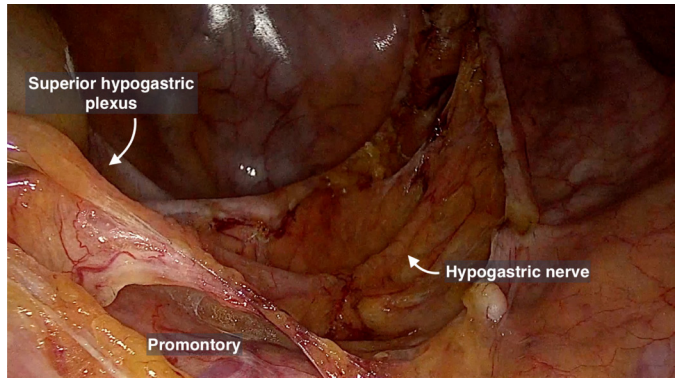

Figure 1. The superior hypogastric plexus at the level of the promontory and the hypogastric nerve completely dissected during a sacrocolpopexy.

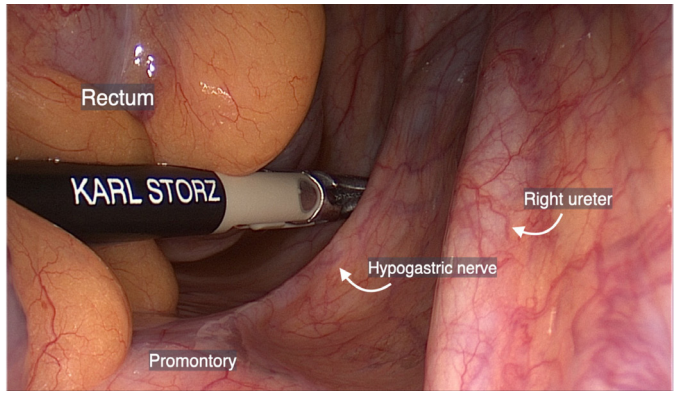

Figure 2. The hypogastric nerve seen transperitoneally at the beginning of the surgery and its relationship to the ureter.

The IHP, also referred to as the pelvic plexus, is the neurological hub for autonomic control of pelvic viscera. Approximately 2 × 2 cm in size, the IHP is located in the visceral pelvic fascia, between the anterolateral surface of the rectum and the posterolateral surface of the vaginal fornix.[16,17] Its branches, categorized as medial, cranial, and anterior efferent bundles, innervate the rectum, uterus, vagina, and bladder.[6] The vesical branches within the anterior bundle supply the bladder and urethra, playing a central role in voiding function. Preservation of the IHP during surgery is essential to avoid severe bladder dysfunction.[18]

The vesical branches of the IHP pass beneath the inferior vesical vein and run parallel to the blood vessels of the paracolpium in close proximity to the vaginal wall before reaching the bladder (Figure 4).[19] These are responsible for motor innervation to the detrusor muscle and coordination of the micturition reflex. Identification of these branches is facilitated by careful dissection of the posterior leaf of the vesicouterine ligament, where meticulous separation of the middle vesical vein and inferior vesical vein allows for the visualization and preservation of the bladder branches.

Sensory signals from the bladder are primarily transmitted via the HNs, with additional minor nociceptive contributions from the PSNs. These fibres relay critical information about bladder fullness and nociceptive stimuli to the central nervous system, enabling proper coordination of the micturition reflex.[10] The integration of sensory and motor inputs ensures the delicate balance required for bladder function. The somatic innervation, mediated by the pudendal nerve, controls the external urethral sphincter, ensuring voluntary control over urination.[9]

These interconnected plexuses and their efferent branches represent a delicate balance of motor, sensory, and autonomic functions, and nerve-sparing approaches and intraoperative neuro-navigation are pivotal in preserving these structures and optimising functional outcomes.[20] Damage to any component of this network can lead to bladder storage and voiding dysfunctions, emphasising the need for meticulous surgical planning and execution.[21]

Radical Hysterectomy (Cervical Cancer Surgery)

Radical hysterectomy is among the most challenging pelvic surgeries and demands meticulous dissection of the parametrial and paracervical regions.[19] While this

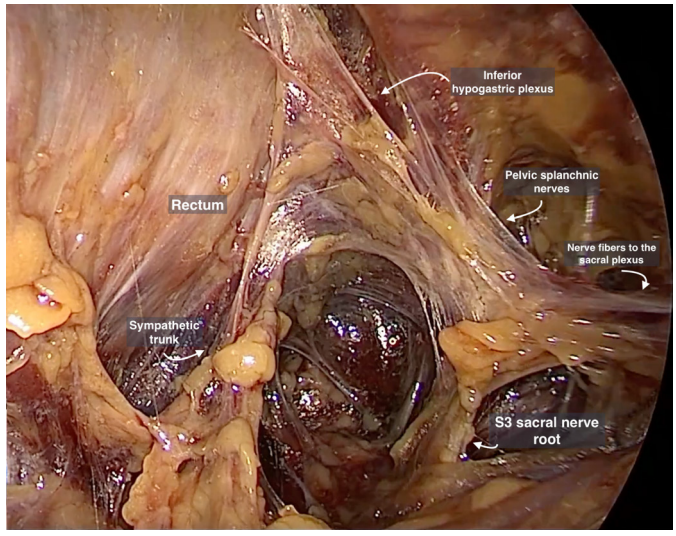

Figure 3. The pelvic splanchnic nerves arise from S2-S2 sacral nerve roots and merge with the hypogastric nerves and the sympathetic trunks on both sides of the rectum to form the inferior hypogastric plexus. Cadaveric dissection, ESGE Annual Congress 2022.

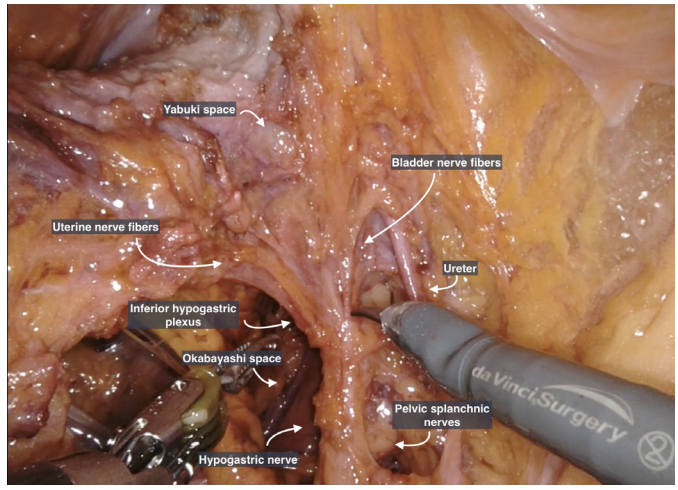

Figure 4. The bladder branches from the inferior hypogastric plexus run in close proximity to the vaginal wall and are prone to injury in extensive vaginal excisions. Cadaveric dissection, ESGE Annual Congress 2023.

procedure is effective in achieving oncological control, it carries significant risks to the autonomic nerves critical for bladder function, with patients presenting voiding dysfunction in up to 80% of cases.[22] The most vulnerable structures during radical hysterectomy include the HNs and the IHP, mainly, its vesical branches which run in the lateral parametrium.[23]

Dissection of the dorsal parametrium poses a particular risk to the HNs, which are essential for bladder storage. These nerves facilitate detrusor relaxation and contribute

to the tone of the internal urethral sphincter. Damage to these nerves can result in stress urinary incontinence due to decreased sphincter tone, as well as bladder overactivity caused by parasympathetic dominance.[24,25] Maneschi et al.[26] have demonstrated that injury to the HNs during parametrial dissection often leads to decreased bladder compliance and altered sensitivity to fullness, resulting in symptoms such as urgency and incomplete voiding.

The vesicouterine ligament is another critical site. This structure houses the vesical branches of the IHP, which provide motor innervation to the detrusor muscle. Resection of this ligament can cause denervation of the bladder, leading to detrusor atony and voiding dysfunction.[19] Plotti et al.[25] emphasize that damage to these branches not only impairs bladder emptying but also increases the risk of chronic urinary retention and associated complications, such as recurrent infections.

Early bladder complications after radical hysterectomy primarily manifest within the first 3-6 months and are characterized by parasympathetic dominance.[23] This results in a hypertonic bladder with low compliance and reduced capacity, affecting up to 85% of patients.[22] Additionally, some patients may experience loss of bladder sensation and urinary retention, with a residual urine volume exceeding normal limits in 10-15% of cases. If unmanaged, this can lead to irreversible changes such as detrusor hypertrophy and myogenic damage.

Late bladder complications, occurring beyond 6 months post-surgery, often stem from incomplete nerve recovery or aberrant nerve regeneration.[18] These include chronic urinary retention, overactive bladder symptoms, and stress urinary incontinence due to loss of internal sphincter tone. Reduced maximal urethral closure pressure, as reported in up to 40% of patients, exacerbates the risk of incontinence.[3] Inadequate management of early complications can predispose patients to long-term sequelae, such as bladder fibrosis and permanent detrusor dysfunction.[27]

Deep Endometriosis Surgery

Deep endometriosis (DE) poses significant challenges, as infiltration around pelvic autonomic nerves is common and leads to severe anatomical distortion. Bladder dysfunction following DE surgery arises through two primary mechanisms: direct infiltration of the nerve fibres by endometriotic lesions and collateral damage caused by surgical dissection or resection.[1,28] These surgeries aim for complete removal of diseased tissue but are fraught with risks to autonomic nerve integrity.

