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Complex Hysterectomy in Endometriosis: Bridging Pathophysiology With Surgical Decision-Making

Tiago Meneses Alves[1,2*], Hélder Ferreira[1,2,3]

Abstract

Objectives: Endometriosis is a chronic, estrogen-dependent inflammatory disease characterized by the presence of endometrium-like tissue outside the uterus, leading to a wide spectrum of clinical manifestations. This condition can be profoundly debilitating, and its management often poses significant clinical challenges. This narrative review aims to explore the role of hysterectomy in the management of endometriosis, highlighting the challenges associated with complex surgical cases and the importance of understanding the underlying pathophysiology to guide clinical decision-making.

Methods: A comprehensive review was conducted to examine the current literature on the surgical management of complex endometriosis. Emphasis was placed on specific indications, technical considerations, anatomical challenges, multidisciplinary strategies, and outcomes related to hysterectomy in this context.

Results: While medical therapy is the first-line treatment for endometriosis-associated pain, a subset of patients remains refractory. In these cases, hysterectomy may be required to achieve definitive symptom relief. However, surgical management can be challenging due to distorted pelvic anatomy, dense adhesions, and the potential involvement of adjacent organs. A pathophysiology-informed approach, combined with multidisciplinary planning, is essential to minimize intraoperative risks and enhance outcomes.

Conclusions: Hysterectomy for endometriosis should be informed by a comprehensive understanding of the disease's pathophysiology and the potential surgical complexities involved, in order to optimize patient outcomes.

Keywords: Endometriosis, Hysterectomy, Pathophysiology, Patient care team

Introduction

Endometriosis affects approximately 10% of women of reproductive age worldwide, with an estimated prevalence of up to 50% among those with infertility or chronic pelvic pain (1,2). However, endometriosis can manifest at all stages of a woman's life, including the premenarchal and postmenopausal phases (3,4). It is a complex syndrome characterized by the presence of endometrium-like implants outside the uterine cavity, typically in the pelvis, but also in other locations (5). In the literature, endometriosis is traditionally categorized into three main types: superficial peritoneal, ovarian, and deep infiltrating endometriosis (6).

It can manifest through a broad spectrum of symptoms, including dysmenorrhea, heavy menstrual bleeding, chronic pelvic pain, dyspareunia, and infertility. Gastrointestinal involvement may include dyschezia, hematochezia, and constipation, whereas urinary tract involvement may present with hematuria, dysuria, colicky flank pain, or urinary frequency and urgency (2). In cases of extrapelvic endometriosis, though less common, clinical manifestations vary depending on the organ system involved, with rare sites including the thorax (presenting as cyclic chest pain, hemoptysis, pneumothorax, or hemothorax), peripheral nerves (manifesting as sciatica), and the diaphragm or pericardium (2,7).

Diagnosing endometriosis presents significant challenges due to its heterogeneous clinical presentation and the overlap of symptoms with other medical conditions. These challenges are further compounded by the absence of specific biomarkers, limited awareness among both the public and healthcare professionals, and concerns regarding stigma or the normalization of symptoms (2). Furthermore, symptom severity does not always correlate with disease extent, complicating both diagnosis and management (4). As a result, endometriosis is often underdiagnosed, with diagnostic delays that can extend up to 10 years from the onset of initial symptoms (2,4,8). This delayed diagnosis contributes to ongoing patient suffering, progression of the disease, and an increased burden on the healthcare system. Indeed, studies have shown that the combined direct and indirect costs associated with endometriosis are comparable to those of other chronic diseases, such as diabetes, Crohn's disease, or rheumatoid arthritis (9). Laparoscopy is no longer considered the diagnostic gold standard. It is currently reserved for cases in which less invasive procedures, such as negative imaging findings and/or empirical treatment

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[1]Department of Gynecology and Obstetrics, Centro Materno Infantil do Norte – Unidade Local de Saúde de Santo António (CMIN-ULSSA), Porto, Portugal. [2]Instituto Ciências Biomédicas Abel Salazar – ICBAS, University of Porto, Porto, Portugal. [3]Gynecology Minimally Invasive Surgery & Endometriosis Unit, Department of Gynecology and Obstetrics, CMIN-ULSSA, Porto, Portugal.
*Corresponding Author: Tiago Meneses Alves, Email: u13415@chporto.min-saude.pt

Key Messages

- A thorough understanding of endometriosis pathophysiology is essential for informed surgical decision-making in complex hysterectomy cases.
- Multidisciplinary collaboration is pivotal to mitigate surgical morbidity and optimize outcomes in the management of advanced endometriosis.
- A pathophysiology-guided approach improves patient selection and enhances long-term symptom relief following hysterectomy

with analgesics or hormonal therapy, have failed or are deemed inappropriate (4).

