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THE ASSOCIATION OF MAHARASHTRA OBSTETRIC & GYNAECOLOGICAL SOCIETIES AMOGS

in collaboration with

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THE MUMBAI OBSTETRIC & GYNAECOLOGICAL SOCIETY MOGS

MAHA ENDO CONCLAVE 2026

Advancing Evidence, Enhancing Care, Empowering Women.

Consensus statements and clinical recommendations for the Diagnosis & Management of Endometriosis

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Dr Ritu Hinduja
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Dr. Riddhi Desai
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Dr Nilesh Balkawade
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Foreword

Dear Colleagues,

It gives me immense pleasure to pen this foreword for the AMOGS TOG Endometriosis Expert Consensus, developed following the enriching scientific deliberations and expert exchanges at the MAHA ENDO Conclave 2026 in Mumbai.

This initiative, conceived as a joint conclave by AMOGS in collaboration with IAGE, MSR and MOGS, reflects our collective commitment to bridging the gap between evolving scientific evidence and day-to-day clinical practice. It is a step forward in advancing the understanding, diagnosis and management of endometriosis—one of the most challenging conditions affecting women across all stages of reproductive life.

Through insightful presentations, panel discussions and expert interactions, the conclave brought together valuable perspectives on early recognition, advances in imaging, fertility preservation, medical and surgical management, multidisciplinary care pathways and long-term follow-up strategies.

This expert consensus, designed as a concise yet comprehensive reference, aims to support informed clinical decision-making, promote standardised care and encourage the adoption of best practices across diverse healthcare settings.

I congratulate Dr. Ameya Purandare, President, AMOGS; Dr. Rohan Palshetkar, Hon. Secretary, AMOGS; and all the organisational leaders and contributors whose expertise and commitment have made this valuable resource possible.

I am confident that these consensus statements will serve as an important reference for clinicians and will contribute meaningfully to improving outcomes for women living with endometriosis.

Warm Regards

Dr. Bhaskar Pal
President, FOGSI 2026

Preface

Dear Colleagues,

It gives me great pleasure to share the outcomes of MAHA ENDO Conclave 2026, a landmark initiative dedicated to advancing endometriosis care. The conclave brought together experts to discuss key aspects of diagnosis, imaging, fertility preservation, medical and surgical management, and multidisciplinary care. These rich scientific exchanges have culminated in a practical expert consensus to guide clinicians in everyday practice. I thank all faculty, contributors, and partner organizations for their invaluable support. Together, we continue our commitment to improving the lives of women affected by endometriosis.

Warm Regards

Dr. Ameya Purandare
President, AMOGS

Dear Colleagues,

MAHA ENDO Conclave 2026 marked an important step in fostering meaningful scientific dialogue on endometriosis. The comprehensive discussions spanning diagnosis, imaging, fertility, medical and surgical management, and long-term care have enriched our collective understanding of this complex condition. The resulting expert consensus reflects our commitment to evidence-based practice and improved patient outcomes. I sincerely thank all faculty, delegates, and collaborating organizations for their valuable contributions. May this initiative continue to guide and inspire excellence in endometriosis care.

Warm Regards

Dr. Rohan Palshetkar
Honorary Secretary, AMOGS

Messages from Luminaries

Dear Colleagues,

I congratulate AMOGS for organizing the Maha Endo Conclave, a timely initiative dedicated to advancing endometriosis care. The thoughtfully curated scientific program promises valuable insights into the latest diagnostic and surgical advancements. Such focused academic platforms are essential for enhancing clinical expertise and improving patient outcomes. I extend my best wishes to AMOGS and I believe these consensus statements will guide clinical practice and help deliver better outcomes for women living with endometriosis.

Warm Regards

Dr. Sudha Tandon

President, Indian Association of Gynaecological Endoscopists (IAGE)

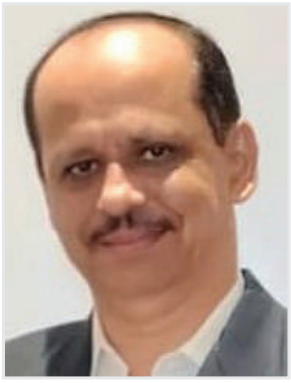
Dear Colleagues,

It is a pleasure to congratulate AMOGS on organizing the Maha Endo Conclave. Endometriosis remains a significant challenge in reproductive medicine, making such focused educational programs and consensus highly relevant. The excellent scientific content and the multidisciplinary discussions will undoubtedly benefit practitioners and patients alike. I wish AMOGS all the best wishes.

Warm Regards

Dr. Ameet Patki

Chairperson, Maharashtra Chapter of Indian Society of Assisted Reproduction (MSR)



Dear Colleagues,

I commend AMOGS for hosting the Maha Endo Conclave, an important academic initiative addressing the complexities of endometriosis. The comprehensive scientific program reflects a strong commitment to advancing women's healthcare through education and collaboration. Such dedicated forums help bridge knowledge gaps and promote evidence-based practice. My sincere congratulations to AMOGS.

Warm Regards

Dr. Shailesh Kore

President, Mumbai Obstetric & Gynaecological Society (MOGS)

Convener

Dr. Priti Vyas

Endometriosis Committee, AMOGS

Dr. Ritu Hinduja

Endocrinology Committee, AMOGS

Dr. Riddhi Desai

Endoscopy & Robotics Committee, AMOGS

Dr. Nilesh Balkawade

Infertility Committee, AMOGS

CONSENSUS STATEMENTS AND CLINICAL RECOMMENDATIONS FOR THE

DIAGNOSIS AND MANAGEMENT OF ENDOMETRIOSIS

Endometriosis Diagnosis Committee

Lead: Dr. Shailesh Kore, Dr. Bharati Abhyankar

Convener: Dr. Priti Vyas

Moderator: Dr. Shreya Prabhoo, Dr. Madhuri Mehendale

Experts: Dr. Uma Wankhede, Dr. Komal Chavan, Dr. Priya Vora, Dr. Chander Lulla, Dr. Mayuri More

Endometriosis Medical Management Committee

Lead: Dr. Kiran Kurtkoti, Dr. Niranjan Chavan

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Moderator: Dr. Jiteeka Thakkar, Dr. Roopali Sehgal

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Endometriosis and IVF Committee

Lead: Dr. Nandita Palshetkar, Dr. Ameet Patki

Convener: Dr. Nilesh Balkawade

Moderator: Dr. Shrutika Thakkar

Experts: Dr. Kundan Ingale, Dr. Chaitanya Ganapule, Dr. Neha Lad, Dr. Nalini Bagul, Dr. Sheetal Sawankar, Dr. Biswanath Ghosh Dastidar, Dr. Sreedevi Tanksale, Dr. Tejal Poddar

CONTENTS

Introduction

Endometriosis is a chronic inflammatory estrogen-dependent disease characterized by the presence of endometrium-like tissue outside the uterus, primarily affecting pelvic organs and peritoneum, ovaries, and causing extensive fibrosis.[1,2,3] Extra-pelvic endometriosis is a rare type of endometriosis, which occurs in a distant site from gynecological organs.[4]

Endometriosis affects nearly 10% of reproductive-aged women worldwide, corresponding to approximately 247 million girls and women globally and around 42 million in India.[5] While some individuals may remain asymptomatic, the condition can significantly impair quality of life and is commonly associated with chronic pelvic pain and subfertility or infertility in 35–50% of cases.[1] Common symptoms include dysmenorrhea, dyspareunia, dyschezia, dysuria, and headache, often leading to absenteeism from work or school, reduced productivity, and social withdrawal.[3,6]

Despite its high prevalence, endometriosis is often diagnosed late, which adversely affects quality of life. Early diagnosis and individualized management are essential for effective symptom control, fertility preservation where desired, and improved outcomes.[2,3,7]

Table 1. Level of evidence and grading strength of recommendations

Level of evidence	Description
Level A	Data derived from multiple randomized trials or meta-analyses, or evidence-based clinical practice guidelines
Level B	Data derived from a single randomized trial or a large non-randomized trial
Level C	Consensus of experts or small studies, retrospective studies or registries, or narrative/ literature reviews
Level D	Data derived from Clinical experience
Class of recommendations	
Class I	Evidence and or general agreement that a given treatment or procedure is beneficial, useful or effective. It is recommended.
Class IIa	Evidence is in favor of efficacy/usefulness and should be considered
Class IIb	Efficacy/usefulness is less well established, and recommendations may be considered
Class III	Evidence and or general agreement that a given treatment or procedure is not beneficial, useful or effective, and in some cases may cause harm. Not recommended

The European Society of Human Reproduction and Embryology (ESHRE) 2022 guideline prioritizes medical therapy, reserving surgery for selected cases, with regular follow-up recommended to monitor recurrence.[8]

Scope

These consensus statements are intended to support evidence-based diagnosis and management of endometriosis, facilitate informed clinical decision-making, and optimize patient outcomes across diverse clinical settings.

Methodology

The practice points were developed following a comprehensive review of current evidence, published literature, and established clinical guidelines related to the diagnosis and management of endometriosis. A multidisciplinary expert task force comprising specialists in Obstetrics and Gynecology critically evaluated the available evidence and formulated recommendations through iterative discussions and consensus-building exercises. The initial draft was prepared by the task force and subsequently reviewed and endorsed by the expert panel. Practice points were appraised and graded using a predefined evidence grading system (Table 1) to assess the quality of evidence and strength of recommendations.

DIAGNOSIS OF ENDOMETRIOSIS

Non-invasive workup

Clinical presentation and physical examination

CONSENSUS STATEMENT

A comprehensive initial evaluation including detailed medical, gynecological menstrual, and family history, along with systematic assessment of symptom characteristics and impact on quality of life along with physical examination is essential for identifying suspected endometriosis. (Level A, Class I; Consensus: 100% Agreement)

Discussion

Clinical presentation

Endometriosis diagnosis is often delayed by 4–11 years after symptom onset, allowing disease progression, worsening symptoms, reduced quality of life, and higher healthcare costs. Organizations like American College of Obstetricians and Gynecologists (ACOG), National Institute for Health and Care Excellence (NICE), ESHRE, and Canadian bodies recommend the use of a clinical diagnostic approach for the initial evaluation of suspected endometriosis.[9,10,11,12]

ACOG specifically states that symptom-based assessment and/or physical examination are sufficient to begin empiric medical therapy. Initial evaluation for endometriosis should include a thorough medical, gynecologic, menstrual, and family history, along with a detailed symptom review covering location, intensity, frequency, duration, and impact on quality of life.[9]

Endometriosis should be suspected in patients presenting with symptoms such as chronic pelvic pain, dysmenorrhea, dyspareunia, dysuria, dyschezia, or infertility, especially when multiple symptoms coexist. Although these symptoms can arise from other conditions, their combination increases the likelihood of endometriosis and warrants further evaluation.[9, 10]

A real-world study involving 27,840 women with endometriosis reported that 87.8% were diagnosed based on clinical symptoms. Dysmenorrhea (61.8%), heavy or irregular bleeding (50.8%), and pelvic pain (37.2%) were the most common symptoms, with over half of the women also reporting significant psychological distress, including depression and hopelessness.[12]