The localization and extent of endometriotic nodules play a critical role in determining the risk of postoperative bladder dysfunction. According to Boulus et al.,[4] urinary retention occurs in up to 30% of patients following DE surgery, with approximately 83% regaining normal voiding function within 18 months, while 17% may suffer from persistent dysfunction due to irreversible nerve damage. The risk strongly correlates with the proximity of lesions to autonomic structures such as the PSNs and the IHP.

Parametrial infiltration significantly increases the likelihood of autonomic nerve injury. Posterior DE nodules involving the rectovaginal septum, uterosacral ligaments, and the parametrium have been associated with a higher incidence of postoperative voiding difficulties.[29,30] Imboden et al.[31] also identified that ENZIAN B lesions larger than 3 cm significantly increase the risk of bladder dysfunction, likely due to their impact on the IHP and PSNs.These findings highlight the necessity of targeted nerve-sparing techniques when excising parametrial disease.

The need for colorectal resection further compounds the risk. Roman et al.[28] and Ballester et al.[32] showed that segmental colorectal resections—especially when combined with bilateral uterosacral ligament excision—lead to higher rates of postoperative neuropathy and prolonged bladder rehabilitation. Similarly, Landi et al.[33] found that even unilateral parametrectomy may cause bladder dysfunction, reinforcing the vulnerability of autonomic pathways. Dubernard et al.[34] demonstrated that extensive resections involving the uterosacral ligaments or ischial spine correlate with increased rates of intermittent self-catheterization (ISC).

Bladder dysfunction after DE surgery typically arises from either reversible neuropraxia or irreversible axonal injury. Neuropraxia, due to inflammation or thermal injury, preserves axonal continuity and often resolves over time. This explains the relatively high recovery rates observed in studies such as those by Boulus et al.[4] and Gabriel et al.[35]. In contrast, direct nerve transection during extensive parametrial or colorectal dissection may lead to permanent dysfunction.[36] Kovoor et al.[37] noted that transient urinary retention usually resolves within 5–7 days, while long-term retention—observed in 4–10% of cases—is more common after bilateral USL excisions or bowel resections.

It is also important to recognize that patients with endometriosis may present with lower urinary tract symptoms that are preexisting and attributable to the disease itself, rather than being solely iatrogenic in origin. Preoperative bladder dysfunction caused by nerve damage and infiltration by the endometriosis strongly predicts postoperative outcomes. According to Boulus et al.,[4] patients with preexisting nerve damage are more likely to experience persistent bladder voiding dysfunction postoperatively. This correlation underscores the importance of thorough preoperative assessments, including urodynamic testing and pelvic imaging, to identify patients at higher risk. Ballester et al.[32] emphasized that preoperative urodynamic testing provides valuable insights into baseline bladder function, helping to anticipate the likelihood of postoperative dysfunction and guide surgical planning. Similarly, Panel et al.[38] found that lower urinary tract symptoms identified preoperatively due to nerve damage caused by the disease in patients with DE strongly correlated with postoperative outcomes, indicating that early recognition of voiding disturbances allows for better perioperative counselling and tailored postoperative management. These findings highlight the need for comprehensive preoperative evaluation to mitigate long-term bladder dysfunction following DE surgery.

Sacrocolpopexy for Pelvic Organ Prolapse

Abdominal and minimally invasive sacrocolpopexy remain the gold standards for managing pelvic organ prolapse.[39] However, these procedures are associated with a significant risk of nerve injury, particularly during promontory dissection and vesicouterine ligament manipulation. Injuries to the SHP, HNs, and vesical branches of the IHP can result in debilitating bladder and bowel dysfunction.

Dissection at the sacral promontory poses a high risk to the SHP and HNs. According to Ercoli et al.,[40] the use of an inverted "L-shaped" peritoneal incision, medial to the right common iliac artery, minimizes nerve injury during promontory dissection. They emphasize that the presacral fascia must be carefully medialised to preserve the HNs and prevent iatrogenic denervation. [40] Cosma et al.[41] further demonstrated that nerve-sparing sacrocolpopexy significantly reduces the incidence of postoperative voiding dysfunction compared to the standard technique.

The vesical branches within the vesicouterine ligament are particularly vulnerable during anterior vaginal wall fixation. Shiozawa et al.[42] highlighted that precise delineation of the vesicouterine ligament and identification of the anterior longitudinal ligament during dissection can mitigate this risk. Preservation of these branches is crucial to maintaining bladder contractility and avoiding postoperative catheter dependency.

Nerve-sparing Techniques and Preventive Strategies

Nerve-sparing techniques have become a cornerstone in minimising autonomic nerve damage during pelvic surgeries. These approaches require a deep understanding of pelvic anatomy and surgical precision, emphasising the preservation of key autonomic structures while ensuring oncological and functional outcomes.

The concept of nerve-sparing was first introduced in oncological surgery, particularly in the context of radical hysterectomy, to reduce the significant morbidity associated with pelvic organ dysfunction.[43,19] The benefits of nerve-sparing approaches have been substantiated by numerous studies. Magrina et al.[44] demonstrated that patients undergoing nerve-sparing radical hysterectomy experienced significantly lower rates of urinary dysfunction without compromising oncological outcomes. Similarly, Kavallaris et al.[45] reported improved bladder function recovery in cases where precise nerve preservation techniques were employed during cervical cancer surgeries. According to Possover et al.,[46] laparoscopic exposure and precise dissection of PSNs markedly improved postoperative bladder function, significantly reducing dysfunction rates. Their findings highlighted the importance of meticulous surgical planning and real-time nerve identification in minimising complications, with reported rates of severe dysfunction being significantly low among patients undergoing radical pelvic surgeries. This approach underscores the critical role of nerve-sparing techniques in optimising both oncological and functional outcomes.

Over time, these principles have been adapted to other complex pelvic surgeries, including procedures for deep infiltrating endometriosis and prolapse surgery, to optimize outcomes and improve quality of life. Volpi et al.[47] was among the first to describe the identification and sparing of the nervous structures during DE surgery, with further advancements by Landi et al.[48] and Ceccaroni et al.,[13] who standardized the nerve-sparing technique for DE

excision. Their findings consistently demonstrated shorter catheterization times, lower rates of urinary retention, and better functional outcomes in nerve-sparing groups compared to standard techniques. Despite the benefits, nerve-sparing may not always be feasible due to disease infiltration, necessitating individualized surgical planning to balance functional preservation with disease control. According to Roman and Darwish,[1] bilateral involvement of critical structures, such as the uterosacral ligaments, significantly increases the likelihood of autonomic nerve damage, particularly to the IHP. This can result in profound bladder dysfunction, including detrusor atony and chronic urinary retention. They emphasized that preoperative imaging and advanced laparoscopic techniques are pivotal in assessing the extent of infiltration and guiding a nerve-sparing approach, even in complex cases. By employing precise dissection within avascular planes and preserving neural pathways where possible, the risk of severe postoperative bladder dysfunction can be minimized.

Emerging technologies such as artificial intelligence and augmented reality are providing new opportunities for enhancing pelvic nerve preservation. According to Kinoshita et al.,[49] Artificial intelligence (AI)-based nerve recognition models have demonstrated significant potential in improving intraoperative nerve identification. Their deep learning algorithm, trained on surgical videos, enhances surgeons' ability to accurately recognize autonomic nerves in real-time, reducing the risk of inadvertent nerve damage. Additionally, AI-assisted surgical education has shown improved learning outcomes for junior surgeons by enhancing nerve recognition skills through visual analysis, further supporting the integration of AI in nerve-sparing strategies.

The fundamental principle of nerve-sparing surgery is to minimize unnecessary nerve dissection, handling, and manipulation to prevent potential nerve damage. These techniques should be employed only when the nerves are directly affected by the disease, ensuring that interventions are justified and beneficial. It is strongly advised against performing unnecessary nerve dissection, as preserving nerve integrity is essential for maintaining postoperative function. Studies have emphasized that systematic full surgical dissection of pelvic nerves is not required unless there is direct nerve entrapment, reinforcing the importance of a tailored approach in complex gynaecological procedures. Research further supports that unnecessary nerve handling can increase the risk of postoperative dysfunction, making precise surgical planning crucial. A simplified approach to nerve-sparing using the HNs as landmarks has been proposed[50] to reduce the amount of nerve dissection while still providing the advantage for the direct visualization proposed by Possover.[46] These principles align with the article of Aleksandrov et al.[5] and the Strasbourg consensus by Wattiez et al.,[51] which stress that full nerve dissection should only be undertaken when absolutely necessary to preserve function and optimize patient outcomes.