Determining the appropriate management strategy for endometriosis is challenging and often requires a multidisciplinary approach. It may encompass medical therapy and/or surgical intervention, tailored to the individual patient's symptoms, disease severity, and reproductive goals. Medical therapy is often the first-line treatment, particularly for endometriosis-associated pain (4). Standard initial options include nonsteroidal anti-inflammatory drugs (NSAIDs) in association with combined oral contraceptives or progestins due to their low side-effect profile and effectiveness in relieving symptoms for many patients (10,11). In cases of inadequate response, and following appropriate patient counseling regarding potential adverse effects, second-line agents such as gonadotropin-releasing hormone (GnRH) analogs (agonists or antagonists), danazol, or aromatase inhibitors may be considered (8). Surgical treatment, by contrast, should be considered for patients with endometriosis-associated pain that is refractory to medical therapy, as well as in cases involving bowel or urinary tract obstruction, or infertility (12). Surgical options range from conservative procedures, such as excision or ablation of endometriotic lesions, to definitive interventions, including hysterectomy with or without bilateral salpingo-oophorectomy (BSO) (2). A systematic review by Alkatout et al found no significant difference in postoperative outcomes between total and subtotal hysterectomy for the treatment of endometriosis (13). However, total hysterectomy is generally preferred as it obviates the need for ongoing cervical cancer screening. Endometriosis is frequently associated with distorted pelvic anatomy due to extensive adhesions and infiltration of adjacent organs, which can substantially increase the complexity of hysterectomy procedures, regardless of the surgical route (14,15). Consequently, these patients are at a higher risk of major perioperative complications compared to those undergoing surgery for other benign indications (16).

Integrating pathophysiological insights into the planning and execution of hysterectomy may improve surgical precision and outcomes. A comprehensive understanding of the multifactorial nature of endometriosis, including hormonal, immunological, and genetic factors, enables more targeted surgical strategies and informs preoperative assessment, intraoperative decision-making, and postoperative management. This review synthesizes current evidence on applying pathophysiological knowledge to the surgical management of endometriosis, with a particular focus on complex hysterectomy. By highlighting the interface between advanced scientific understanding and surgical practice, we aim to provide a structured framework for optimizing outcomes in this challenging clinical setting.

A comprehensive narrative literature review was conducted using PubMed/MEDLINE and the Cochrane Library databases. The search strategy included the terms: "endometriosis", "pathophysiology", "deep infiltrating endometriosis", "hysterectomy", "complex hysterectomy", "surgical outcomes", and "complications," alone and in combination. Articles published in English up to July 2025 were considered. Reference lists of relevant studies were screened to identify additional eligible articles. Inclusion criteria were: (a) original clinical studies, systematic reviews, meta-analyses, international guidelines, or expert surgical reviews directly addressing endometriosis pathophysiology or surgical management; and (b) studies reporting outcomes related to hysterectomy, surgical technique, or perioperative risk in endometriosis. Exclusion criteria were: case reports, conference abstracts, non-peer-reviewed material, and studies not relevant to the scope of this review. Table 1 provides an overview of the types of evidence sources included in this narrative review.

Endometriosis: Exploring Pathophysiological Mechanisms

The exact etiology and pathogenesis of endometriosis remain unclear. The origin of endometrial tissue at ectopic sites is still debated, and several complementary theories have been proposed (7,17). Endometriosis is recognized as a multifactorial disorder involving genetic, epigenetic, immunological, and hormonal mechanisms that collectively support implantation, survival, and proliferation of endometrium-like tissue outside the uterus (18). This biological complexity contributes to the heterogeneous surgical presentation of the disease, in which pelvic anatomy may be significantly distorted and operative planes are often unpredictable, emphasizing the need for individualized surgical planning during complex hysterectomy.