Physical examination

A focused bimanual abdominopelvic examination can help detect signs of endometriosis, rule out other conditions, and guide further evaluation. Pelvic examination may reveal findings such as reduced organ mobility, enlargement, tenderness, nodularity in the posterior fornix, or visible lesions.[9,10] A rectovaginal exam is recommended when posterior abnormalities are suspected. Signs suggestive of deep endometriosis (uterosacral nodularity or posterior fornix thickening) warrant referral to a specialist. However, a normal physical exam does not rule out endometriosis.[9,10]

A meta analysis has shown that physical examination has moderate accuracy for detecting deep endometriosis.[13]

Imaging

CONSENSUS STATEMENTS

- **Imaging can be routinely considered in the initial evaluation of suspected endometriosis, even when physical examination is normal.** (Level A, Class I; Consensus:100% Agreement)
- **Transvaginal ultrasound (TVS) should be the first-line modality to - detect endometriotic lesions, exclude alternative diagnoses, guide management, and assist in preoperative planning. TVS adds additional benefits of being dynamic mode of examination in addition to being cost effective and easy availability** (Level A, Class I; Consensus: 100% Agreement)
- **TVS is the preferred first-line imaging modality for suspected deep endometriosis, including bladder and rectosigmoid involvement, due to its high specificity, adequate sensitivity, and strong evidence base.** (Level A, Class I; Consensus: 100% Agreement)
- **Transabdominal ultrasound as an alternative when TVS is not feasible. In cases of atypical endometrioma, colour Doppler and/ or contrast magnetic resonance imaging (MRI) aids in differentiating them from borderline ovarian tumors.** (Level D, Class IIa; Consensus: 100% Agreement)
- **MRI consistently demonstrates higher sensitivity for selected deep pelvic compartments (including rectosigmoid, uterosacral ligaments, rectovaginal septum, vagina, and bladder). This makes MRI a reliable modality for comprehensive preoperative mapping.** (Level A, Class I; Consensus: 100% Agreement)
- **MRI is especially valuable when transvaginal ultrasound is inconclusive, not feasible, or technically inadequate.** (Level A, Class I; Consensus:100% Agreement)

Discussion

Imaging plays a key role in endometriosis diagnosis, with TVS and MRI assessing the presence of disease, and also its type, location, and extent. The International Deep Endometriosis Analysis (IDEA) group recommends a detailed ultrasound evaluation of both anterior (bladder, ureter) and posterior (bowel, uterosacral ligaments, rectovaginal septum, pouch of Douglas) compartments to detect ovarian and deep endometriosis as well as adhesions. MRI is useful for identifying multifocal and extra-pelvic disease. When performed by experts, TVS and MRI are reported to have similar accuracy, but TVS is preferred as the first-line imaging due to its accessibility, lower cost, and dynamic assessment (soft signs of site specific tenderness, localized collection and sliding sign).[7]

Ultrasound

- **The ACOG 2026 guideline recommends imaging in the initial evaluation, even with a normal physical exam, to detect lesions, rule out other causes, guide management, and assist preoperative planning. TVS is the preferred initial modality, with transabdominal ultrasound as an alternative if TVS is not suitable. Empiric treatment should be started alongside imaging to avoid delays.[9]**
- **According to NICE guidelines, a TVS should be offered to all patients with suspected endometriosis, even if examination findings are normal. TVS can detect endometriomas and deep disease, rule out other causes, and guide management and referral. If not suitable, a transabdominal ultrasound can be considered. Normal examination or imaging does not exclude endometriosis.[10]**

Discussion

Ultrasonography can aid preoperative planning in endometriosis. In a multicenter retrospective study (N=878), preoperative ultrasound staging matched surgical staging (according to the 2021 American Association of Gynecologic Laparoscopists Endometriosis Classification system) in 66.7% of cases. It was most reliable for identifying patients without disease and those with stage 1 or stage 4 endometriosis.[14] A systematic review assessing imaging for suspected bladder deep endometriosis found that TVS has excellent specificity and the strongest supporting evidence, making it the preferred first-line diagnostic modality.[15]

MRI

ACOG 2026 guideline recommends pelvic MRI when additional characterization of deep endometriosis is required to guide treatment planning.[9] ESHRE 2022 advises the use of imaging (ultrasound or MRI) in the diagnostic work-up, while emphasizing that negative imaging does not rule out endometriosis, particularly superficial peritoneal disease.[8]

A systematic review and meta-analysis showed that while both TVS and MRI have excellent specificity for detecting deep endometriosis in the uterosacral ligaments, rectovaginal septum, and vagina, MRI consistently demonstrates higher sensitivity. This makes MRI the more reliable modality for detecting these lesions, particularly in preoperative evaluation.[16,17]

The Society of Radiologists in Ultrasound consensus states that when transvaginal imaging is not feasible or technically inadequate, and clinical suspicion for endometriosis remains high, expert pelvic MRI should be used as the next diagnostic modality.[18]

An international consensus states that MRI can reliably predict, preoperatively, the presence of deep endometriosis in the rectosigmoid, uterosacral ligaments and torus uterinus, rectovaginal septum, vagina, and bladder.[19]

> **According to updated guidelines from the European Society of Urogenital Radiology, MRI for endometriosis should include multiplanar T2-weighted, T1-weighted, and kidney visualization sequences, with reporting based on a standardized compartmental approach. This is essential for accurate disease mapping and clear communication with patients and surgeons.[20]**

Contrast-enhanced MRI serves as a valuable adjunctive imaging modality for differentiating endometriosis from other pelvic masses. It enhances the assessment of lesion morphology, inflammation, and vascularity while improving visualization of deep infiltrating and complex lesions, particularly when ultrasound findings are inconclusive.[8,21]

Biomarkers

CONSENSUS STATEMENTS

- **Cancer Antigen 125 (CA-125) cannot be considered as a reliable biomarker for diagnosis of endometriosis in routine clinical practice. A normal CA-125 result does not necessarily rule out the disease.** (Level A, Class I; Consensus: 100% Agreement)
- **No biomarker is currently recommended for screening or diagnosis in routine practice. Salivary miRNA profiling is an emerging non-invasive tool.** (Level D, Class I; Consensus: 100% Agreement)

Discussion

The international guidelines, like the ACOG, ESHRE, or NICE, do not recommend biomarkers for the diagnosis of endometriosis.[8, 9,10]

According to the The Federation of Obstetric and Gynaecological Societies of India-Indian College of Obstetricians and Gynaecologists (FOGSI-ICOG) Good Clinical Practice Recommendations (GCPR), no biological marker currently has sufficient reliability to confirm or exclude endometriosis definitively. Markers such as CA-125 have limited diagnostic and follow-up value, and a negative CA-125 result does not rule out the disease.[22]

Invasive diagnosis of endometriosis

Diagnostic laparoscopy

CONSENSUS STATEMENTS

- **Diagnostic laparoscopy should be reserved for cases with diagnostic uncertainty, failure of empiric treatment, or when definitive confirmation is desired by the patient.** (Level A, Class I; Consensus: 86% Agreement, 14% Disagreement)
- **Biopsy of suspected lesions should be considered during laparoscopy in atypical lesions or suspected malignancy** (Level A, Class I; Consensus: 96% Agreement, 4% Disagreement)
- **During diagnostic laparoscopy, treatment of visible endometriotic lesions during the initial procedure should be considered to reduce the need for repeat surgeries.** (Level A, Class I; Consensus: 100% Agreement)

Discussion

Advances in imaging, improved understanding of endometriosis, and concerns regarding diagnostic delays have reduced the routine use of diagnostic laparoscopy.[9]

- According to the FOGSI–ICOG GCPR, diagnostic laparoscopy may be considered for patients with suspected endometriosis when the diagnosis is uncertain, when patients seek definitive confirmation before treatment, or when empiric therapy is unsuccessful.[22]
- ACOG 2026 guideline recommends considering biopsy of suspected lesions during diagnostic laparoscopy for histologic confirmation, although a negative biopsy does not rule out endometriosis. Because endometriosis is associated with an increased risk of ovarian cancer, biopsy and histopathologic evaluation are particularly important when malignancy is suspected based on preoperative or intraoperative findings.[9]
- ACOG 2026 guideline recommends treating suspected endometriotic lesions during the initial laparoscopy whenever feasible to reduce the need for repeat surgery. However, surgical risks, the possibility of inconclusive findings, and the need for additional procedures in extensive disease should be carefully considered. Preoperative imaging can aid surgical planning and help minimize unexpected intraoperative findings beyond the surgeon's expertise.[9]

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MEDICAL MANAGEMENT OF ENDOMETRIOSIS

CONSENSUS STATEMENTS

- **NSAIDs, combined oral contraceptives (COCs), and progestogens form the cornerstone of medical management for suspected endometriosis-associated pain and may be used alone or in combination according to symptom burden and patient profile.** (Level A, Class I; Consensus: 90% Agreement; 10% Disagreement)
- **Hormonal treatment selection should follow a patient-centric and shared decision-making approach, considering efficacy, tolerability, adverse effects, fertility goals, recurrence risk, cost, and long-term treatment expectations.**(Level A, Class I; Consensus: 100% Agreement).
- **COCs either cyclic or continuous regimen is effective, safe, and represents an appropriate early-line therapeutic option in women with mild endometriosis-associated pain.(**Level C, Class IIa; Consensus: 100% Agreement).
- **Progestogens like medroxyprogesterone acetate (MPA), Dydrogesterone, Dienogest given continuously are effective, safe, and represents an appropriate early-line therapeutic option in women with mild endometriosis-associated pain.** (Level B, Class IIa; Consensus: 90% Agreement; 10% Disagreement).
- **Dydrogesterone administered either in a cyclical or continuous manner, is particularly meaningful where preservation of ovulatory function and fertility potential are important treatment goals.** (Level A, Class I; Consensus: 100% Agreement)
- **Oral GnRH antagonists represent an important advancement in endometriosis management by enabling rapid suppression of endometriosis-associated pain with early return of ovarian function. It supports flexible dosing and treatment duration, improved tolerability and better symptom relief across different patient profiles.** (Level A, Class I; Consensus: 100% Agreement)
- **GnRH agonists may be considered in women with inadequate response to combined hormonal contraceptives or progestogens, although their use is limited by flare phenomenon, hypoestrogenic adverse effects like vasomotor symptoms, loss of bone mineral density, and delayed recovery of ovarian function.** (Level A, Class I; Consensus:100% Agreement).
- **Aromatase inhibitors may be considered in women with refractory endometriosis-associated pain not adequately controlled with conventional medical or surgical treatment.**(Level B, Class I; Consensus:100% Agreement).
- **Cabergoline 0.5 mg twice weekly can be given as a non-hormonal treatment upto period of 24 weeks** (Level D, Class IIa; Consensus: 100% Agreement)
- **Add back Calcium and Vitamin D3 therapy to be added to long-term medical management with GnRH analogue.** (Level D, Class IIa; Consensus:100% Agreement)