The successful application of nerve-sparing strategies in pelvic surgeries relies on a combination of advanced anatomical knowledge, precise surgical techniques, and the integration of innovative tools such as neuro-navigation and artificial intelligence. These approaches facilitate real-time nerve identification, minimising intraoperative damage and optimising functional recovery. By prioritising nerve preservation, these methods contribute to improved patient outcomes, reduced postoperative complications, and an overall better quality of life.

Postoperative Management of Voiding Dysfunction

The management of voiding dysfunction following neurological damage during pelvic surgeries is crucial to restoring normal voiding function and preventing long-term bladder complications. Early identification and management of voiding dysfunction is critical. Clear, structured protocols for catheter removal and trial without catheter (TWOC) should be implemented postoperatively. While often implied, this step must be explicitly recognized as one of the most effective and straightforward strategies to ensure timely diagnosis and prevent long-term complications.

TWOC is a standardized protocol used to assess a patient's ability to void spontaneously after catheter removal. It typically involves removing the indwelling catheter 24–72 hours postoperatively, depending on the extent of nerve dissection, followed by close monitoring of spontaneous urination and post-void residual (PVR) volume measured with bladder ultrasound or catheterization. A PVR less than 100 mL is generally considered a successful trial. Higher residuals may necessitate ISC or reinsertion of the catheter. The implementation of a TWOC protocol enables early detection of voiding impairment, prevention of bladder overdistension, and timely initiation of rehabilitative strategies.

Patients with a post-void residual volume exceeding 100 mL are typically advised to perform ISC four to six times daily to prevent bladder overdistension and maintain low residual volumes.[4,52] Research, including studies by Boulus et al.[4] and de Resende et al.,[36] demonstrates that short-term bladder dysfunction is often attributed to neuropraxia caused by surgical manipulation, dissection, or thermal injury to the nerves. Neuropraxia generally resolves within 12-18 months when managed appropriately. To minimize unnecessary damage, excessive handling of or dissection near neural structures should be avoided, and neurosurgical principles should guide surgical interventions near delicate nerve pathways.[5]

In addition to ISC, pharmacological interventions such as alpha-adrenergic blockers are effective in reducing hypertonicity of the internal urethral sphincter, facilitating voiding, and alleviating retention.[4] Possover has highlighted the importance of addressing detrusor-sphincter dyssynergia, a common consequence of nerve damage, with pharmacological and supportive therapies.[2]

Electrostimulation therapy targeting the sacral or tibial nerves provides additional support in managing bladder dysfunction. Tibial nerve stimulation offers retrograde activation of sacral plexus pathways governing bladder function.[53] This can be achieved using percutaneous needle electrodes, transcutaneous surface electrodes, or wireless implantable devices. In the study by Boulus et al.,[4] all patients with bladder dysfunction were discharged with a transcutaneous tibial nerve electrostimulation device to stimulate the splanchnic nerves and promote recovery of voiding function. Regular follow-up assessments, including urodynamic studies and bladder ultrasounds, are essential for tracking recovery and tailoring therapeutic strategies. These evaluations guide decisions regarding the continuation or cessation of supportive treatments, ensuring that management aligns with individual patient needs.

Sacral Nerve Stimulation

Sacral nerve stimulation (SNS) involves the implantation of electrodes to deliver mild electrical pulses to the sacral nerves, particularly the S3 segment, to regulate bladder and anal sphincter activity. This procedure comprises a two-stage process: the initial phase involves the percutaneous insertion of a temporary electrode wire through the S3 sacral foramen to evaluate efficacy, followed by the second stage in which the electrode is connected to a permanent implantable pulse generator.[54] SNS has demonstrated success in alleviating symptoms of urinary incontinence, urgency, and retention in up to 70% of treated patients.[55] Aublé et al.'s[56] retrospective analysis of SNS for voiding dysfunction following endometriosis surgery revealed that 60% of patients experienced significant improvements in bladder function and quality of life after a median follow-up of 55 months. More than half of those who required clean ISC (CISC) before SNS were able to discontinue CISC post-treatment. However, complications such as infections, paraesthesia, and electrode migration were noted, highlighting the importance of careful patient selection and follow-up.

Agnello et al.[57] similarly reported that 69.2% of patients undergoing SNS following deep infiltrating endometriosis DE surgery demonstrated significant improvements in symptoms, including bladder sensitivity and emptying.[57] The study emphasized that SNS not only improves voiding efficiency but also reduces the need for daily catheterizations, making it a promising option for managing persistent voiding dysfunction.

The LION procedure, pioneered by Possover, provides a targeted approach by directly stimulating pelvic nerves, such as the SHP or pudendal nerve.[14,58] Unlike SNS, which modulates sacral nerves indirectly, the LION procedure delivers focused neuromodulation through laparoscopically placed electrodes adjacent to the target nerves. The nervous structures that could be reached and stimulated using the LION procedure are the sacral nerve roots S2-S4, which play a role in the treatment of bladder and bowel dysfunction after nerve injury, the SHP, in cases of bladder atonia secondary to radical pelvic surgery the pudendal nerve, stimulation of which might help patients with bladder or faecal incontinence, or the sciatic or lumbar nerves L1-L5, which might play a role in management of chronic pain or motor dysfunction. Possover's studies have demonstrated the efficacy of the LION procedure in treating refractory bladder atonia, showing significant improvements in voiding function and reductions in complications related to urinary retention.[59] This is a more invasive and complex procedure than SNS, which could be considered in select cases where SNS has failed.

Importance of Adequate Follow-up in Preventing Chronic Morbidity

The long-term outcomes of bladder dysfunction are closely tied to the quality of postoperative follow-up.

As detailed by Possover, inadequate follow-up can lead to insidious and irreversible complications.[2] Among the 47 patients evaluated in his study for bladder retention following DE surgeries, those without consistent postoperative monitoring often presented with advanced neurogenic bladder conditions, including chronic atony and severe detrusor dysfunction years after the surgery.

Failure to identify early signs of sensory or motor deficits with flow deterioration on postoperative uroflowmetry or clinical red flags such as reduced urinary frequency or the need for Valsalva manoeuvres to complete emptying, allows for progressive bladder overdistension. This can result in secondary myogenic damage, reduced elasticity, and eventual loss of detrusor contractility. Possover emphasized that regular assessments of post-void residual volumes and bladder sensation, paired with timely interventions like ISC, are critical to preventing such outcomes.

Without proactive management, complications such as recurrent urinary tract infections, overflow incontinence, and even renal impairment due to bilateral ureterohydronephrosis may develop. The findings from Possover's study underline the necessity for structured follow-up protocols focusing not only on voiding function but also on sensory and neurological assessments of the bladder. This approach ensures early detection of dysfunctions, timely interventions, and preservation of long-term bladder health.

Conclusion

Bladder dysfunction following advanced pelvic surgeries remains a significant challenge that can greatly affect a patient's quality of life. A comprehensive approach incorporating meticulous surgical planning, a profound understanding of pelvic neural anatomy, and the implementation of nerve-sparing techniques are essential to minimize the risk of autonomic nerve injury. Avoiding unnecessary nerve dissection and manipulation is paramount, as excessive handling can result in irreversible damage and long-term functional impairment.

A tailored surgical approach, guided by preoperative imaging and intraoperative neuro-navigation, allows for precise dissection while preserving essential nerve structures. When disease infiltration creates the need for nerve resection, selective dissection should be employed to balance oncological control with functional preservation. Emerging technologies such as artificial intelligence and augmented reality further enhance intraoperative nerve identification, reducing the risk of inadvertent damage and improving surgical outcomes.

Beyond intraoperative strategies, postoperative management plays a crucial role in bladder function recovery. Multimodal rehabilitation, including pharmacological therapies, electrostimulation, and neuromodulation techniques, is essential for restoring autonomic control and preventing long-term complications such as detrusor hypotonia or atonia or chronic urinary retention. Early and structured follow-up, incorporating urodynamic and uroflowmetry assessments and targeted interventions, is critical in identifying dysfunction at an early stage and preventing irreversible sequelae.

Ultimately, optimising patient outcomes in pelvic surgery requires a multidisciplinary effort that integrates advanced surgical techniques, technological innovations, and individualized patient care strategies. By prioritising nerve preservation and ensuring meticulous postoperative management, the risk of bladder dysfunction can be significantly mitigated, leading to improved patient recovery, functional outcomes, and overall quality of life.

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VIDEO ARTICLE

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Laparoscopic hysterectomy for deep infiltrating endometriosis: anterior colpotomy first technique

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ABSTRACT

Background: Deep infiltrating endometriosis, particularly involving the rectovaginal space, represents one of the most challenging surgical benign gynaecologic conditions. While hysterectomy is a definitive option in women without fertility desire, these procedures are technically complex and associated with higher risks of complications. The anterior colpotomy first technique has been developed as an alternative approach to simplify dissection and improve surgical safety in such advanced cases.

Objectives: Stepwise video demonstration of laparoscopic hysterectomy for deep infiltrating endometriosis involving rectovaginal space by the anterior colpotomy first technique.