The retrograde menstruation (Sampson's) theory remains the most widely accepted explanation for typical pelvic disease (6,18). However, it does not fully explain deep infiltrating endometriosis (DE) or extrapelvic lesions. Alternative mechanisms, including coelomic metaplasia, lymphovascular dissemination, iatrogenic implantation, and Müllerian embryonic rests, likely contribute to anatomical variability and lateral disease spread (6,18). These diverse pathogenetic pathways reflect

Table 1. Summary of Evidence Sources Included in the Review

Evidence source	No. of references	Contribution to review
International guidelines (eg, ESHRE, ACOG)	3	Diagnostic criteria and evidence-based management recommendations
Surgical observational studies (cohort/case series)	25	Data on hysterectomy complexity, complications, and operative strategy
Systematic and narrative reviews	33	Contextualization of current evidence
Pathophysiology and molecular studies	20	Mechanistic foundations for surgical planning
Imaging and diagnostic evaluation studies	8	Disease mapping and preoperative staging
Surgical technique and operative strategy papers	23	Operative decision-making in complex hysterectomy
Consensus statements and multidisciplinary recommendations	3	Integration of MDT principles and advanced pelvic surgery

ACOG: American College of Obstetricians and Gynecologists; ESHRE: European Society of Human Reproduction and Embryology; MDT: Multidisciplinary team.

the clinical observation that surgical disease distribution does not always correlate with symptom severity. Disease involvement may extend to parametrial, ureteral, bladder, or intestinal compartments. This variability reinforces the importance of thorough preoperative imaging and maintaining a high index of suspicion for extrauterine involvement (19).

Emerging mechanistic studies support a fundamental role of immune dysfunction in the pathogenesis and persistence of endometriosis. Peritoneal macrophage activation, impaired natural killer (NK) cell cytotoxicity, and aberrant T-cell responses allow ectopic cells to evade clearance (20-22). Elevated inflammatory cytokines, such as interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-α), promote angiogenesis by increasing vascular endothelial growth factor (VEGF) expression (23), resulting in vascularized, adhesive, and fibrotic lesions. These inflammatory changes pose significant technical challenges during hysterectomy, as they are frequently associated with dense adhesions, obliteration of tissue planes, and friable vascular surfaces, which increase the risk of hemorrhage and adjacent organ injury (24,25).

Genetic susceptibility further contributes to disease heterogeneity. Women with an affected first-degree relative have a sevenfold higher risk of endometriosis (7), and recent evidence implicates Kirsten Rat Sarcoma Viral Oncogene Homolog (KRAS) polymorphisms and microRNA (miRNA) dysregulation in more aggressive phenotypes (26-28). These molecular alterations correlate clinically with parametrial fibrosis, ureteral encasement, and postoperative recurrence, suggesting that genetic and epigenetic signatures may help predict surgical complexity and guide early multidisciplinary team involvement (29).

Hormonal imbalance plays a central pathogenic role. Local aromatase overexpression and increased prostaglandin E2 (PGE2) production enable estrogen hyperactivity within lesions, while progesterone resistance, driven by altered progesterone receptor isoforms A and B (PR-A/PR-B) expression and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) activation, reduces response to medical therapy (30,31). These mechanisms explain why some patients develop refractory pain and progress even under hormonal suppression, ultimately requiring definitive surgery. Estrogen-driven angiogenesis also increases intraoperative vascularity, underscoring the importance of meticulous hemostatic technique, surgical energy selection, and postoperative strategies to prevent recurrence.

Epigenetic dysregulation, including aberrant DNA methylation and altered miRNA expression (miR-155, miR-29c, miR-196a, miR-9, and miR-21), contributes to invasiveness, fibrosis, and disease chronicity (31-33). These molecular drivers may explain the persistence of DE lesions despite prior surgeries, supporting long-term follow-up and individualized postoperative suppression in high-risk cases.