Discussion

Medical therapy serves as a first-line strategy to control symptoms in Endometriosis, suppressing disease activity, delaying progression, and minimizing the need forsurgery that could compromise ovarian reserve.[1,2] Contemporary management of endometriosis focused on purely symptom-based approach that is evolving towards apatient-centric

and phenotype-driven treatment strategy.[3] Current treatment options recommended by the 2022 ESHRE guideline and 2024 FOGSI-GCPR, include non-hormonal therapies such as non-steroidal anti-inflammatory drugs (NSAIDs) and hormonal therapies such as COCs, progestins, gonadotrophin-releasing hormone (GnRH) agonists and GnRH antagonists.[4]

NSAIDs

NSAIDs remain widely used for symptomatic relief of endometriosis-associated pain throughinhibition of prostaglandin productionand reduction of inflammatory pain pathways. However, they do not reduce or eliminate ectopic endometrial lesions.[5] According to ESHRE guidelines, NSAIDs may provide effective short-term pain reliefeither as monotherapy or in combination with hormonal treatments.[6]

Combined oral contraceptives

COCs are the most commonly prescribed hormonal therapiesfor endometriosis, as they suppress ovarian activity, reduce disease progression, and promote decidualization of endometriotic tissue.[7] COCs offer ease of administration, favorable tolerability profile,and better patient adherence that make them an important component of endometriosis management.[8]

- **ESHRE 2022 recommends combined hormonal contraceptives (oral, vaginal ring, or transdermal) to manage endometriosis-associated dysmenorrhea, dyspareunia, and non-menstrual pain.[6]**
- **FOGSI-ICOG 2024 guideline recommends continuous oral contraceptive pills (OCPs) use over cyclic regimens as it is more effective in reducing symptom recurrence and cyst formation.[9]**

However, patient selection remains important due to contraindications in women with thromboembolic risk factors or smokers above 35 years of age.[9] COCs containing newer estrogen formulations i.e. 17β-estradiol (E2) or estetrol (E4) showed greater improvement in chronic pelvic pain and dysmenorrhea than ethinylestradiol (EE)-containing COCs. Estetrol-containing COCs demonstrated efficacy comparable to dienogest, suggesting a potential role as an alternative therapeutic option in women not seeking pregnancy.[10]

Progestogens (Progestins)

Progestins manage endometriosis by suppressing ovulation and estrogen activity, exerting anti-inflammatory effects that inhibit endometriotic lesion growth and pain. Available in oral, injectable, implant, and intrauterine forms, they are generally well tolerated, with common adverse effects including irregular uterine bleeding/spotting, weight gain, mood changes, and bone loss with long-term depot MPA use. Treatment should be individualized based on patient preferences, fertility goals, and tolerability.[11]

ESHRE 2022 strongly recommends progestogens to reduce endometriosis-associated pain while emphasizing the importance of individualized selection according to tolerability and patient profile.[6]

Dydrogesterone

Dydrogesterone is a retroprogesterone characterized by high selectivity for progesterone receptors and potent progestogenic activity.[12] It helps relieve endometriosis symptoms, reduce lesion size, and improve pregnancy rates in infertile women. The drug induces atrophy of ectopic endometrial tissue and prevents new lesion formation without affecting the normal endometrium. Unlike several suppressive

hormonal therapies used in endometriosis, dydrogesterone preserves ovulatory function and menstrual cyclicity, making it appropriate as an early-line therapeutic option, particularly in women with fertility considerations or those seeking symptom control without complete ovarian suppression. Additionally, dydrogesterone demonstrates favorable safety and tolerability profile with minimal androgenic, estrogenic, glucocorticoid, or mineralocorticoid effects and is not associated with side effects such as weight gain or edema.[13] Dydrogesterone for endometriosis may be prescribed either cyclically (from days 5–25 of the menstrual cycle) or continuously, at daily doses of 20–30 mg.[12]

The ORCHIDEA study demonstrated that both prolonged cyclical 10 mg 2 or 3 times daily, either between the 5th and 25th days of the menstrual cycle)and continuous dydrogesterone regimens administered for 6 months significantly reduced endometriosis-associated chronic pelvic pain, with comparable efficacy. Treatment was associated with improvements in dysmenorrhea, reduced analgesic use, improved sexual well-being, and overall quality of life, while maintaining a favorable safety profile with no serious adverse drug events, supporting dydrogesterone as an effective and well-tolerated long-term treatment option.[14]

An evidence mapping and meta-analysis found that dydrogesterone was more effective than gestrinone in relieving dysmenorrhea, improving pregnancy rates, and reducing adverse events. Compared with GnRH agonists, dydrogesterone was associated with lower recurrence rates and fewer side effects, while avoiding hypoestrogenic symptoms and potential bone loss. Furthermore, postoperative dydrogesterone therapy significantly improved pregnancy rates within 12 months compared with no treatment.[13] Dydrogesterone has a well-established safety and tolerability profile, supported by over 60 years of clinical use, reinforcing its role as a reliable treatment option in women's reproductive health.[15]

GnRH agonists

GnRH agonists induce a hypoestrogenic state by suppressing the hypothalamic–pituitary–ovarian axis, leading to regression of endometriotic lesions. Their use is limited by an initial flare effect, hypoestrogenic adverse effects, delayed recovery of ovarian function, and unsuitability for women seeking pregnancy.[7]

ESHRE recommends GnRH agonists as second-line therapy for endometriosis-associated pain when first-line hormonal treatments fail, with add-back therapy advised to reduce hypoestrogenic side effects including bone loss.[6] The limitations of long-term GnRH agonist therapy have driven interest in GnRH antagonists, which provide rapid, reversible, and dose-dependent estrogen suppression without the initial flare effect.

GnRH antagonists: A contemporary paradigm shift in the management of endometriosis

Endometriosis management should focus on sustained symptom control, prevention of recurrence, preservation of quality of life, and reduction in surgical burden, with therapy individualized according to patient phenotype, disease chronicity, and patient preference.[6]

Elagolix for the management of endometriosis-associated pain

CONSENSUS STATEMENTS

- **Elagolix 150 mg once daily or 200 mg twice daily represents a novel and effective therapeutic option for rapid and effective control of moderate-to-severe endometriosis-associated pain.** (Level A, Class I; Consensus:100% Agreement)
- **Elagolix is particularly useful for short-to-intermediate duration therapy; may serve as an effective bridge between conventional hormonal therapy and long-term chronic disease management strategies.** (Level A, Class IIa; Consensus:100% Agreement)
- **Elagolix therapy should be individualized based on symptom response, BMD, and reproductive goals with periodic reassessment after 6 months of therapy to optimize efficacy, minimize adverse effects, and may be continued for long-term with add-back therapy.** (Level A, Class I; Consensus:100% Agreement)
- **Dose titration with Elagolix allows greater flexibility in balancing efficacy and tolerability across different patient profiles.** (Level C, Class IIa; Consensus:100% Agreement)

Discussion

The advent of oral GnRH antagonists has enabled individualized, long-term, and flexible medical management of endometriosis. Treatment should aim to reduce pain, prevent recurrence, preserve quality of life, and minimize the need for repeat surgery through sustained medical suppression.

Elagolix is an oral, non-peptide GnRH receptor antagonist approved by the United States Food and Drug Administration (USFDA) and Health Canada in 2018, and more recently approved by health authorities in Israel and India, for the management of moderate-to-severe endometriosis-associated pain.[4] It acts by competitively inhibiting GnRH receptors in the anterior pituitary, blocking endogenous GnRH stimulation and suppressing LH and FSH secretion, thereby producing a dose-dependent reduction in estradiol and progesterone levels.[17]

The estrogen threshold hypothesis proposes that estradiol levels above 60 pg/mL may promote endometriotic lesion growth, while levels of 10–20 pg/mL can suppress lesions but cause bone loss and vasomotor symptoms. Therefore, maintaining an "estradiol therapeutic window" of 30–45 pg/mL may help control lesion progression while reducing adverse skeletal effects.[4,18]

Elagolix induces rapid, dose-dependent estradiol suppression within hours of the first dose, with partial suppression observed at 150 mg daily (median estradiol concentration of ~42 pg/mL) and near-maximal suppression achieved at doses of 200 mg twice daily or higher (estradiol concentration approaching the lower limit of quantification [~12 pg/mL]).[19] This dose-dependent modulation of estradiol levels allows individualized suppression according to symptom severity and therapeutic goals while potentially minimizing excessive hypoestrogenic exposure.[19]

Thus, dose-dependent estrogen suppression with elagolix enables individualized balancing of efficacy, tolerability, and reproductive planning. Elagolix 150 mg maintains serum estrogen levels within the proposed estrogen threshold window, thereby suppressing endometriotic lesion activity while avoiding the need for add-back therapy.[4]

Unlike GnRH agonists, elagolix provides rapid, reversible, and dose-dependent estrogen suppression without an initial flare effect, offering greater treatment flexibility, improved tolerability, and preservation of ovarian reserve. Its quick onset, reversible action, and flexible dose-dependent suppression make it an effective bridge between conventional hormonal therapies and longer-duration chronic disease management.[1,2,3]

The phase 3 Elaris Endometriosis I and II (EM-I and EM-II) trials demonstrated that elagolix significantly improved dysmenorrhea and non-menstrual pelvic pain over 6 months in women with moderate-to-severe endometriosis-associated pain. Benefits were dose-dependent and accompanied by predictable hypoestrogenic effects, supporting elagolix as an effective option for patients with moderate-to-severe pain, symptom flares, and/or persistent or severe symptoms.[20]

The EM-III and EM-IV extension trials showed that elagolix maintained sustained improvements in dysmenorrhea and non-menstrual pelvic pain for up to 12 months, with reduced analgesic use, supporting its role in prolonged medical management of endometriosis.[21]

> **An 2026 expert opinion from the Federation of Obstetric and Gynaecological Societies of India identifies elagolix as a preferred option for women with severe dysmenorrhea, non-menstrual pelvic pain, and dyspareunia, with regular reassessment recommended to optimize treatment duration, safety, and fertility planning.[4]**

Relugolix/Ethinyl Estradiol/ Norethindrone acetate combination therapy for long-term management of endometriosis-associated pain

CONSENSUS STATEMENTS

- **Relugolix combination therapy provides symptom control in women with chronic and/or recurrent endometriosis-associated pain; and, represents a comprehensive extended duration treatment approach focused on pain control, tolerability, and quality of life.** (Level A, Class IIa; Consensus: 84% Agreement; 16% Disagreement)
- **Once-daily oral fixed dose combination therapy containing relugolix 40 mg, ethinylestradiol 1 mg, and norethindrone acetate 0.5 mg is particularly useful in women with endometriosis associated pelvic pain improving the quality-of-life.** (Level A, Class I; Consensus: 87% Agreement; 13% Disagreement)
- **Relugolix combination therapy offers the benefit of mitigating hypoestrogenic symptoms associated with other GnRH-based therapies, thereby improving treatment adherence and support long-term treatment.** (Level A, Class IIa; Consensus: 96% Agreement; 4% Disagreement)