Participant: A 47-year-old woman presented with dysmenorrhea, dyspareunia and dyschezia unresponsive to medical treatment. Transvaginal ultrasound and magnetic resonance imaging (MRI) revealed bilateral 5 cm endometriomas, 2 cm endometriotic nodules on both utero-sacral ligaments, and a 4 cm nodule in the Douglas pouch. A further 3 cm superficial endometriotic nodule on the rectosigmoid colon was also revealed on MRI. According to the Enzian classification, the score was A3, B2/2, C3. Laparoscopic hysterectomy, bilateral salpingo-oophorectomy and endometriotic excision of lesions were planned. Operation time was 210 minutes, and blood loss was 50 mL. On the postoperative fourth day patient was discharged. The patient remained pain-free at 25 months follow-up.

Intervention: Surgical steps for anterior colpotomy first technique could be divided into following steps: 1) entry into retroperitoneum, 2) ligation of uterine artery at the branching point from hypogastric artery, 3) development of vesicouterine space, 4) dissection of ureter and transection of lateral parametrium, 5) combining lateral and anterior compartments, 6) anterior colpotomy, 7) developing rectovaginal space from lateral to midline, 8) completion of posterior colpotomy, 9) excision of endometriotic nodule and leaving nodule on rectosigmoid colon, 10) completion of hysterectomy, 11) rectal shaving and resection of endometriotic lesions, 12) Bubble test, assessment of ureteral integrity and ladder filling with saline. In this technique, it is more feasible to do anterior colpotomy first and to develop rectovaginal space from lateral sides towards midline instead of dealing with the posterior compartment at the beginning of surgery. Ultimately endometriotic nodule between the rectosigmoid colon and the uterus is cut, leaving the endometriotic nodule on the rectosigmoid colon.

Conclusions: Laparoscopic hysterectomy with anterior colpotomy first technique makes complicated hysterectomies easier in patients with deep infiltrating endometriosis.

What is New? This video article presents a stepwise demonstration of the anterior colpotomy first technique for laparoscopic hysterectomy in deep infiltrating endometriosis. By prioritising anterior colpotomy and developing the rectovaginal space from lateral to midline, this approach simplifies complex dissections, reduces the risk of rectal injury, and offers a safer, more reproducible strategy for advanced endometriosis cases.

Keywords: Deep infiltrating endometriosis, laparoscopic hysterectomy, anterior colpotomy, endometriosis surgery

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Introduction

Endometriosis is a debilitating chronic disease associated with significant pelvic pain.[1,2] In women without a desire for fertility, hysterectomy with or without salpingo-oophorectomy is the definitive treatment. As these women were previously operated on multiple times, the final surgery is challenging, frequently includes radical organ resections.[3,4] In our department, in the last 8 years, we have been using the anterior colpotomy first technique when hysterectomy is planned for deep infiltrating endometriosis rather than approaching from the posterior compartment first. In this technique, dissection of the posterior compartment (pararectal and rectovaginal spaces) is performed after the anterior colpotomy procedure. By following predetermined steps, the so-called "anterior colpotomy first technique", this complicated surgery turns into a simpler and faster operation. In this video article, a stepwise demonstration of laparoscopic hysterectomy for deep infiltrating endometriosis by the anterior colpotomy first technique is demonstrated.

Methods

A 47-year-old woman with 3 prior surgeries for endometriosis had significant dysmenorrhea (9/10), dyspareunia (8/10) and dyschezia (7/10) unresponsive to medical treatment. She underwent a colonoscopy with normal findings. Transvaginal ultrasound and magnetic resonance imaging (MRI) revealed bilateral 5 cm endometriomas, 2 cm endometriotic nodules on both uterosacral ligaments, and a 4 cm nodule in the Douglas pouch. A further 3 cm superficial endometriotic nodule on the rectosigmoid colon was also revealed on MRI. According to the Enzian classification, the score was A3, B2/2, C3. Laparoscopic hysterectomy, bilateral salpingo-oophorectomy and endometriotic excision of lesions were planned.

Results

The trocar configuration follows a diamond-shaped arrangement. The surgeon stands on the left side of the patient, while the first assistant is on the right. At the beginning of the surgery, the initial laparoscopic view revealed bilateral "kissing ovaries" and a frozen pelvis with an endometriotic nodule (Figure 1). The surgical approach (laparoscopic hysterectomy for deep infiltrating endometriosis involving rectovaginal space by anterior colpotomy first technique) could be divided into following steps: 1) entry into retroperitoneum by ligation and transection of round ligament, 2) ligation of uterine artery at the branching point from hypogastric artery, 3) development of vesicouterine space, 4) dissection of ureter up to ureteric tunnel and transection of lateral parametrium, 5) combining lateral and anterior compartments, 6) anterior colpotomy, 7) developing rectovaginal space from lateral to midline, 8) completion of posterior colpotomy, 9) excision of endometriotic nodule and leaving nodule on rectosigmoid colon, 10) completion of hysterectomy, 11) rectal shaving and resection of endometriotic lesions, 12) bubble test assessment of ureteral integrity bladder filling with saline.

In this video, the patient underwent bilateral salpingo-oophorectomy. Ovaries could be preserved depending on the patient and involvement of the ovaries, and this is not an essential step of this surgery. Moreover, the radicality of the hysterectomy is tailored according the extent of the disease in the parametrium. In this case, 1-2 cm lateral parametrium was involved with the disease and was excised. The size of the superficial rectal nodule was 3 cm without any sign of obstruction or involvement of the rectal mucosa. Rectal shaving to clear the endometriotic lesion was decided. The integrity of the rectosigmoid colon was confirmed using a bubble test. The serosa was reinforced with three interrupted sutures at the end of the surgery. Total operation time was 210 minutes, and total blood loss was 50 mL without any intraoperative complications. On the postoperative fourth day patient was discharged. It has been 25 months since the surgery, and she has no pain symptoms (pelvic pain 1/10, dyspareunia 1/10 and dyschezia 0/10).

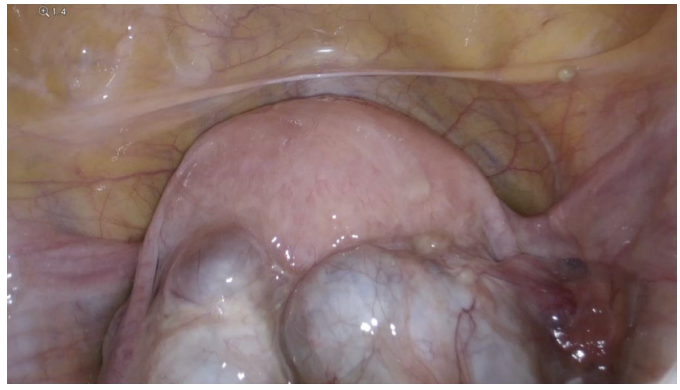

Figure 1. Laparoscopic view demonstrating bilateral kissing ovaries in a frozen pelvis associated with an endometriotic nodule on Douglas.

Discussion

Total hysterectomy is an option and has an additional benefit for the control of endometriosis-associated pain compared to conservative surgery when fertility is not a concern.[5] However, the dissections carried out in this complicated surgery are extensive, and the type of operation is not a simple hysterectomy, but a more radical approach should be performed to preserve vital structures.

The rate of intraoperative complications is about 3% and any major postoperative complication is 9% in women undergoing surgery for complex endometriosis. About 10% severe complication rate (Clavien-Dindo grade >2) was reported for women undergoing laparoscopic hysterectomy with stage 3-4 endometriosis.[3,6,7] When deep infiltrating endometriosis is of concern, even in highly specialised surgical departments, these are high-risk surgeries with a higher possibility of significant complications.

In a standard fashion, surgery proceeds from the lateral compartment (development of pararectal spaces, ureterolysis) to posterior spaces (rectovaginal pouch), (i.e., lateral to medial approach). On the contrary, in our anterior colpotomy first technique, in our opinion, it would be more feasible to do anterior colpotomy first and then to develop rectovaginal space from lateral sides towards midline instead of dealing with the posterior compartment at the beginning of the surgery.[3] Ultimately, the endometriotic nodule between the rectosigmoid colon and uterus is transected, leaving an endometriotic nodule on the rectosigmoid colon, which will subsequently be resected. In this technique, when anterior colpotomy is performed, the healthy tissue and right dissection plane in the rectovaginal pouch is clearly visible, and the most distal part of the lesion on the rectosigmoid colon is easily seen. In this way, dissection of the rectovaginal space becomes easier, and a possible injury to the rectosigmoid colon is significantly reduced, particularly when rectal shaving is planned. Beginning from 2017, we have been performing hysterectomies for deep infiltrating endometriosis by using the anterior colpotomy first technique, and we did not experience any surgery-related bowel complication.

There are a number of studies reporting surgical outcomes of hysterectomy performed for endometriosis, but only in a limited number of these studies, anatomical and surgical details of the type and hysterectomy had been addressed. Rosati et al.[8] presented 23 patients undergoing radical hysterectomy for deep infiltrating endometriosis with the parametria involved. In this study, the steps of the procedure were described and functional results were presented. The so called "nerve-sparing radical hysterectomy for parametrial deep endometriosis" was described as adhesiolysis and ovarian surgery if needed, transection of round ligaments, incision of broad ligament, identification of uterine arteries and veins branching from internal iliac vessels, formation of medial and lateral pararectal spaces, development of medial paravesical space, dissection of vesicouterine space and exposition of 1-2 cm distal vagina, ligation of uterine artery at its origin, lateralization of ureters and ureterolysis, lateralization of hypogastric nerves, dissection of rectavaginal space, nerve sparing tailored parametrectomy and finally colpotomy and uterus removal. The technique resembles a radical hysterectomy performed for cervical cancer. The rate of complications (Clavien-Dindo grade 1, 2) was 34%.