Collectively, these biological insights demonstrate that endometriosis is not a uniform disease but rather a spectrum of phenotypes influenced by inflammatory, hormonal, genetic, and immunologic mechanisms. Acknowledging this heterogeneity has direct surgical implications: operative planning must account for potential multicompartmental involvement, altered tissue response, and recurrence risk, supporting the need for structured, pathophysiology-informed surgical strategies in complex hysterectomy.

Pathophysiological Considerations in Surgical Management

A personalized, pathophysiologically informed approach is essential for optimizing hysterectomy in endometriosis. Surgical planning must account not only for disease extent but also for individual patient factors, including reproductive goals, pain phenotype, prior response to medical therapy, and comorbidity risk profile. Biological variability, such as progesterone resistance, KRAS/miRNA-associated lesion aggressiveness, and chronic inflammatory burden, can influence disease behavior, surgical difficulty, and recurrence risk (34). Imaging phenotype (superficial, ovarian, or deep infiltrating endometriosis) and associated anatomical distortion determines the route of hysterectomy, the extent of dissection, and the need for multidisciplinary involvement. Understanding these biological and clinical variables is critical to anticipate surgical complexity and tailoring the operative strategy accordingly (19,35). Within this context, the following parameters must be considered:

- Disease phenotypes and preoperative evaluation: a thorough physical examination and detailed assessment of the patient's symptomatology are essential components of the initial clinical evaluation, as they may raise suspicion for DE or extrapelvic disease (19). Subsequent imaging studies, particularly magnetic resonance imaging (MRI) and transvaginal ultrasound (TVUS), are pivotal for establishing a presumptive diagnosis and characterizing the anatomical distribution and extent of endometriotic lesions (19). Additional diagnostic procedures, such as cystoscopy or colonoscopy, are not routinely recommended and should generally be reserved for specific indications (36,37).
- Surgical considerations: the surgical management of hysterectomy in the context of endometriosis requires a meticulously individualized approach that balances complete excision of disease with preservation of organ function and minimization of morbidity (38). Conservative surgery aims to preserve reproductive organs and fertility, often focusing on excising endometriotic lesions while maintaining the uterus and ovaries and restoring normal pelvic anatomy (39,40). This approach is generally considered the first-line surgical option for most women, as it is less invasive and associated with lower perioperative morbidity (39). It preserves both fertility and endogenous hormonal production (39). In contrast, definitive surgery may be indicated for those with severe or refractory symptoms despite maximal medical therapy, recurrent or persistent pain unresponsive to conservative surgery, coexisting conditions such as adenomyosis or fibroids, and completed childbearing (Table 2) (38,39). In selected cases, it may be performed in combination with BSO, particularly when ovarian endometriosis or recurrent disease is present. The choice between conservative and definitive approaches must be guided by multiple factors, including the patient's age, symptom severity, reproductive goals, prior surgical history, and the extent and distribution of disease (41). Minimally invasive surgery (MIS) is widely preferred in gynecology and has become the standard of care in specialized centers (42). Both laparoscopy and robotic-assisted laparoscopy are favored for their association with superior pelvic visualization, reduced intraoperative blood loss, decreased postoperative pain, shorter hospitalization, faster recovery, and improved cosmetic outcomes (42). Robotic-assisted surgery offers enhanced dexterity and precision, particularly in anatomically complex regions such as the pouch of Douglas, owing to articulated instruments and a stable, magnified three-dimensional view (43). However, in cases of extensive disease or challenging anatomical involvement, laparotomy may be necessary to ensure safe dissection and enable complex reconstructive procedures. Table 3 summarizes the main surgical routes, their respective indications, and technical considerations.
- Multidisciplinary approach: the complex nature of endometriosis, particularly in cases of DE involving the gastrointestinal or urinary tract, often necessitates a multidisciplinary surgical team (46) Preoperative findings suggestive of multiorgan involvement should prompt collaborative planning to optimize individualized surgical strategies and achieve complete resection (47,48).
- Patient education and counseling: shared decision-making is a cornerstone of patient-centered care. Comprehensive patient education regarding the pathophysiology, clinical manifestations, potential impact on fertility, and the increased risk of recurrence in advanced-stage disease is essential. Clear communication of these aspects enables patients to better understand their condition and the rationale behind different treatment options, particularly