Discussion

Relugolix is an oral GnRH receptor antagonist that suppresses estradiol and progesterone production, effectively reducing moderate-to-severe endometriosis-associated pain, including dysmenorrhea, nonmenstrual pelvic pain, and dyspareunia. The development of relugolix combination therapy reflects the evolving paradigm

of endometriosis management toward sustained symptom control, improved quality of life, reduction in recurrence burden, and minimization of repeated surgical interventions through prolonged medical suppression.[22,23]

Although relugolix monotherapy effectively suppresses ovarian hormone production, prolonged hypoestrogenism may result in vasomotor symptoms andBMD loss. To address this, relugolix has been combined with low-dose estradiol (1 mg) and norethindrone acetate (0.5 mg), which helps maintain therapeutic estrogen levels while reducing hypoestrogenic adverse effects, supporting long-term treatment, improving quality of life, and delaying or avoiding surgery.[22] The convenience of a once daily oral dosing regimen, together with integrated add-back therapy, provides a practical long-duration treatment option for women requiring sustained symptom control.[23]

Relugolix 40 mg combined with estradiol 1 mg and norethindrone acetate 0.5 mg is the first and only once-daily oral GnRH antagonist fixed-dose combination approved for the management of moderate-to-severe endometriosis-associated pain.[22] Relugolix combination therapy is a valuable option for women with recurrent or persistent endometriosis symptoms, offering sustained efficacy, improved tolerability, and support for long-term disease management and quality of life. However, this therapy is contraindicated in women with current or high risk of thrombotic or thromboembolic disorders, pregnancy, known osteoporosis, current or prior hormone-sensitive malignancy, hepatic impairment or liver disease, undiagnosed abnormal uterine bleeding, or known hypersensitivity to any formulation component, necessitating careful patient selection before long-term use.[24]

The phase III SPIRIT 1 and 2 trials demonstrated that once-daily relugolix combination therapy for 24 weeks significantly improved dysmenorrhea, non-menstrual pelvic pain, dyspareunia, quality of life, and daily functioning while reducing analgesic use, with minimal impact on bone mineral density due to add-back therapy.[25]

The SPIRIT extension study showed that relugolix combination therapy provides sustained pain relief, improved quality of life, reduced analgesic use, and stable bone mineral density for up to 104 weeks, supporting its long-term use in chronic or recurrent endometriosis-associated pain.[26]

Linzagolix for the management of endometriosis-associated pain

Linzagolix, administered orally once daily at a dose of 200 mg in combination with add-back therapy (ABT), demonstrated superior efficacy and safety compared with placebo for the treatment of moderate-to-severe endometriosis-associated pain. The addition of ABT improved quality of life while minimizing hypoestrogenic adverse effects, including bone mineral density loss and vasomotor symptoms. Linzagolix 75 mg monotherapy may represent a potential option for long-term management of endometriosis-associated pain without the need for concomitant hormonal ABT. This regimen may provide an alternative for women who prefer to avoid ABT or in whom ABT is contraindicated. Both linzagolix 200 mg with ABT and linzagolix 75 mg alone have shown to significantly reduce dysmenorrhea and non-menstrual pelvic pain after 6 months of treatment.[27]

Patient selection for GnRH-based management of endometriosis

CONSENSUS STATEMENTS

- **GnRH-based therapy (with or without add back) should be individualized according to fertility intent, prior treatment exposure, surgical history, recurrence risk, and patient-specific therapeutic goals.** (Level A, Class I; Consensus: 100% Agreement)
- **Adolescentwith persistent dysmenorrhea or chronic pelvic pain despite empiric hormonal therapy should be evaluated for possible endometriosis, and in selected refractory cases beyond the age of 16 years, GnRH-based therapy with add-back may be considered under specialist supervision** (Level C, Class IIa; Consensus: 96% Agreement; 4% Disagreement)
- **In perimenopausal women with persistent or recurrent endometriosis-related symptoms, GnRH-based strategies with add-back therapy should be individualized after careful assessment of symptom persistence, recurrence risk, prior hormone exposure, comorbidities, bone health, and the potential risk of malignant transformation.** (Level C, Class IIa; Consensus: 93% Agreement; 7% Disagreement)

Discussion

Patients with severe or acute pain may require rapid symptom suppression, while those with chronic recurrent disease often benefit from prolonged, well-tolerated therapy. Treatment should be individualized through shared decision-making, considering efficacy, safety, fertility goals, and patient preferences.[6]

Fertility planning and reproductive goals

Fertility intentions are a key factor in treatment selection for endometriosis, with management focused on preserving ovarian reserve while providing effective symptom control in women seeking future pregnancy. Hormonal suppression does not improve fertility directly but may help control symptoms before surgery or assisted reproduction. In women with endometriosis-associated infertility, ovarian stimulation and assisted reproductive techniques, including IVF, should be considered when conception is delayed or fertility is time-sensitive.[6,28]

In women not seeking immediate pregnancy, treatment should be guided by symptom severity, previous treatment response, and long-term goals. Following conservative surgery, prolonged hormonal suppression can significantly reduce disease recurrence and is recommended as part of long-term management.[29]

Treatment history and chronic disease management

Prior treatment response and disease chronicity should guide escalation of therapy in endometriosis management. COCs and progestogens remain important therapeutic options in symptomatic women, while GnRH-based therapies may be considered in women with persistent or recurrent symptoms despite conventional hormonal treatment.[30,31]

Women with recurrent disease, severe pain phenotype, impaired quality of life, or prior treatment failure may particularly benefit from GnRH-antagonist management strategies. In such patients, prolonged medical suppression may help reduce recurrence burden, improve daily functioning, and minimize the need for repeated surgery. Relugolix combination therapy in a once-daily fixed-dose regimen with integrated add-back therapy, represents a long-duration treatment option.[23]

Special populations

Adolescents

Adolescents with persistent dysmenorrhea or chronic pelvic pain despite hormonal therapy should be

evaluated for endometriosis. Early diagnosis and management can reduce disease burden and improve quality of life, while GnRH-based therapy with add-back may be considered for selected cases under specialist supervision.[6]

Perimenopausal / Postmenopausal Disease

Although endometriosis is primarily a disease of reproductive age, persistent or recurrent symptoms may occur during the peri-menopausal period. In such patients, management should be individualized after careful evaluation of symptom persistence, prior disease history, hormone exposure, recurrence risk, and the potential risk of malignant transformation.[6]

Therapeutic decisions in perimenopausal women should balance symptom control with age-related comorbidities, bone health considerations, cardiovascular risk, and potential contraindications to prolonged hormonal therapy.[6]

Surgical considerations in GnRH-based management

Repeated surgical intervention should be minimized whenever possible, particularly in women with recurrent disease or concerns regarding preservation of ovarian reserve. Increasing evidence suggests that repeated ovarian surgery may adversely affect ovarian reserve and future reproductive potential, emphasizing the importance of optimized long-term medical management in selected patients.[32,33]

Aromatase inhibitors

Aromatase inhibitors are used in endometriosis because ectopic endometrial tissue exhibits increased aromatase activity, leading to local estrogen production that promotes lesion growth. Estrogen also stimulates PGE_2 synthesis, which further induces aromatase activity, creating a self-perpetuating cycle. Aromatase inhibitors help break this cycle by reducing local estrogen production.[16]

ESHRE recommends aromatase inhibitors for women with endometriosis-associated pain refractory to standard medical or surgical treatments, either alone or in combination with oral contraceptives, progestogens, GnRH agonists, or antagonists to improve efficacy.[6]

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SURGICAL MANAGEMENT OF ENDOMETRIOSIS

Surgical indications and technique selection

CONSENSUS STATEMENTS

- **Surgical management should be considered in women with symptomatic endometriosis-associated pelvic pain presenting with advanced-stage disease, deep infiltrating endometriosis (DIE), ovarian endometriomas >4 cm or bilateral endometriomas, infertility where restoration of pelvic anatomy may improve reproductive outcomes, failure/intolerance/inadequate response to medical therapy, or when malignancy is suspected.**
  (Level A/Class I; Consensus: 82% Agreement, 18% Disagreement)
- **Laparoscopic surgery is the gold-standard surgical approach for the management of endometriosis.** (Level A/Class I; Consensus: Consensus: 82% Agreement, 18% Disagreement)
- **Laparoscopic excision is preferred over drainage/ aspiration/ ablative techniques for the management of ovarian endometriomas. To preserve ovarian reserve during endometrioma surgery, hydrodissection with diluted vasopressin is recommended to facilitate cyst wall dissection and reduce bleeding. Excessive electrosurgery should be avoided, particularly in the ovarian hilum where the major vascular supply enters the ovary.**
  (Level A/Class I; Consensus: 96% Agreement, 4% Disagreement)
- **Women undergoing surgical treatment for endometriosis should be appropriately counselled regarding the risk of disease recurrence.** (Level A/Class I; Consensus: 100% Agreement)
- **Women with endometriosis-associated infertility undergoing surgery should be counselled regarding the possible risk of diminished ovarian reserve following surgical intervention.**
  (Level A/Class Ia; Consensus: 100% Agreement)
- **Counselling regarding attempts at natural conception versus further assisted reproductive treatment should be individualized and guided by the Endometriosis Fertility Index (EFI) surgical staging.** (Level A/Class I; Consensus: 100% Agreement)
- **Women undergoing surgery for endometriosis should be counselled regarding the need for appropriate postoperative hormonal suppression therapy for a suitable duration, where indicated.** (Level B/Class IIa; Consensus: 100% Agreement)
- **Endometriosis surgery should be performed by an expert in an adequately equipped centre.**
  (Level A/Class I; Consensus: 100% Agreement)
- **Symptomatic DIE warrants surgery to be done by an experienced surgeon having a multi-disciplinary team.** (Level A/Class I; Consensus: 100% Agreement)
- **For superficial peritoneal endometriosis, either excision or ablative techniques can be used during surgery to treat endometriotic lesions and improve pain symptoms.**
  (Level A/Class IIa; Consensus: 100% Agreement)
- **During surgery, it is essential to restore the tubo-ovarian relationship.**
  (Level D/Class IIa; Consensus: 96% Agreement, 4% Disagreement)
- **Recurrent endometriosis is a complex condition, Ginvolving surrounding pelvic structures, requiring a multi-disciplinary approach.** (Level A/Class I; Consensus: 100% Agreement)
- **Detailed anatomical mapping and extension of the disease using the #Enzian classification system enables compartment-based surgical planning.**
  (Level C/Class I; Consensus: 96% Agreement, 4% Disagreement)

Discussion

Surgical indications and thresholds

Endometriosis is a progressive disease that can lead to anatomical destruction of the reproductive organs, making surgical therapy an important component of management.[1] Surgical management of endometriosis may be indicated in women with severe pain symptoms associated with significant functional impairment, advanced disease causing substantial anatomical distortion of pelvic organs and/or endometriomas, failure of expectant or medical management, or intolerance to medical therapy.[2] Surgery may also be considered in patients who cannot or do not wish to continue medical treatment, have deep infiltrating endometriosis (DIE), require concomitant management of other gynecologic disorders, or are seeking fertility treatment in the presence of pain.[3] Emergency surgery may be required in cases of endometrioma rupture or torsion, obstructive uropathy, or bowel obstruction.[2]