Hysterectomy for deep infiltrating endometriosis is a challenging surgical intervention compared to other benign indications. The surgery requires significant expertise, and strict steps should be followed to complete the surgery without any visible endometriotic lesions. Different techniques have been described for hysterectomy associated with endometriosis, but there is no consensus for the optimal surgical approach. Anterior colpotomy technique is an alternative way to perform hysterectomy for complex endometriosis cases, and in our opinion, makes the dissection of the rectovaginal pouch easier and faster.

Conclusion

Laparoscopic hysterectomy with anterior colpotomy first technique makes complicated hysterectomies easier in patients with deep infiltrating endometriosis involving the pouch of douglas.

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Data sharing: Data and related information are available from the corresponding author upon request.

Transparency: The authors affirm that the manuscript is an honest, accurate, and transparent account of the studies assessed.

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Video 1. https://www.youtube.com/watch?v=ETkU31rrbYA

VIDEO ARTICLE

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Innovative laparoscopic technique for #ENZIAN C3 intestinal endometriotic nodule and concurrent uterine fibroids: NOSES

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ABSTRACT

Background: Deep infiltrating endometriosis (DIE) is a severe condition which requires innovative surgical approaches to address complex anatomical distortions, reduce operative risks, and enhance outcomes.

Objectives: To demonstrate the effectiveness of integrating three advanced surgical techniques-reverse laparoscopic technique, natural orifice specimen extraction surgery (NOSES), and advanced intraoperative bleeding control strategies-in managing a complex case of DIE.

Participant: A 29-year-old nulligravida patient presented with hypermenorrhea, dysmenorrhea, urinary symptoms, and bowel dysfunction. Magnetic resonance imaging revealed a 3.3 cm #ENZIAN C3 intestinal nodule, bilateral ovarian endometriomas and multiple uterine fibroids.

Intervention: Advanced techniques reverse laparoscopic technique, associated with intraoperative bleeding control strategies such as vasopressin injection, temporary ligation of uterine arteries, and infundibulopelvic ligaments; combined with NOSES for specimen extraction. Patient included in this video gave consent for the publication of this video article and its online posting, including social media, journal's website, scientific literature websites, and other applicable sites. Operative time, estimated blood loss, preservation of anatomical structures, postoperative recovery time, symptom resolution, and complications were assessed. Surgery was completed in 180 minutes, with minimal blood loss (40 cc). The patient tolerated a general anti-inflammatory diet by postoperative day two and was discharged without complications. One month postoperatively, the patient showed significant symptom improvement.

Conclusions: The combination of different techniques in the same surgery can clearly lead to favourable results and outcomes, ensuring optimal recovery with superior cosmetic and functional outcomes, particularly in fertility-preserving surgeries.

What is New? The combination of NOSES, the reverse laparoscopic technique, and advanced bleeding control strategies ensures optimal management for complex procedures in DIE surgeries with fertility preservation.

Keywords: Natural orifice specimen extraction surgery, deep infiltrating endometriosis, infundibulopelvic ligament, magnetic resonance imaging, estimated blood loss, operative time, rectal endometriosis, uterine fibroids, laparoscopic colorectal resection

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Introduction

Deep infiltrating endometriosis (DIE) is a severe form of endometriosis characterised by the invasion of endometrial-like tissue into structures such as the bowel, bladder, and uterine ligaments. An #ENZIAN C3 nodule, according to this classification, describes endometriosis involving the lower rectum, often causing significant anatomical distortion and intestinal obstructive symptoms. Surgical management requires advanced techniques to mitigate risks, such as nerve injury, excessive blood loss, and long operative time (OT).

Unlike the traditional technique, which involves identifying and removing the diseased areas first, the Reverse Technique begins with the separation of healthy from affected tissues, moving toward the diseased.[1] The final step in the reverse technique involves dissection of the affected tissues and rectal nodules, allowing the surgeon to establish clean surgical planes and minimise trauma to critical structures.

Additionally, advanced intraoperative bleeding control strategies, such as vasopressin injection into the uterine muscle, temporary ligation of uterine arteries during myomectomy, and temporary ligation of the infundibulopelvic (IP) ligaments during endometrioma cystectomy, significantly reduce blood loss and the need for extensive coagulation, preserving ovarian and uterine integrity.[2,3] Together, these methods increase surgical precision and optimise patient outcomes. When combined with natural orifice specimen extraction surgery (NOSES), which utilizes natural orifices for specimen extraction, this approach reduces operative time and enhances recovery by avoiding large abdominal incisions.[4-6]

Methods

This case involves a 29-year-old nulligravida patient presenting with severe hypermenorrhoea, dysmenorrhea, urinary symptoms (hesitancy, incomplete voiding), and bowel symptoms (severe constipation). Magnetic resonance imaging (MRI) findings revealed:

- A 3.3 cm ENZIAN C3 endometriotic nodule located 14.5 cm from the anal verge, infiltrating 40% of the circumference of the rectum.

- Bilateral ovarian endometriomas (7 cm on the left and 2.9 cm on the right).

- Uterine fibroids (UF) (largest measuring 4.3 cm, FIGO 2-5).

- Obliteration of the rectouterine septum with associated uterosacral ligament thickening.

- #ENZIAN (2021): P0, O3/2, T3/3, A2, B1/1, C3, FA.

Patient included in this video gave consent for the publication of this video article and it's online posting, including social media, journal's website, scientific literature websites, and other applicable sites.

Main Outcomes

1. OT.

2. Estimated blood loss (EBL).

3. Preservation of critical anatomical structures.

4. Postoperative recovery time.

5. Symptom resolution and cosmetic results.

6. Immediate and mediate postoperative complications.

Results

The surgery was completed in 180 minutes (Video 1). EBL was minimal at 40 cc. The patient was monitored during hospitalisation with procalcitonin and C-reactive protein levels as a parameter of colorectal anastomosis dehiscence, and the comparison curve at 24, 48, and 72 hours remained stable without significant increases. She was discharged from the hospital and resumed a general anti-inflammatory diet after the second day of hospitalisation, with no further complications. The patient showed significant improvement of symptoms one month after surgery.

Discussion

The NOSE technique offers significant advantages in the management of intestinal endometriosis. By utilizing the anus as the natural extraction site, it eliminates the need for a mini-laparotomy, thereby reducing surgical trauma, postoperative pain, and recovery time. Unlike conventional laparoscopic colorectal resection (CLR), which requires an additional 4-5 cm incision for specimen extraction and anvil insertion, NOSE eliminates the need for abdominal wall opening, avoiding muscle and aponeurosis incision, while also reducing intestinal manipulation, decreases postoperative ileus risk, and allows for faster return of bowel function.[7] Furthermore, the absence of external incisions lowers the incidence of wound infections and incisional hernias, providing both functional and cosmetic benefits.[6-8] Large case series and randomised controlled trials have demonstrated

that NOSE patients require less postoperative analgesia, contributing to an overall better recovery experience. While the technique requires a specific learning curve, when performed by experienced surgeons, it does not increase surgical time and may, in fact, shorten it. With no significant drawbacks, NOSE represents a safe, efficient, and superior alternative to traditional CLR in endometriosis patients requiring intestinal surgery. The only potential limitation is the learning curve associated with mastering the technique. However, in surgical teams proficient in both NOSE and CLR, we have observed that surgical time is reduced, further improving efficiency.

The reverse technique further improves surgical outcomes by prioritising the dissection of healthy tissue planes before addressing the diseased areas.[1,9] By starting the dissection in less affected areas, the surgeon gains better visibility and access to deeper regions, reducing the risk of injury to vital structures. In contrast, starting from the more severely affected areas, as in standard techniques, can lead to accidental damage due to poor visibility or complex anatomical distortions.[10,11] Therefore, this approach reduces operative complexity as it improves visibility in affected regions and minimises the risk of injury to critical structures such as the hypogastric nerves and ureters. By preserving these anatomical structures, the Reverse Technique optimises surgical precision and patient safety.

Advanced intraoperative bleeding control strategies significantly contributed to the success of this surgery. Vasopressin injection into the uterine muscle effectively reduced intraoperative bleeding during the myomectomy, limiting the need for blood transfusions and enhancing surgical efficiency by improving visualisation of the surgical field due to reduced bleeding.[2] Temporary ligation of the uterine arteries provided additional control over blood loss, further decreasing the need for postoperative interventions. Additionally, temporary ligation of the IP ligaments during the endometrioma cystectomy minimised bleeding and reduced the necessity for extensive coagulation energy, preserving ovarian tissue integrity and function.[3] In fertility-preserving surgeries like this, these strategies play a pivotal role in ensuring minimal damage to reproductive structures while achieving optimal outcomes.[3,11]

This case highlights the significance of integrating multiple advanced techniques in one procedure. The fusion of the reverse laparoscopic technique, NOSES, and bleeding control strategies not only optimises surgical time and minimises complications but also ensures improved cosmetic and functional outcomes. By integrating these advanced techniques, the OT was reduced to 180 minutes, significantly shorter than the conventional approach, which typically averages 4 hours. Additionally, the procedure resulted in minimal blood loss of only 40 cc, and the patient achieved an optimal postoperative recovery, free from complications.