Table 2. Indications for Hysterectomy ± BSO in Endometriosis

Indication	Clinical context	Considerations
Severe symptoms or refractory to medical therapy/previous conservative surgery	Persistent pelvic pain, severe dysmenorrhea, heavy menstrual bleeding, dyspareunia, or other debilitating symptoms unresponsive to medical or conservative therapy.	Assessment of treatment duration and patient adherence; evaluation of effects on quality of life and daily functioning.
Anatomical distortion	Pelvic anatomy significantly altered by adhesions, large endometriomas, or deep infiltrating lesions.	Preoperative imaging and multidisciplinary evaluation may be required.
Presence of associated conditions	Coexistent pathology: adenomyosis, large uterine fibroids, breast cancer gene (BRCA) 1 and 2 mutations, or Lynch syndrome.	Consider these factors in surgical decision-making and planning.
Desire for definitive treatment	Patient preference for definitive symptom control after appropriate counseling.	Discuss fertility implications and alternative options.
Significant impact on quality of life	Severe physical, psychological, or social impairment due to endometriosis-related symptoms.	Consider when childbearing is complete or not desired. Psychological support should be offered.

Table 3. Surgical Approaches for Hysterectomy in Endometriosis (44,45)

Routes of hysterectomy	Clinical indications	Contraindications/relative contraindications	Technical considerations
Abdominal	Multiorgan involvement; severely distorted anatomy	Mild disease with minimal adhesions	Provides full exposure; reserved for cases of highest surgical complexity
Laparoscopy	Moderate to severe endometriosis; DE with accessible anatomy	Extensive adhesions; poor visualization	Preferred in specialized centers; allows magnification and precision
Robotic- assisted laparoscopy	Deep fibrosis or complex DE	Cost limitations; unavailable platform	Enhanced ergonomics; useful for parametrial and deep pelvic dissection
Vaginal	Minimal adhesions; mobile uterus	DE or obliteration of cul-de-sac	Suitable for selected, uncomplicated cases

DE: deep infiltrating endometriosis.

when more invasive surgical interventions are being considered (41).

To translate these biological and anatomical considerations into clinical practice, a structured approach to case selection and operative planning is essential. Figure 1 presents the Pathophysiology-Anchored Triage and Hysterectomy Strategy decision flowchart, which synthesizes patient profiling, reproductive goals, disease phenotype, imaging findings, and multidisciplinary evaluation into a practical preoperative strategy for hysterectomy in endometriosis.

Surgical Management of Complex Hysterectomy

The complex pathophysiology of endometriosis results in progressive disruption of the typical architecture and obliteration of anatomical planes, thereby posing significant intraoperative challenges (49). Consequently, several technical considerations must be taken into account when performing a hysterectomy for endometriosis.

Surgical Entry and Initial Exploration

In patients with suspected extensive adhesions, particularly those with prior abdominal or pelvic surgery or significant anatomical distortion on preoperative imaging studies, laparoscopic entry via an open (Hasson) technique or Palmer's point is recommended to minimize visceral injury (50). Following safe access, a systematic evaluation of the abdominal and pelvic cavities should be performed to assess disease extent and involvement of adjacent structures, and to guide surgical planning for hysterectomy (with or without BSO) and excision of endometriotic lesions.

Distorted Pelvic and Obliterated Tissue Planes

Dense adhesions between the uterus and surrounding structures, such as the bowel, bladder, or pelvic sidewalls, can complicate dissection. Sharp dissection is preferred to minimize tissue trauma and preserve anatomical integrity (24). Hydrodissection, in conjunction with the use of cold scissors, facilitates delineation of tissue planes, while laparoscopic magnification enhances precise identification of anatomical landmarks (24,49).

Ureteral Involvement or Anatomical Displacement

Ureteral involvement in endometriosis presents a significant challenge during hysterectomy, as ureters may be displaced, encased in fibrotic tissue, or directly infiltrated by endometriotic lesions (51). These alterations increase the risk of iatrogenic ureteral injury, particularly near the uterosacral and infundibulopelvic ligaments (52). Early and systematic ureterolysis, initiated at the pelvic brim, is recommended to ensure safe identification and mobilization. Indocyanine green (ICG) fluorescence imaging has emerged as a valuable adjunct for intraoperative ureteral mapping. Following preoperative cystourethroscopy and retrograde ICG instillation, ureters can be visualized in real-time using near-infrared (NIR) imaging systems (53). ICG fluorescence imaging is a safe and feasible method for ureteral mapping during complex MIS (53).