Laparoscopy remains the gold standard for both diagnosis and treatment of endometriosis-associated infertility, while laparotomy may be considered in selected patients requiring complex multiorgan procedures or when advanced laparoscopic expertise is unavailable. For young patients experiencing infertility and/or pain, conservative surgical management should be considered. This approach is recommended as the initial surgical strategy because it is minimally invasive while helping preserve reproductive potential and hormone production.[4]

Evidence evaluating the efficacy of laparoscopic surgery has shown variable but generally favorable outcomes.[5] A comprehensive review of 34 randomized controlled trials (RCTs) further showed that laparoscopic treatment of endometriosis was associated with a reduction in pain symptoms and improvement in fertility outcomes.[6]

The 2022 ESHRE and updated 2024 NICE guidelines recommend laparoscopic surgery as an effective treatment option for reducing endometriosis-associated pain, provided there are no contraindications.[7,8]

Technique selection

The ESHRE and NICE guidelines suggest that clinicians may consider excision over ablation for endometriosis and endometriomas to improve pain outcomes, while taking fertility goals and ovarian reserve into account.[8,9]

A systematic review and meta-analysis demonstrated that laparoscopic excision was associated with significantly greater improvement in dysmenorrhea (mean difference [MD] = 0.99; 95% confidence interval [CI], -0.02 to 2.00; p=0.05) and dyschezia (MD=1.31; 95% CI, 0.33-2.29; p=0.009) compared with ablation. Data from one study demonstrated that laparoscopic excision was associated with significant reductions in chronic pelvic pain (MD=2.57; 95% CI, 1.27–3.87; p=0.0001) and Endometriosis Health Profile-30 (EHP-30) core pain scores (MD=13.20; 95% CI, 3.70–22.70; p=0.006) compared with ablation. Thus, laparoscopic excision provides greater improvement in dysmenorrhea, dyschezia, and chronic pelvic pain at 12 months post-surgery compared with ablation.[10]

A 2024 Cochrane review of 9 studies involving 578 women reported that, in the management of ovarian endometriomas, excisional surgery may lower the risk of dysmenorrhea, dyspareunia, and endometrioma recurrence, and the need for further surgical intervention compared with ablative surgery. At 1 year, endometrioma recurrence rates were 5–17% following excision *vs* 37% after ablation, while the need for further surgery was substantially higher after ablative surgery (32% vs 3–16%).[11]

During cystectomy, care should be taken to avoid the ovarian hilum to preserve the vascular supply from the ovarian and infundibulopelvic ligaments. Hydrodissection with saline or diluted synthetic vasopressin solution (0.1–1 unit/ml) can facilitate cyst wall dissection and reduce bleeding. For large endometriomas, a combined excision and ablation technique may help minimize ovarian tissue loss. Excessive use of electrosurgery should be avoided because thermal injury may damage healthy ovarian tissue and adversely affect ovarian reserve.[12]

Patient counselling

Women should be counselled of their chances of becoming pregnant after surgery. To identify patients who may benefit from ART after surgery, the Endometriosis Fertility Index (EFI) should be used, as it is validated, reproducible, and cost-effective.[9]

When surgery is indicated in women with an endometrioma, clinicians should perform ovarian cystectomy, instead of drainage and electrocoagulation, for the secondary prevention of endometriosis-associated dysmenorrhea, dyspareunia, and non-menstrual pelvic pain. However, the risk of reduced ovarian reserve should be taken into account. The ESHRE guideline development group (GDG) recommends that adolescents with endometriosis are informed of the potential detrimental effect of ovarian endometriosis and surgery on ovarian reserve and future fertility.[9]

For DIE: According to the ESHRE guidelines, surgical removal of DIE may reduce endometriosis-associated pain and improve QoL. The guidelines further recommend referral of women with DIE to specialised centres of expertise and emphasize that patients undergoing surgery should be counselled regarding the potential risks, benefits, and long-term impact on QoL.[9]

For DIE by compartment

The ESHRE GDG recommends that nerve-sparing laparoscopic procedures should be performed in specialized centres with expertise and the evidence should be collected in a standardized format to evaluate the potential risks and benefits.[9]

ESHRE suggests that is advisable to discuss the diagnosis and management of extrapelvic endometriosis in a multidisciplinary team in a centre with sufficient expertise.[9]

Surgical treatment of superficial peritoneal endometriosis includes excision or ablation.[13]

Pre-operative workup

Accurate preoperative assessment of lesion location and disease severity is essential for surgical planning in endometriosis. Dedicated transvaginal ultrasound (TVS) and magnetic resonance imaging (MRI) allow detailed mapping of deep endometriotic lesions using the #Enzian system, thereby facilitating compartment-based surgical planning. A narrative review of 19 studies evaluating the #Enzian, 2021 American Association of Gynecologic Laparoscopists (AAGL) classification, and Numerical Multi-Scoring System of Endometriosis (NMS-E), highlighted their complementary roles in preoperative assessment of endometriosis. While revised American Society for Reproductive Medicine (r-ASRM) remains important for disease staging, #Enzian enables detailed anatomical mapping, AAGL 2021 focuses on surgical complexity, and NMS-E incorporates symptom severity and adhesions. However, none independently fulfil all the requirements of an ideal preoperative classification system.[14]

A retrospective study involving 139 patients undergoing laparoscopic surgery for endometriosis demonstrated that, unlike the r-ASRM classification,

the AAGL 2021 and #Enzian classifications can be effectively utilized as preoperative diagnostic tools, with the #Enzian system providing more detailed anatomical coding.[15]

Post-surgical suppression therapy

CONSENSUS STATEMENTS

- **Postoperative hormonal therapy should be considered following surgical management of endometriosis in women not seeking immediate conception, with the aim of reducing symptom recurrence and minimizing the risk of disease recurrence.** (Level A/Class I; Consensus: 96% Agreement, 4% Disagreement)
- **For women undergoing surgery for endometriosis and desiring pregnancy, Dydrogesterone may be considered as an appropriate postoperative hormonal treatment** (Level A/Class IIa; Consensus: 90% Agreement, 10% Disagreement)
- **GnRH antagonists represent an early postoperative therapeutic option for women with endometriosis-associated pain to achieve improved symptom control and reduce the risk of symptom recurrence following surgery. (**Level B/Class IIa; Consensus: 100% Agreement)
- **Elagolix offers faster reversal of hormonal suppression after treatment discontinuation facilitating earlier return of reproductive function and potentially improving the chances of conception after laparoscopic surgery** (Level C/Class I; Consensus: 100% Agreement)
- **Elagolix is recommended for the management of DIE-associated symptoms and can be considered as a part of post surgical management.** (Level A/Class IIa; Consensus: 100% Agreement)

Discussion

Post-operative medical therapy is effective in treating microscopic endometriotic lesions that may not be detected or completely excised during surgery. It helps suppress residual disease that cannot be surgically removed and reduces the risk of recurrence of endometriosis.[16] According to the ESHRE guidelines, postoperative hormonal therapy may be offered to improve outcomes of surgery for pain in women with endometriosis who do not desire immediate pregnancy. After surgical treatment of ovarian endometrioma, long-term hormonal therapy is recommended to prevent endometrioma and the recurrence of endometriosis-related symptoms in women not immediately seeking conception. In cases of DIE, long-term postoperative hormonal therapy can be considered to reduce recurrence.[9]

Dydrogesterone

Dydrogesterone effectively controls endometriosis symptoms, reduces disease progression, and may improve fertility outcomes while maintaining a favorable tolerability profile.[17]

Clinical studies including the ORCHIDEA trial and meta-analysis of 19 studies (n = 1709 women) suggest dydrogesterone may improve pelvic pain and dysmenorrhea and reduce recurrence-related symptoms, with a favorable safety profile.[18,19] In an Indian clinical trial, dydrogesterone was associated with a reduction in endometrioma size, improvement in endometriosis-associated pelvic pain, decrease in serum VEGF levels, and significant enhancement in QoL.[20] However, although dydrogesterone acts on several pathways involved in endometriosis, it does not completely address the multifactorial nature of the disease, particularly due to its limited ability to suppress local estrogen production.[21]

A retrospective study showed that long-term dydrogesterone therapy effectively reduced endometriotic lesions, improved dysmenorrhea and quality of life, decreased analgesic use, and enhanced menstrual regularity and hemoglobin levels.[22]

An Indian multicentre study demonstrated that dydrogesterone is an effective and safe post-laparoscopic treatment for endometriosis, producing marked reductions in pelvic pain, dysmenorrhea, and dyspareunia, with significant clinical improvement in most patients.[23]

Another study showed that postoperative dydrogesterone therapy in women with stage III–IV endometriosis significantly improved spontaneous and cumulative pregnancy rates at 12 months compared with GnRH agonist therapy.[24]

GnRH antagonist

GnRH antagonists rapidly and dose-dependently suppress LH, FSH, and ovarian estrogen production through competitive GnRH receptor blockade. Unlike GnRH agonists, they provide immediate hormonal suppression without an initial flare effect and are associated with fewer hypoestrogenic adverse effects.[25]

Elagolix and Relugolix (Oral GnRH Antagonists)

Relugolix and elagolix, both oral GnRH receptor antagonists, represent innovative therapeutic options for the management of moderate-to-severe pain in patients with endometriosis.[26] Elagolix is the first oral GnRH antagonist approved for the management of moderate-to-severe endometriosis-associated pain.[27]

The pivotal Elaris trials (EM-I and EM-II evaluated elagolix at doses of 150 mg once daily (lower-dose group) and 200 mg twice daily (higher-dose group) for endometriosis-associated pain. Both dosing regimens demonstrated significant improvement in dysmenorrhoea and non-menstrual pelvic pain over 6 months compared with placebo.[27] Long-term extension studies (EM-III and EM-IV) confirmed sustained efficacy up to 12 months, supporting the long-term efficacy of elagolix in the management of endometriosis-associated pain.[28]

Elagolix has been associated with significant improvements in dyspareunia, fatigue, and health-related QoL, with a favourable safety profile. Compared with conventional therapies, it demonstrates comparable efficacy with fewer hypoestrogenic adverse effects.[29]

- **According to expert opinion from FOGSI, elagolix may be considered a potential first-line option for patients with endometriosis presenting with severe dysmenorrhoea or non-menstrual pelvic pain in clinical practice. Experts suggest that elagolix provides effective pain relief, reduces dyspareunia, and improves DIE, thereby leading to meaningful improvements in QoL.[29]**
- **The ESHRE, Collège National des Gynécologues et Obstétriciens Français (CNGOF), and American Academy of Family Physicians (AAFP) guidelines collectively support elagolix as an effective therapeutic option for the treatment of endometriosis-associated pain.[25]**

Relugolix, alone or in combination with estrogen and progestogens, represents an effective and well-tolerated therapeutic option for the management of endometriosis-associated pain.[26] Two large, replicate phase 3 randomized, double-blind trials (SPIRIT 1 and SPIRIT 2) demonstrated significant reduction in dysmenorrhea and non-menstrual pelvic pain,

improvement in functional outcomes, and low rates of hypoestrogenic effects, with minimal bone mineral density loss (<1%) with relugolix combination therapy.[30] The SPIRIT open-label extension study further confirmed sustained efficacy for up to 2 years, with continued improvement in menstrual and non-menstrual pain, dyspareunia, and functional outcomes. After an initial decline of less than 1%, mean bone mineral density remained stable with ongoing treatment (Table 1).[31]