The combination of advanced laparoscopic techniques allows for improved surgical times, reduced blood loss, and lower risk of complications. It highlights the potential for comprehensive management of complex cases of DIE, offering a paradigm shift in the surgical treatment of this challenging condition.

Conclusion

This video article demonstrates three advanced and innovative surgical techniques, combining the reverse laparoscopic technique, the NOSES, and advanced intraoperative bleeding control strategies, for the treatment of DIE involving an #ENZIAN C3 intestinal nodule and concurrent UF. The combination of different techniques in the same surgery can clearly lead to favourable results and outcomes, ensuring optimal recovery with superior cosmetic and functional outcomes, particularly in fertility-preserving surgeries.

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Data sharing: The data supporting the findings of this study are not publicly available due to concerns regarding patient confidentiality and institutional restrictions. However, de-identified data may be made available from the corresponding author upon reasonable request, in accordance with ethical and legal standards.

Transparency: The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported. No important aspects of the study have been omitted, and any deviations from the original protocol have been clearly explained within the manuscript.

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Video 1. The Video demonstrates multiple innovative and advanced techniques for laparoscopic pelvic surgery in cases of deep endometriosis with intestinal involvement, while reinforcing critical concepts of pelvic anatomy.

https://youtu.be/yqaXMWxC3SY

VIDEO ARTICLE

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Laparoscopic management of presacral retroperitoneal haematoma after sacrocolpopexy

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ABSTRACT

Background: Minimally invasive sacrocolpopexy (SCP) has emerged as the gold standard procedure for pelvic organ prolapse. However, it entails a deep surgical dissection, essential for proper mesh positioning, and is not devoid of intraoperative and postoperative complications, including sporadic cases of potentially life-threatening intraoperative bleeding or postoperative haematomashaematomas. The appropriate management of bleeding complications in this area varies depending on the individual case and presence of hemodynamic instability, from emergency open surgery to a conservative wait-and-see approach.

Objectives: To illustrate an effective method for the management of bleeding complications of SCP and raise awareness about this unusual complication.

Participant: A 69-year-old woman underwent laparoscopic revision surgery due to evidence of a voluminous presacral haematoma on the second postoperative day after SCP.

Intervention: The effectiveness of minimally invasive revision surgery for the management of voluminous presacral haematoma following laparoscopic SCP was assessed. Laparoscopic revision surgery allowed for the complete drainage of the haematoma without complications, resulting in discharge on postoperativeday seven.

Conclusions: The video reviews the steps of the laparoscopic approach for performing a successful and safe revision surgery to manage presacral haematomas after SCP, and illustrates the procedure's adaptability, also providing specific tips and tricks to successfully perform this procedure without the need for mesh removal, thereby preserving the best outcome for the patient.

What is New? This is the first description of the surgical management of a retroperitoneal hematoma following colposacropexy. The study's conclusions provide a valuable resource for gynecologists facing patients presenting with a retroperitoneal presacral hematoma after prosthetic surgery for prolapse.

Keywords: Sacrocolpopexy, laparoscopy, surgical complications, presacral bleeding, retroperitoneal haematoma, revision surgery

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Introduction

Minimally invasive sacrocolpopexy (SCP) has emerged as one of the preferred surgical approaches for managing pelvic organ prolapse (POP) but it is not devoid of intraoperative and postoperative complications. Sporadic life-threatening complications, including vascular lesions leading to intraoperative bleeding and postoperative haematomas, have also been reported. Overall, the incidence of serious vascular injuries, bleeding events requiring blood transfusion, and postoperative haematomas is lower than 1%, with presacral space and sacral promontory being the most common anatomical sites.[1-4]

Therefore, an adequate and careful dissection of the presacral space during SCP is mandatory.[5]

The appropriate management of bleeding complications in this area varies depending on the individual case. Instances of significant and active bleeding resulting in hemodynamic instability often necessitate emergency open surgery. Conversely, postoperative bleeding or haematomas without notable alterations in vital signs may be addressed through minimally invasive surgery or a conservative "wait-and-see" approach.[4,6]

If conservative measures fail due to the patient's clinical condition or the haematomas size, surgical treatment becomes necessary, especially if the haematoma is adjacent to the prosthetic material. This underscores the importance for gynaecologists to be adept at managing such cases with simple and effective procedures to drain it in the least invasive way.

Methods

We present the case of a 69-year-old woman who developed a retroperitoneal haematoma following laparoscopic sacrocolpopexy (LSCP) intervention for multicompartmental POP.

The patient, a Caucasian non-smoker with a body mass index of 26.7 kg/m^2, was referred to our Urogynaecology Department at Fondazione Policlinico Universitario A. Gemelli IRCCS for symptomatic POP. She had a history of three pregnancies with three caesarean deliveries and entered menopause at 44 years of age. Her past medical history included hypertension, arrhythmia, and prior laparoscopic cholecystectomy.

Prior to surgery, the patient received detailed surgical counselling on the different surgical approaches, including prosthetic surgery and native tissue repair techniques. She was made aware of the risks of the procedure and signed an informed consent allowing the use of personal data.

Following appropriate preoperative evaluation, the patient underwent a standard nerve-sparing LSCP procedure,[5,7] with a total operating time of 160 min and an estimated blood loss of less than 100 mL. On the second postoperative day, the patient experienced abdominal pain and anaemia, with haemoglobin levels decreasing from 12.1 g/dL to 9.1 g/dL. The patient's vital signs were within normal limits, except for mild hypotension and moderate tachycardia. Physical examination revealed abdominal swelling and perineal ecchymosis. Thus, an abdominal ultrasound was performed, revealing the presence of a voluminous haematoma in the soft tissue of the presacral region, which was confirmed by a computed tomography (CT) scan having a cranial-caudal extension of 10.5 cm and a lateral-lateral extension of 5.5 cm. Following this, the patient underwent emergency minimally invasive revision surgery.

Results

Under general anaesthesia, the patient underwent emergency minimally invasive surgery for the drainage of the presacral retroperitoneal haematoma and abdominal cavity lavage (Video 1). The ports were placed in the same positions as previous surgery. At the exploration of the abdominal cavity, there was no evidence of hemoperitoneum, but the epiploic appendixes of the sigmoid colon were filled with ecchymosis. The parietal peritoneum was reopened at the presacral level. The mesh was correctly positioned but surrounded by a voluminous haematoma, partly organised and mixed with clots, which filled the retroperitoneal space up to the plane of the levator ani (Figure 1a). After clots removal, active haemorrhage was observed at the lateral pelvic wall near the levator ani muscle, likely of venous origin. After appropriate identification of anatomical landmarks, including ipsilateral ureter, the vessel was coagulated, and the haemostasis was finalised with a haemostatic matrix (Floseal®) (Figure 1b). The peritoneal pocket was closed with 2-0 Stratafix (Figure 1c). Subsequently, a pelvic excavation toilet was performed with repeated washing. Total operating time was 78 min with an estimated blood loss of 100 ml. After reoperation, the postoperative course proceeded uneventfully, leading to the patient's discharge a few days later (day 7).

At the 1- and 6-month postoperative follow-up, the patient reported a complete resolution of all symptoms related to POP.

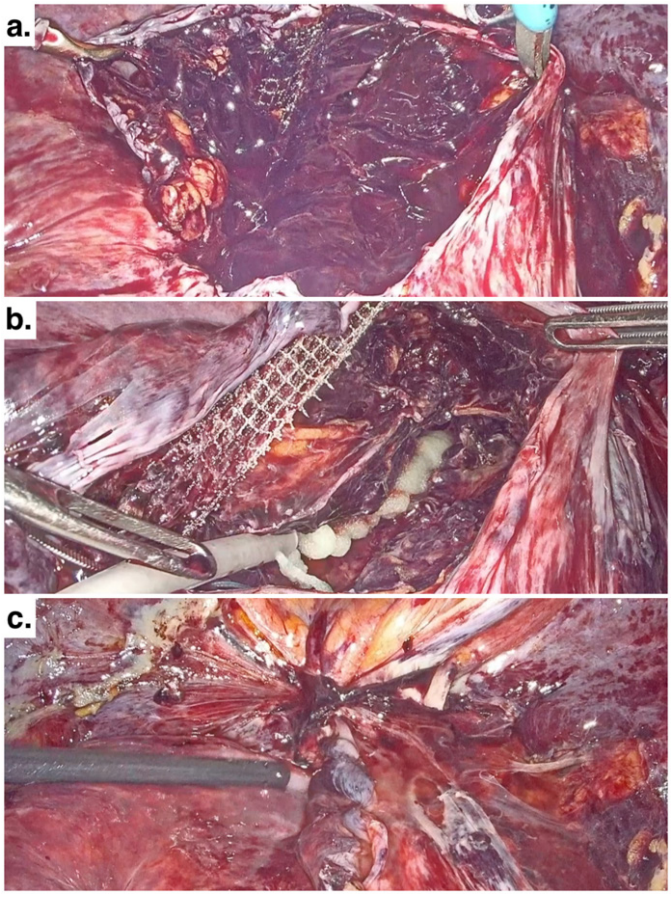

Figure 1. Key steps of revision surgery. a) Shows a view of the retroperitoneal haematoma at the presacral region before drainage. b) Shows the presacral space after blood clots removal and insertion of a haemostatic agent using a flexible cannula. c) Shows the field at the end of the procedure after reclosure of the peritoneum.