Furthermore, a recent systematic review of nine RCTs (> 8,000 women with endometriosis) concluded that both agents, used as monotherapy or with add-back therapy, are effective and generally well tolerated for the management of endometriosis-associated pain.[26]

Despite the benefits of laparoscopic excision, postoperative recurrence remains a major challenge in endometriosis management. The FOGSI Experts suggested that elagolix offers faster reversal of hormonal suppression after treatment discontinuation compared with GnRH agonists, which may facilitate earlier return of reproductive function and potentially improving the chances of conception after laparoscopic surgery. This makes elagolix a potential therapeutic option in both pre- and postoperative management of endometriosis. Experts also consider elagolix to have a favorable safety profile with efficacy comparable to conventional therapies, along with the added advantage of convenient oral administration. Additionally, elagolix has demonstrated potential for pain resolution in cases of scar endometriosis.[29]

> • **The 2024 FOGSI-ICOG GCPR guidelines recommend elagolix for the management of DIE-associated symptoms, with notable improvements when administered either before or after surgery.[4]**

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IVF AND ENDOMETRIOSIS

Pathophysiology of endometriosis-related infertility

Endometriosis impairs fertility through multiple mechanisms, including pelvic adhesions and anatomical distortion, chronic inflammation, immune dysregulation, reduced endometrial receptivity, and diminished ovarian reserve. Inflammatory mediators can adversely affect sperm function, oocyte and embryo quality, and implantation, while ovarian endometriomas may lower AFC and AMH levels and reduce ovarian responsiveness during ART, particularly when lesions are large or bilateral. These effects highlight the importance of individualized fertility-preserving management.[1]

Endometriosis and adenomyosis frequently coexist and together may worsen fertility outcomes. Adenomyosis contributes to infertility through increased junctional zone thickness, altered uterine peristalsis, and endometrial dysfunction, and has also been associated with adverse obstetric outcomes including preterm birth, placental abnormalities, cesarean delivery, and postpartum hemorrhage.[2]

In symptomatic women with rASRM stage I/II, treatment decisions should consider pain, age, ovarian reserve, previous surgeries, other infertility factors, and Endometriosis Fertility Index (EFI). IVF is generally preferred in moderate-to-severe disease (stage III/IV), low EFI, tubal dysfunction, or recurrent treatment failure.[1,2]

Pre-IVF hormonal downregulation: Rationale and emerging therapeutic strategies

CONSENSUS STATEMENTS

- **Hormonal downregulation in women seeking IVF may improve endometrial receptivity in women with endometriosis and/or adenomyosis by reducing inflammation, lesion activity, and abnormal uterine peristalsis** (Level B/Class IIa; Consensus: 100% Agreement).
- **Progestin therapy or ultra-long GnRH agonist downregulation before embryo transfer may improve uterine quiescence and implantation outcomes; however, treatment should be individualized considering treatment delay, hypoestrogenic adverse effects, and ovarian reserve status** (Level B/Class IIa; Consensus: 100% Agreement).
- **Elagolix-based approaches may allow greater flexibility in IVF scheduling and potentially shorter time to treatment initiationcompared with prolonged GnRH agonist downregulation.** (Level A/Class IIa; Consensus: 100% Agreement).
- **Dose-adjustable oral antagonists such as Elagolix therapy may enable individualized therapy with lower doses offering improved bone safety and higher doses providing greater symptom control with reversible ovarian suppression** (Level A/Class IIa; Consensus: 100% Agreement).
- **An oral GnRH antagonist strategy may improve patient convenience and reduce injection burden during IVF cycles.** (Level D/Class IIa; Consensus: 100% Agreement).
- **Oral antagonists such as Elagolix represent a promising strategy that may bridge symptom control and fertility planning in women with endometriosis undergoing ART, particularly where flexibility, rapid reversibility, and reduced treatment burden are prioritized.** (Level D/Class IIa; Consensus: 100% Agreement).

Discussion

Pre-IVF hormonal downregulation aims to restore endometrial receptivity, reduce peritoneal and uterine inflammatory burden, induce lesion quiescence, and suppress adenomyosis-associated uterine peristalsis, thereby creating a more favorable implantationenvironment. Progestin-based therapie may provide symptom relief and uterine quiescence with associated reductions in junctional zone thickness and abnormal uterine contractility on ultrasound.[3]

Ultra-long GnRH agonist downregulation, typically administered for 2–3 months prior to frozen embryo transfer, has been associated with improved implantation and pregnancy outcomes by inducing profound hypoestrogenism, reducing junctional zone thickness, and improving endometrial receptivity. However, this approach may delay IVF timelines by 3–6 months and may be limited by vasomotor symptoms, vaginal dryness, mood changes, and potential ovarian over-suppression in women with reduced ovarian reserve.[3]

Elagolix may be considered a potential first-choice therapy in women with severe dysmenorrhea or non-menstrual pelvic pain (NMPP).[4,5]Elagolix 150 mg once daily achieves partial estrogen suppression (~42 pg/mL), associated with a comparatively lower magnitude of BMD reduction at lower doses without the need for add-back therapy, whereas 200 mg twice daily provides near-complete estrogen suppression (~12 pg/mL) with greater symptomatic control.[4] This dose flexibility, together with its rapid onset of action, absence of the initial flare effect, and rapid recovery of ovarian function after treatment discontinuation, may help balance efficacy and safety in fertility-preserving treatment strategies.[4,5]

Elagolix 150 mg may be administered for 6 months with subsequent reassessment of treatment response and bone mineral density, and therapy may be extended up to 2 years when clinically indicated.[4]

> **Supported by clinical evidence and FOGSI Expert Opinion, Elagolix has emerged as a promising option for reducing endometriosis-associated pain and improving quality of life with fewer hypoestrogenic effects compared with conventional therapies.[4]**

GnRH antagonist in endometriosis management in women undergoing ART

CONSENSUS STATEMENTS

- **GnRH antagonist protocols may be preferred in women with endometriosis undergoing IVF/ICSI, particularly poor responders and those with diminished ovarian reserve following endometrioma or endometrioma surgery, owing to effective prevention of premature LH surge and improved cycle flexibility** (Level B/Class IIa; Consensus: 89% Agreement; 11% Disagreement).
- **Oral antagonists such as Elagolix are emerging as potential alternatives to injectable GnRH antagonists for ovarian suppression during IVF cycles.** (Level B/Class IIa; Consensus: 91% Agreement; 9% Disagreement).
- **Oral GnRH antagonists are an emerging option in women where prolonged hypoestrogenism or delayed IVF timelines associated with ultra-long GnRH agonist protocols are undesirable.** (Level D/Class IIb; Consensus: 96% Agreement; 4% Disagreement).

Discussion

The GnRH antagonist protocol is considered an appropriate option for poor responders, including women with diminished ovarian reserve secondary to ovarian endometrioma or following surgical

excision of endometrioma in IVF cycles, as it provides immediate suppression of the luteinizing hormone (LH) surge. In women undergoing IVF/ICSI treatment, the GnRH antagonist protocol should be preferred, and an elective frozen embryo transfer strategy may also be considered.[6]

Current evidence suggests that oral GnRH antagonists may effectively suppress premature ovulation during IVF cycles, with outcomes comparable to injectable GnRH antagonists. Relugolix, at an oral dose of 40 mg, demonstrates a prolonged plasma half-life of approximately 45 hours. Elagolix, an orally active nonpeptide GnRH antagonist, reaches peak plasma concentrations within 30–60 minutes and has a short plasma half-life of approximately 4–6 hours, enabling rapid, dose-dependent ovarian suppression with quick reversibility after discontinuation.[7]

Across both Phase III ELARIS EM-I and EM-II trials, Elagolix demonstrated significant dose-dependent reductions in dysmenorrhea, nonmenstrual pelvic pain, and dyspareunia, with improved quality of life and reduced rescue analgesic use at both 150 mg once-daily and 200 mg twice-daily regimens. Compared with leuprolide acetate, Elagolix provided effective ovarian suppression with a lower magnitude of bone mineral density loss, without the initial flare effect, and with rapid reversibility following treatment discontinuation.[4]

Management across IVF profiles

CONSENSUS STATEMENTS

1. Elagolix in ovulation induction for normo responders

- **Elagolix is emerging as an effective oral alternative to injectable GnRH antagonists for ovulation suppression during fresh IVF cycles in women with adequate ovarian reserve, owing to its rapid and effective LH suppression, flexible administration, and rapid reversibility after discontinuation.** (Level C/Class IIb; Consensus: 92% Agreement; 8% Disagreement).

2. Elagolix for PCOS women/ high BMI

- **Elagolix 200 mg BID from Day 6 until trigger day may be considered as aneffective oral option in PCOS and high-BMI women, which may support controlled ovarian stimulation witheffective LH suppression.** (Level D/Class IIb; Consensus: 88% Agreement; 12% Disagreement).

3. Elagolix 'early start' for high responders

- **Early-start Elagolix 200 mg BID from Day 1 of stimulation until trigger day may improve LH control, follicular synchronization, and oocyte retrieval efficiency in high responders undergoing IVF.** (Level D/Class IIb; Consensus: 96% Agreement; 4% Disagreement).

4. Elagolix in OHSS prevention

- **Elagolix may potentially support OHSS risk mitigation strategies in selected high responders, owing to its ability to control LH and estradiol rise while maintaining comparable oocyte yield with a safer hormonal profile.** (Level D/Class IIb; Consensus: 96% Agreement; 4% Disagreement).

5. Rescue antagonist add-on (for LH escape)

- **In women with LH escape despite Elagolix, adding an injectable GnRH antagonist to Elagolix 200 mg BID until trigger day may rapidly control premature LH surge and maintain cycle continuation in the majority of IVF cycles.** (Level D/Class IIb; Consensus: 100% Agreement).