Discussion

SCP usually has a low rate of intra- and postoperative complications. Early postoperative issues include urinary tract and surgical site infections, respiratory or thromboembolic events. Minimally invasive techniques are associated with fewer complications, reduced blood transfusions, shorter hospital stays, and fewer readmissions compared to the abdominal approach.[1,8-11] Although rare, serious complications of SCP include vascular haemorrhage, bowel injury, discitis, mesh erosion, and death. Life-threatening bleeding complications, such as left iliac venotomy, right hypogastric vessel injury, and presacral bleeding, may require conversion to laparotomy. The incidence of major vascular injuries, transfusion-requiring bleeding, and retroperitoneal haematomas is less than 1%, with presacral space and sacral promontory being the most common sites for significant bleeding.[1-4,8,12]

A thorough understanding of surgical anatomy is crucial to minimise complications in SCP. The procedure involves deep dissection for mesh placement, extending from the presacral space to the avascular regions between vaginal walls and adjacent organs. Identifying anatomical boundaries is essential to avoid vascular injury.[5]

The presacral space is critical due to the risk of haemorrhage and ureteral injury. On average, the distances between the right ureter and iliac vessels to the midsacral promontory are 3 cm. Nevertheless, there is a wide interindividual variability concerning vessel diameter, presence of anatomical vascular variants, and distance from the vessels and ureter to the midline. The left common iliac vein is often less than 1 cm from the sacral promontory. These anatomical differences highlight the importance of careful dissection, starting with an incision along the medial border of the right common iliac artery, followed by medial displacement to identify key structures, including the right inferior hypogastric nerve and middle sacral artery and vein.[5,13-15] For these reasons, bleeding complications may arise from injuries to the vessels of the presacral region. Nevertheless, in our case, the bleeding source was identified at the level of levator ani muscle, highlighting the need for careful dissection and haemostasis also at this level.

Pelvic haematomas are often diagnosed through clinical signs such as abdominal pain, swelling, and fluctuating vital signs, with contrast-enhanced CT scans being the gold standard for diagnosis.[4,6,16] Bleeding complications are managed based on severity. Active bleeding causing hemodynamic instability usually requires emergency open surgery, while less severe bleeding or haematomas can be addressed conservatively or with minimally invasive techniques.[4,6,17]

Conservative treatment may include antibiotics, drainage, or embolisation. If these fail, surgical intervention is required, utilising haemostatic agents, electrocoagulation, suturing, vessel ligation, or packing in case of significant or unclear bleeding. Intraoperative identification of the bleeding source is essential for selecting the appropriate haemostatic technique. Electrocoagulation is effective for mild bleeding from small vessels but requires caution due to the risk of vessels' damage and retraction, possibly leading to bleeding worsening.[4,6,16,18]

In our case, minimally invasive revision surgery was performed as the first choice due to the haematomas dimensions and risk for postoperative infection related to the proximity to prosthetic material.

Video review from the original procedure, if available, can aid in guiding revision surgery. Complete haematoma drainage is essential, particularly near prosthetic material, with warm saline irrigation helping to dissolve clots. Local haemostatic agents can be used, especially when the bleeding source is unclear or involves smaller vessels.

Conclusion

Presacral bleeding represents a potentially life-threatening complication of pelvic surgery, particularly SCP. The occurrence of this complication underscores the importance of understanding the anatomical intricacies of presacral and retroperitoneal spaces during SCP procedures. To our knowledge, this study presents the first report of minimally invasive surgical management of a retroperitoneal haematoma following LSCP intervention for POP. By providing this detailed video of a complex minimally invasive revision surgery and sharing these tips, we hope that it may be a valuable resource for gynaecologists when faced with a patient presenting with a retroperitoneal presacral haematoma after prosthetic surgery for POP.

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Data sharing: This statement describes the availability of data supporting the results reported in the paper. Due to the nature of this video case report describing a single clinical case, no additional datasets were generated or archived in a public repository. The video material supporting the case is included within the article. Sharing additional data is not applicable as it may compromise patient confidentiality and ethical standards. Further information can be made available upon reasonable request.

Transparency: The lead author affirms that this manuscript is an honest, accurate, and transparent account of the clinical case being reported; that no important aspects of the case have been omitted; and that any deviations from standard clinical practice have been fully explained.

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Video 1. Laparoscopic revision surgery. Steps of laparoscopic approach for performing a successful and safe revision surgery to manage presacral haematomas after laparoscopic sacrocolpopexy.

https://youtu.be/80cYYew02ZE

VIDEO ARTICLE

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10-step approach for laparoscopic pectopexy combined with supracervical hysterectomy

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ABSTRACT

Background: Apical prolapse, characterised by the descent of the vaginal apex, uterus, or cervix, is commonly treated by laparoscopic sacrocolpopexy, the current gold standard. Laparoscopic pectopexy (LP) has emerged as an effective alternative, particularly advantageous for obese patients due to its technical approach.

Objectives: To demonstrate a standardised 10-step surgical technique for performing laparoscopic pectopexy combined with supracervical hysterectomy, aiming to provide a safe and reproducible method for the treatment of apical prolapse.

Participant: A 68-year-old female patient presenting with symptomatic, advanced apical pelvic organ prolapse (POP-Q stage IV) consented to the procedure.

Intervention: The patient underwent LP following a 10-step surgical protocol: (1) division of the round ligaments and dissection towards the pelvic sidewall, (2) identification of the iliopectineal ligament, (3) division of the uterovesical peritoneum and development of the vesicovaginal space, (4) supracervical hysterectomy, (5) opening of the rectovaginal space, (6) closure of the cervical canal, (7) mesh insertion and fixation to cervix, anterior and posterior vagina, (8) bilateral anchoring of the mesh lateral arms to the iliopectineal ligaments, (9) closure of the overlying peritoneum, and (10) morcellation of the uterine corpus. The surgery was completed with minimal blood loss and no intraoperative complications.

Conclusions: LP combined with supracervical hysterectomy is a safe, effective, and reproducible surgical option for apical prolapse repair, demonstrating favourable perioperative outcomes and early discharge.

What is New? This video-based demonstration introduces a standardised 10-step approach to LP combined with supracervical hysterectomy, facilitating adoption of this technique by surgeons with advanced minimally invasive skills, and highlighting its potential benefits, especially in obese patients.

Keywords: Pectopexy, pelvic organ prolapse, laparoscopy

Introduction

Pelvic organ prolapse (POP) is defined as a protrusion or herniation of the pelvic organs through the vaginal walls and pelvic floor, a commonly-occurring condition which has a significant negative impact on women's quality of life.[1,2] Apical compartment prolapse is the result of the descent of the cervix or the vaginal vault after hysterectomy. The gold-standard method of surgical correction is sacrocolpopexy.[3,4] The laparoscopic approach is preferred to laparotomy due to its numerous benefits for the patients, such as shorter recovery time, shorter hospitalisation and less postoperative pain.[5,6] In 2010, a novel laparoscopic

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technique, known as laparoscopic pectopexy (LP), was introduced by Banerjee and Noé[7] for the treatment of apical prolapse. LP was initially developed as an alternative to laparoscopic sacrocolpopexy (LS) for obese patients, in whom access to os sacrum and longitudinal ligament may be technically challenging. The anchoring points of the mesh in LP are the iliopectineal ligaments bilaterally.[7] In this video article, we present a step-by-step surgical technique of LP with concomitant supracervical hysterectomy.

Methods

A 68-year-old patient was referred to our outpatient department with a one-year history of "vaginal dragging sensation" without co-existent urinary incontinence. The patient had 2 normal deliveries, a body mass index 27 kg/m^2, no previous abdominal surgeries and suffered from mild hypertension. Our clinical examination revealed the presence of a POP-quantification system (Q) IV prolapse. The patient was thoroughly counselled about management options of her condition and opted to undergo LP combined with supracervical hysterectomy. Informed written consent was obtained.

Under general anaesthesia, the patient was placed in lithotomy position and a vaginal examination was performed, confirming the presence of POP-Q IV prolapse. A urinary bladder catheter was inserted and the uterus instrumented. Pneumoperitoneum was established using the Veress needle in the base of the umbilicus. A 0-degree laparoscope was then, introduced through a 10-millimetre trocar in the base of the umbilicus and three further ports were placed under direct vision, two 5 mm lateral and one suprapubic 10 mm, under vision. The procedure was completed by performing the following 10 consecutive steps, using 1 Metzenbaum scissor, a universal grasping forceps, 1 bipolar forceps and 1 needle holder.