Discussion

Elagolix in ovulation induction

The oral GnRH antagonist elagolix appears to provide ovulation suppression comparable to that achieved with the injectable GnRH antagonist ganirelix, with similar embryological and clinical IVF outcomes. Oral elagolix offers a less invasive, potentially more cost-effective, and patient-friendly alternative for pituitary suppression during assisted reproduction.[8] A study comparing oral elagolix (50 mg every other day) with daily injectable ganirelix/cetrorelix during controlled ovarian stimulation have demonstrated comparable IVF outcomes, including the number of oocytes retrieved, mature oocytes obtained, fertilization rates, blastocyst formation rates, euploidy rates, and endometrial thickness at the time of trigger.[9]

Elagolix for women with PCOS/high BMI

Elagolix has demonstrated effective suppression of LH secretion and prevention of premature ovulation when administered during controlled ovarian stimulation and continued until trigger. Evidence suggests that oral elagolix can be a convenient alternative to injectable GnRH antagonists in selected IVF patients, particularly those at risk of premature LH surge.[10]Additional evidence of elagolix's LH-suppressive effects are shown in women with PCOS, where treatment significantly reduced LH levels as early as week 1 compared with placebo. FSH levels remained relatively stable, while serum estradiol and testosterone concentrations were consistently lowered across various dosing regimens. These findings highlight the potent LH-suppressive activity of elagolix and support its potential use in IVF stimulation protocols. Although evidence from IVF-specific studies remains limited, data suggest that elagolix may serve as a promising oral alternative to injectable GnRH antagonists.[11]

Elagolix 'early start' for high responders

The early follicular phase is the most quiescent stage of the HPO axis and an ideal period for hormonal suppression. Studies have shown that elagolix (200 mg twice daily) effectively suppresses FSH, LH, estradiol, and progesterone when administered during the early follicular phase, with dose-dependent inhibition of gonadotropins and ovulation. These findings suggest that early initiation of elagolix during controlled ovarian stimulation may enhance LH suppression, improve follicular synchronization, and potentially increase oocyte yield in selected high responders.[12,13]

Elagolix in OHSS prevention

GnRH antagonist protocols are effective in reducing the risk of ovarian hyperstimulation syndrome (OHSS) in high responders. Studies have shown lower cycle cancellation and OHSS rates with GnRH antagonist protocols compared with GnRH agonist protocols. Additionally, GnRH antagonist rescue strategies can reduce serum estradiol levels, prevent cycle cancellation, and enable cycle completion without compromising oocyte maturity, fertilization, embryo quality, blastocyst development, pregnancy, or live-birth outcomes.[14,15]

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ANNEXURE

Classification of endometriosis

Staging of endometriosis

According to the revised ASRM (rASRM) scoring system, endometriosis is categorized into four stages based on lesion severity, size, depth, location, and extent. Stage I (minimal) scores 1–5 points, Stage II (mild) 6–15 points, Stage III (moderate) 16–40 points, and Stage IV (severe) more than 40 points. Deep and large (>3 cm) ovarian endometriotic lesions are assigned 20 points, while dense ovarian and tubal adhesions score 16 points. Complete obliteration of the posterior cul-de-sac is assigned 40 points, indicating severe endometriosis.[1]

ENZIAN differs from rASRM in its inclusion of (and the focus on) deep infiltrating endometriosis. In this classification retroperitoneal structures are divided into three compartments:[2]

- Compartment A: vagina, recto-vaginal septum;
- Compartment B: uterosacral ligaments to the pelvic wall (BB: bilateral involvement);
- Compartment C: rectum and sigmoid colon.

Disease severity is classified as:

- Grade 1: invasion <1 cm;
- Grade 2: invasion 1-3 cm;
- Grade 3: invasion >3 cm

Deep endometriosis invasion beyond the lesser pelvis and invasion of organs are recorded separately:

- FA: adenomyosis;
- FB: bladder invasion;
- FU: intrinsic ureteral endometriosis;
- FI: bowel disease cranial to the sigmoid colon;
    - F0: other locations.

The prefix "F" stands for "far" or "foreign", referring to distant retroperitoneal structures.

In 2021, the American Association of Gynecologic Laparoscopists introduced a new anatomy-based staging system for endometriosis, offering improved assessment of surgical complexity compared to the revised ASRM system. This classification enables a more reliable preoperative evaluation, supports informed prognostic counseling, and provides better insight into potential postoperative risks.[1]

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DIAGNOSIS OF

Goal: Early diagnosis, accurate disease mapping, and Individualize

1 CLINICAL EVALUATION & INITIAL ASSESSMENT

Women presenting with symptoms suggestive of endometriosis

- Dysmenorrhea
- Chronic pelvic pain
- Dyspareunia
- Dyschezia
- Dysuria
- Infertility
- Heavy/irregular
  - » menstrual bleeding
- Fatigue / GI symptoms

Clinical assessment

- Detailed medical, menstrual and family history
- Symptom characterization and severity assessment
- Quality-of-life assessment
- Pelvic examination
- Consider differential diagnoses

Clinical suspicion of endometriosis?

- **Low suspicion** → Evaluate alternative causes
- **Moderate/High suspicion** → Proceed to imaging evaluation

Differential diagnoses

- Irritable bowel syndrome
- Adenomyosis
- Primary dysmenorrhea
- Pelvic inflammatory disease
- Interstitial cystitis
- Ovarian cysts
- Pelvic floor disorders
- Leiomyomas
- Bladder disorders
- Congenital, oncologic and non-gynecologic causes

Special clinical considerations

Adolescents

- Persistent dysmenorrhea despite pain management
- Early evaluation recommended
- Early recognition may reduce future disease burden

Infertility

- Assess reproductive goals
- Consider fertility evaluation and referral where appropriate

2 SONOGRAPHY (USG)

Initiate empiric medical therapy* and perform imaging evaluation

First-line imaging

- **Transvaginal Ultrasound (TVS)** — Preferred imaging modality
- **OR**
- **Transabdominal Ultrasound** — When TVS is not feasible

Imaging findings suggestive of endometriosis?

- **YES**
  - **Characterize disease extent**
    - Endometrioma
    - Adhesions
    - Organ involvement
  - → **Proceed to disease mapping and staging**
- **NO/INCONCLUSIVE**
  - **Persistent or high clinical suspicion?**
    - **NO** → **Evaluate alternative diagnoses**
    - **YES** → **Proceed to Pelvic MRI**

Biomarkers

- CA-125 is not recommended for diagnosis
- No currently available biomarker can reliably confirm or exclude endometriosis

IMPORTANT PR

- Normal pelvic examination does not exclude endometriosis.
- Normal TVS does not exclude superficial peritoneal disease.
- Normal MRI does not exclude superficial peritoneal disease.
- TVS is the preferred first-line imaging modality.
- MRI is for dis and ev infiltrat

*Empiric therapy may be initiated based on clinical suspicion while diagnostic evaluation is ongoing.

ENDOMETRIOSIS

ed management while minimizing unnecessary invasive procedures

3 PELVIC MRI

Indications

- Persistent / high clinical suspicion despite negative or inconclusive TVS
- Suspected deep infiltrating endometriosis
- Pre-operative disease mapping
- TVS technically inadequate or not feasible

Imaging findings suggestive of endometriosis?

YES

Disease mapping

- Rectovaginal disease
- Bowel involvement
- Bladder involvement
- Ureteric involvement
- Multifocal disease

NO

Continue clinical management

- Clinical diagnosis remains possible
- Negative MRI does not exclude superficial peritoneal endometriosis

Disease staging

Proceed to classification and management planning

Shared decision-making

Discuss with patient:

- Continued empiric management
- Need for surgical confirmation
- Patient preferences and reproductive goals

4 LAPAROSCOPY

Consider diagnostic / therapeutic laparoscopy + biopsy

When:

- Symptoms persist despite treatment
- Diagnostic remains uncertain
- Patient desires definitive diagnosis
- Surgical management is planned
- Advanced disease is suspected

Diagnostic/therapeutic laparoscopy

- Visual inspection of lesions
- Excision or ablation when feasible
- Histopathological confirmation if biopsy obtained

Surgical classification

- **rASRM Classification**
  Stage I-IV disease
- **#ENZIAN Classification**
  Deep infiltrating endometriosis
- **AAGL 2021 Classification**
  Anatomy-based assessment of surgical complexity

Individualized management plan based on:

- Disease extent and phenotype
- Symptom burden
- Fertility and reproductive goals
- Patient preferences
- Risk-benefit assessment

Individualized management based on disease extent, symptoms, and reproductive goals

ACTICE POINTS

- recommended
- ease mapping
- valuation of deep
- ting disease.

Biomarkers including CA-125, are not recommended for diagnosis.

Diagnostic laparoscopy is not mandatory for all women and should be reserved for selected situations.

Shared decision-making should guide the choice between empiric treatment and surgical diagnosis.

Early recognition and evaluation in adolescents may reduce future disease burden.

Abbreviations: TVS: Transvaginal ultrasound: MRI: Magnetic Resonance Imaging; rASRM: Revised American Society for Reproductive Medicine; AAGL: American Association of Gynecologic Laparoscopists; CA 125: Cancer antigen 125

MEDICAL MANAGEM

Goal: Reduce pain, improve quality of life, suppress disease activity and recu

1 ASSESSMENT & PATIENT PROFILING

Confirm or clinically suspected endometriosis

Assess key determinants

- Reproductive goals & fertility intent
- Previous treatment exposure & response
- Disease recurrence / chronicity
- Disease severity
- Quality of life / functional impact
- Need for rapid symptom control
- Contraindications to hormonal therapy
- Comorbidities

Disease severity

- Mild-Moderate
- Moderate-Severe

Desire for pregnancy/ fertility preservation?

YES

Fertility-conscious management
- NSAIDs as needed
- Dydrogesterone (cyclic or continuous)
- Fertility evaluation if infertility present

→ **Proceed to symptom-based management**

→ **Consider ART / IVF referral + Surgical evaluation when indicated**

→ **Goal: Symptom control while preserving ovulation and reproductive potential**

NO

→ **Proceed to symptom-based management**

Symptom-based management

Mild
- NSAIDs as needed
- Lifestyle & supportive measures

Moderate
- NSAIDS + COCs or Progestins
- Lifestyle & supportive measures

Moderate-severe
- Proceed to Step 28
- (Consider GnRH-based therapies)

2A MILD TO MODERATE DISEASE
Start Treatment With

NSAIDs
For short-term pain relief

Continuous Combined Oral Contraceptives (COCs)
(oral/transdermal / vaginal ring)
Preferred over cyclic regimens

Progestins (choose based on patient profile, tolerability, contraindications & preference)
- Medroxyprogesterone acetate (MPA)
- Norethindrone acetate
- Dydrogesterone (cyclic or continuous)
- Dienogest
- LNG-IUS (Levonorgestrel-releasing intrauterine system)

→ **Progestins preferred in women desiring fertility preservation or maintenance of cyclicity**

→ **Assess Response at 3-6 months**

Adequate Response
- Continue therapy
- Long-term maintenance
- Reassess periodically

Inadequate Response
- Persistent pain
- Significant QoL impairment
- Intolerable adverse effects

ADOLESCENT ENDOMETRIOSIS

- Early recognition important to reduce symptom progression and future disease burden.
- Start with NSAIDS, COCs or progestins as first-line.
- If moderate to severe disease or inadequate response, GnRH antagonist or agonist
- therapy with add-back may be considered under specialist supervision.
- Aim: Preserve quality of life, support normal development, and maintain future fertility potential.

Abbreviations: NSAIDs: Non-steroidal Anti-inflammatory Drugs; COCs: Combined Oral Contraceptives; LNG-IUS: Levonorgestrel-releasing Intrauterine System; GnRH: Gonadotropin-Releasing Hormanne; ART: Assisted Reproductive Technology; QoL: Quality of Life; NMPP: Non-Menstrual Pelvic Pain; IVF: In Vitro Fertilization.

MENT ENDOMETRIOSIS

urrence, and minimize need for surgery while considering reproductive goals

2B MODERATE TO SEVERE DISEASE
OR INADEQUATE RESPONSE TO FIRST-LINE THERAPY CONSIDER GnRH-BASED THERAPIES

Moderate-to-Severe Pain or Inadequate Response to First-Line Therapy

- Severe Dysmenorrhea
- Non-Menstrual Pelvic Pain (NMPP)
- Dyspareunia
- Significant QoL Impairment

Choose Between

GnRH Agonist (Leuprolide Acetate)

- Initial flare effect
- Hypoestrogenic side effects (hot flushes, night sweats, vaginal dryness, mood changes)
- Bone mineral density loss
- Injectable administration
- Delayed onset of action
- Add-back therapy required

GnRH Antagonist

Options

- Elagolix (For moderate-severe disease)
- Relugolix Combination Therapy (For Chronic Recurrent Disease Phenotype)

Relugolix Combination Therapy (Long-term Suppression)
Relugolix 40 mg + Estradiol 1 mg + Norethindrone acetate 0.5 mg (Once daily)

Assess Response at 3-6 months

Response: Yes

- Continue long-term with add-back therapy

OR

- Switch to Relugolix combination therapy with integrated add-back

Inadequate Response

- Persistent symptoms
- Poor tolerability

3 REFRACTORY DISEASE
(Persistent symptoms despite adequate trials)

Consider

- Aromatase inhibitors
- Progestins inhibitors (alternate)
- Multidisciplinary pain management
- Specialist referral
- Re-evaluation for surgery

Consider alternate therapies

- Alternate hormonal therapies
- Trial of other medical options (e.g., aromatase inhibitors)
- Multidisciplinary pain management
- Specialist referral

Consider surgery

- Diagnostic and/or therapeutic laparoscopy in selected cases

4 POST-SURGICAL MEDICAL MANAGEMENT

Conservative surgery performed

Is immediate pregnancy desired?

YES

Attempt conception / ART (IVF if indicated)

NO

Postoperative hormonal suppression
(COCs/Progestins / GnRH antagonist-based strategy based on tolerance and patient preference)
Reduces recurrence risk & improves outcomes

Goals

- Reduce recurrence
- Improve pain control
- Preserve fertility potential

PERI-MENOPAUSAL ENDOMETRIOSIS

- Evaluate symptom persistence, prior disease history, and hormone exposure.
- Consider risk of recurrence and malignant transformation.
- Choose therapy individualized to symptom severity and risk profile.
- Balance benefits with bone health, cardiovascular risk, and potential contraindications to prolonged hormonal therapy.

This algorithm is intended for guidance.
Clinical judgment and patient preference remain paramount.

SURGICAL MANAGEME

Goal: Optimize symptom relief, preserve fertility where appropriate, minimize rec

1 ASSESSMENT & PATIENT SELECTION

Suspected or confirmed endometriosis

Assess surgical indications

Consider surgery when:

- Severe/refractory pain despite medical therapy
- Ovarian endometrioma
- Deep infiltrating endometriosis
- Anatomical distortion
- Infertility associated with pain
- Intolerance or contraindication to medical therapy
- Patient preference
- Concomitant gynecological pathology

Emergency surgical indications

- Endometrioma rupture
- Ovarian torsion
- Bowel obstruction
- Obstructive uropathy

Reproductive goals assessment

Desire Fertility Preservation?

- YES → Conservative surgery preferred
- NO → Individualized surgical planning

Shared decision-making

Discuss:

- Expected symptom relief
- Surgical risks
- Fertility impact
- Risk of recurrence
- Need for postoperative suppression

Reproductive goals assessment

2 PRE-OPERATIVE EVALUATION & DISEASE MAPPING

Imaging Workup

TVS
Preferred first-line imaging

MRI
For Deep Infiltrating Endometriosis and surgical planning

Disease Mapping & Classification

#Enzian Classification
Anatomical mapping

AAGL 2021
Surgical complexity

rASRM
Disease staging

Identify Disease Phenotype

- Superficial Peritoneal Endometriosis (SPE)
- Ovarian Endometrioma (OMA)
- Deep Infiltrating Endometriosis
- Adenomyosis

Proceed to procedure selection

SPECIAL CON

Ovarian Endometrioma
Prefer cystectomy over drainage/ coagulation due to lower recurrence and better pain outcomes.

Deep Infiltrating Endometriosis (DIE)
Refer to specialized centers. Consider multidisciplinary management for complex cases.

Fertility Pr
Conservati technique. surgery wh

Abbreviations: AAGL: American Association of Gynecologic Laparoscopists; COCS: Combinec Oral Contraceptives; GnRH: Gonadotropin-Releasing Hormone; r-ASRM: revised American Society for Reproductive Medicine; TVS: Transvaginal Sonography; MRI: Magnetic Resonance Imaging; ART: Assisted Reproductive Technology; IVF: In Vitro Fertilization; BMD: Bone Mineral Density.

ENT OF ENDOMETRIOSIS

currence, and reduce surgical morbidity through individualized surgical planning

3 SURGICAL TECHNIQUE

Preferred surgical approach

Laparoscopy (Gold Standard)
- Diagnosis
- Pain management
- Fertility preservation
- Reduced recovery time

Laparotomy
(Selected situations only)
- Complex multiorgan disease
- Extensive bowel involvement
- Lack of advanced laparoscopic expertise

Disease-specific surgical strategy

Ovarian Endometrioma

Preferred
Cystectomy
- Lower recurrence
- Better pain reduction

Alternative
CO_2 laser vaporization
- Comparable recurrence beyond first year

Deep Infiltrating Endometriosis
- Refer to specialized centers
- Possible procedures:
- Excision
- Nerve-sparing surgery
- Bowel/bladder procedures when required

Superficial Peritoneal Endometriosis (SPE)
Individualized decision-making Evidence remains limited

Adenomyosis
Uterus-sparing surgery when appropriate

Laparoscopic Surgery Performed

4 POST-SURGICAL MANAGEMENT & RECURRENCE PREVENTION

Immediate pregnancy desired?

YES → Attempt conception or ART / IVF when indicated

NO → **Long-Term Postoperative Suppression** Choose according to patient profile

Dydrogesterone

Suitable for:
- Fertility preservation
- Ovulation maintenance.
- Long-term suppression

Benefits:
- Good tolerability
- Pain improvement
- Potential fertility benefit

GnRH antagonists Elagolix

Useful for:
- Pre-operative symptom control
- Post-operative pain control
- Deep infiltrating endometriosis -associated symptoms

Advantages:
- Rapid onset
- No flare effect
- Oral administration
- Faster reversibility

Relugolix combination therapy

Suitable for:
- Chronic recurrent disease
- Long-term suppression

Benefits:
- Integrated add-back therapy
- Up to 24 months treatment
- Minimal BMD loss

Follow-up goals

Reduce recurrence | Improve pain control | Preserve fertility | Improve quality of life

SIDERATIONS

reservation
ve surgery and meticulous
Minimize repeat ovarian
enever possible.

GnRH Antagonists
May be considered before and after surgery in selected patients for better symptom control and recurrence prevention.

Patient Counseling
Discuss realistic expectations, potential risks, need for postoperative medical therapy, and long-term follow-up.

This algorithm is intended for guidance.
Clinical judgment and patient preference remain paramount.

IVF AND ENDOMETRIOSIS

Woman with Endometriosis Desiring Fertility/Planned IVF

1 COMPREHENSIVE ASSESSMENT

DISEASE CHARACTERISTICS

- Stage I/II disease
- Stage III/IV disease
- Endometrioma
- Deep infiltrating endometriosis
- Adenomyosis
- Tubal disease
- Pain symptoms

FERTILITY & OVARIAN RESERVE ASSESSMENT

- Age
- AMH
- AFC
- Previous ovarian response/ POR history
- EFI (where applicable)
- Duration of infertility
- Male factor assessment

2 SURGERY INDICATED?

NO (Most infertility patients)

- Routine surgery for all endometriosis with infertility cases is not recommended
- Minimal disease: Conservative fertility-preserving approach

YES

ENDOMETRIOMA >4 cm

Consider cystectomy only if:

- Severe refractory pain
- Suspicion of malignancy
- To improve follicular access during IVF

HYDROSALPINX/SEVERE ADHESIONS

Surgical correction before embryo transfer

BILATERAL ENDOMETRIOMA/ DIMINISHED OVARIAN RESERVE

- Avoid aggressive cystectomy
- Prefer direct IVF
- Consider ablation/sclerotherapy\ if intervention is necessary

DEEP ENDOMETRIOSIS

- Surgery mainly for symptom relief
- Not routinely performed solely to improve IVF outcomes

3 NEED FOR PRE-IVF MEDICAL MANAGEMENT?

IMMEDIATE FERTILITY TREATMENT PLANNED

- Routine hormonal suppression before fertility treatment is not indicated

DELAYED IVF/WAITING FOR FERTILITY TREATMENT

Medical therapy may be used for symptom control

ELAGOLIX

- Severe pain
- Adenomyosis-associated symptoms

RELUGOLIX COMBINATION THERAPY

- Option for ovarian suppression and symptom control

SELECTED SEVERE DISEASE / SIGNIFICANT ADENOMYOSIS

- Consider prolonged GnRH agonist suppression before IVF

4 SELECTION OF FERTILITY TREATMENT

FAVOR IUI + CONTROLLED OVARIAN STIMULATION

If:

- Stage I/II disease
- Patent tubes
- Good ovarian reserve
- Younger age group

OR

FAVOR IVF/ICSI

If any of the following:

- Stage III/IV disease
- Tubal factor infertility
- Poor ovarian reserve
- Previous failed fertility treatment
- Significant endometriosis burden
- Age 2 38 years

5 IVF STIMULATION STRATEGY

PREFERRED

- GnRH antagonist stimulation protocol

CONSIDER

- GnRH agonist-based stimulation approach in women with endometriosis

6 EMBRYO TRANSFER STRATEGY

FAVOR FREEZE-ALL + FROZEN EMBRYO TRANSFER (FET)

Particularly in:

- Advanced disease
- Adenomyosis
- High inflammatory burden
- Need for endometrial optimization

Management should be individualized based on patient age, ovarian reserve, symptoms, prior treatment, and patient preferences.

7 POST-IVF CARE

ADEQUATE LUTEAL PHASE SUPPORT

- Dydrogesterone-based or standard luteal support

LONG-TERM MANAGEMENT

- Individualized suppression strategy after completion of fertility treatment
- Ongoing management of pain and recurrence risk

Abbreviations: AMH: Anti-Müllerian Hormone; AFC: Antral Follicle Count; EFI: Endometriosis Fertility Index; POR: Poor Ovarian Response; IVF: In Vitro Fertilization; GnRH: Gonadotropin-Releasing Hormone

For Comprehensive Management of Endometriosis

REGONEU

Relugolix 40 mg + Estradiol 1.0 mg +Norethindrone acetate 0.5 mg

Relieve...Reduce... Renew

Endogolix 150/200

Elagolix Tablets

ENDO PAIN Specialist

Dydrosure SR 30

Dydrogesterone Sustained Release Tablets 20 mg / 30 mg

Better for sure

ALKEM

Inspiring Healthier Lives

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