Results

Step 1: Division of the round ligaments and extension of dissection towards the pelvic sidewall bilaterally. Step 2: Identification of the iliopectineal ligament as the anchoring point of the mesh. Step 3: Division of the uterovesical peritoneum and development of the vesicovaginal space. Step 4: Routine subtotal hysterectomy. Step 5: Opening of the rectovaginal space. Step 6: Closure of the cervical canal. Step 7: Insert the mesh (polypropylene) and fix it with sutures on the cervix, anterior and posterior vagina. Step 8: Anchor the lateral arms of the mesh on the iliopectineal ligaments bilaterally. A non-absorbable suture is placed through the iliopectineal ligament while pushing carefully the external iliac vein laterally. The same suture is then passed through the lateral arm of the mesh, and the knot is tied. It is important to ensure that excessive tension is avoided. Step 9: Closure of the overlying peritoneum with a continuous absorbable suture. Step 10: In-bag Morcellation of the uterine corpus according to the National Institute for Health and Care Excellence and American College of Obstetricians and Gynecologists guidelines.[8,9]

The operation was performed with minimal blood loss and no intra- or post-operative complications. The patient was discharged on the first postoperative day, after fully voiding her bladder and made an uneventful recovery. The patient was examined in our outpatient department 6 weeks following the procedure by the operating surgeon, confirming excellent anatomic reconstruction (POP-Q 0) and symptom resolution.

Discussion

There are many different surgical procedures for the treatment of apical prolapse, which can be divided into obliterative ones (such as Colpocleisis,[10,11] for non-sexually active patients) and restorative ones. The gold standard method for apical suspension is LS.[4,12-14] LP is an alternative method for the reconstruction of apical defects.

There have been many studies and trials which have investigated and compared the complications and outcomes of LP and LS. In LS the mesh is placed between the cervix/vagina and the sacrum, restricting the pelvis and, possibly, leading to defecation problems and post-inflammatory changes of the sigmoid.[12,13,15-18] Moreover, there is a risk of injuring the hypogastric nerves because of the preparation of the anterior sacral bone, which is needed during LS.[19] On the other hand, in LP the mesh follows the natural structures in an organ free area, minimising the risk of such complications and preserving a natural vaginal axis.[7,20] Pectineal ligament has been also proved to be statistically significantly stronger than the sacrospinous ligament and the arcus tendinous of the pelvic fascia.[21] Though the two methods do not seem to differ regarding the relapse rates of apical prolapse, *de novo* central- or lateral-defect and *de novo* rectocele as well as anatomic outcomes, intraoperative blood loss and

hospitalisation duration,[20] LP is associated with reduced procedural time.[22] Noé et al.[20] have shown that the two methods have similar *de novo* stress urinary incontinence and urgency rates postoperatively. Some studies have also demonstrated that patients undergoing LP have a greater improvement in quality of life and sexual function.[23,24] Furthermore, Chuang et al.[23] evaluated and compared the learning curve of LP with LS in a cumulative analysis and showed that LP seems to have a shorter learning curve, possibly explained by the complexity of the surgical field in LS, especially in obese patients.[25,26] On the other hand, LP may offer an easier approach to the surgeon, with the obturator area, corona mortis and external iliac vein being the most important anatomical structures that need to be preserved during preparation of iliopectineal ligament according to Pulatoğlu et al.[27]

In our 10-step approach of LP, we have included a concomitant supracervical hysterectomy. However, nowadays there is an increasing desire of women for uterus-preserving prolapse treatment. LP can also be used to perform a hysteropexy after an effective and appropriate counselling and selection of the patients. In this case, the round ligament should remain intact, and the preparation begins with a superficial incision of the peritoneum adjacent to the ligament and the central part of the mesh can be fixated to the anterior or the posterior part of the uterus.[28]

LP is a safe and effective alternative to LS in the clinical routine. However, it is important to that future multicentre, randomised trials should be conducted with an adequate sample size and follow-up to evaluate efficacy and long-term outcomes of this technique.

Conclusion

We report a simple, effective and reproducible approach for LP, using 10 consecutive steps. The standardised procedure can be adopted and safely performed by surgeons with advanced minimal access skills and with, potentially, a shorter learning curve compared to LS.

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Transparency: The authors affirm that this article is an honest, accurate, and transparent account of the study being reported and that no important aspects have been omitted.

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Video 1. https://youtu.be/0s3kjxKyRow

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Pre-operative GnRH agonists in deep endometriosis: insights beyond the current evidence

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Dear Editor,

Rafique et al.'s[1] article, "Pre-operative GnRH agonist use and surgical outcomes in rectovaginal/colorectal endometriosis," is a comprehensive, multicenter study that combines surgical outcomes and health-related quality of life data to examine patients' experiences postsurgery. However, some methodological issues may necessitate further investigation.[1]

Firstly, gonadotrophin releasing hormone (GnRH) agonists produce hypoestrogenism, but their pharmacokinetics, formulations, and adverse effects vary. The study did not specify the type, dosage, and duration of GnRH therapy, which can affect hormonal suppression and tissue response. Extended use may make surgical dissection more challenging. The validity of the results is not compromised, but methodological challenges exist. Future research should focus on regimen-specific effects, despite the methodological challenges of stratifying large datasets by drug type and dosage.[2]

Secondly, the study, while controlling for variables, lacked information about the location, size, and depth of lesions, which are known to influence surgical risk. The use of terms like "surgical difficulty" or "procedure type" only provides a partial view. Standardized systems like ENZIAN could enhance future registry studies and improve risk assessment.[3]

Thirdly, the study provides valuable information on surgical risks and quality of life for women with severe endometriosis but does not evaluate fertility outcomes. Understanding the impact of major surgery and hormone therapy on fertility is crucial for family planning. However, the results are difficult to apply to real-life decisions. Future research should include information on pregnancy outcomes, whether natural or assisted, to be more beneficial for patients and clinicians.[4]

Lastly, the study, which includes 101 centers from six countries, offers diversity and strength but also introduces uncertainty due to the lack of standardization of surgeon experience, perioperative procedures, and surgical methods. Future research could consider this variability by reporting center-level practices or using random-effects models to reduce bias, as it represents real-world practice.[5]

Rafique et al.[1] provide valuable insights into the function of GnRH analogue in endometriosis surgery, despite its limitations, and their findings may enhance future research.

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Reply: Pre-operative GnRH agonists in deep endometriosis: insights beyond the current evidence

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Dear Editor,

We thank the Bano et al.[1], for their interest in our article. We appreciate the comments on the lack of details of type, dosage and duration of gonadotrophin releasing hormone (GnRH) agonist treatment; location, size and depth of lesions; fertility outcomes and surgeon experience. Our study was a pragmatic analysis of a very large, multicentre surgical database [British Society for Gynaecological Endoscopy (BSGE) Endometriosis Centres Database] from 101 centres, including 9,433 patients.[2] Although the data were entered from six different countries, the vast majority of the entries were from the United Kingdom.

The database did not include the type, dosage or duration of GnRH agonists. However, in practice, the majority of women would have been on long term depot preparations such as leuprorelin acetate 3.75 mg/month or 11.25 mg/3 months, goserelin acetate 3.6 mg/month or 10.8 mg/3 months, or triptorelin 11.25 mg/3 months. The decision to use GnRH agonists, including the specific agent, dosage, and duration, was according to local protocols and clinician discretion. While we agree that stratification by agent and duration could provide further insights, this analysis was not possible. Importantly, the lack of uniformity reflects actual clinical heterogeneity and enhances external validity, while the large sample size provides robustness.

The lesion characteristics were collected to include the location but not depth or size of deep endometriotic nodules. Data regarding the size and depth of deep nodules are disreputably difficult to collect, especially when different teams use different diagnostic methods. In addition, surgical estimates regarding size of these lesions are not reliable. Data collection in the BSGE database started in 2009, when the concept of nodule size was only starting to develop (and the first version of the ENZIAN classification did not exist).[3,4] Thus, analysis of outcomes according to lesion depth and size was not possible with the data available. However, we used proxy measures to reflect surgical complexity instead. This included analysis based on presence or absence of bowel resection, bladder or ureteric nodule excision and hysterectomy. Nevertheless, we agree that lesion-specific staging would improve risk stratification and could be incorporated into future registry studies. It is our understanding that a revision of the BSGE database is close to completion and set to include the latest ENZIAN classification. Fertility related outcomes were not collected in the

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BSGE Database as it was designed to focus on surgical outcomes and health-related quality of life.

We agree that heterogeneity in surgeon experience and perioperative management protocols are important considerations. These parameters are difficult to determine and collect objectively. However, the accredited centres were expected to reach certain requirements, including a minimum number of operations carried out by the centres or individual surgeons annually and submission of an edited video to the BSGE Scientific Advisory Group for assessment every year. The large number of participating centres inevitably introduced practice variability, which we acknowledge as both a strength and a limitation. Further work, including randomised trials and standardised data collection frameworks, is needed to refine and personalise GnRH analogues regimens and predict long-term reproductive and surgical outcomes.

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