Additionally, minimizing thermal energy near the ureters is critical. Lateral thermal spread may lead to devascularization or delayed ureteral necrosis, even in the absence of direct injury (54). Thus, meticulous dissection, precise identification, and continuous visualization of the ureters are essential throughout key operative steps to reduce the risk of complications.

Bladder Involvement and Anterior Dissection

Anterior compartment disease frequently results in adhesions between the bladder and either the uterus or the anterior abdominal wall, which significantly increases the risk of inadvertent cystotomy during surgical dissection (55,56). In such cases, a meticulous, sharp dissection of the uterovesical fold should be performed. Notably, Nezhat et al have also described the reverse vesicouterine fold dissection as an effective technique during laparoscopic hysterectomy for minimizing the risk of incidental cystotomy (57). This approach involves accessing a lateral plane via blunt dissection through the broad ligament, then sweeping medially beneath adhesions to mobilize the bladder from inferior to superior and safely expose the cervix for colpotomy (57).

Following complex dissections, an intraoperative assessment of bladder integrity is essential. It can be effectively achieved through the instillation of ICG

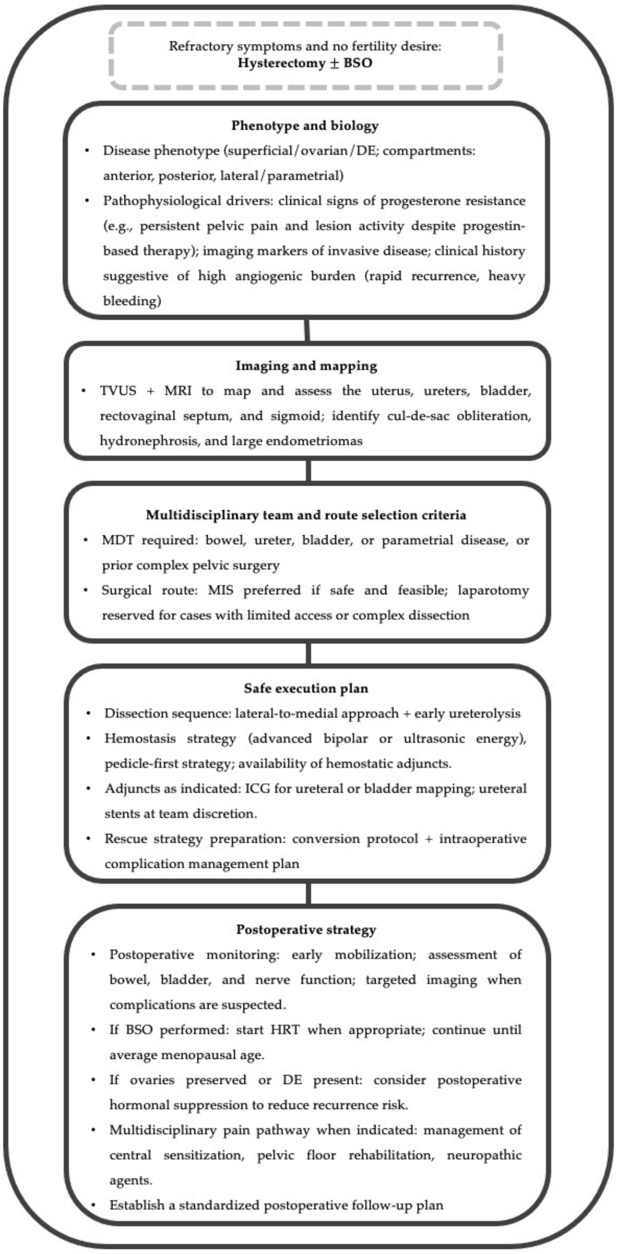

Figure 1. Pathophysiology-Anchored Triage and Hysterectomy Strategy Decision Flowchart. Abbreviations: BSO, bilateral salpingo-oophorectomy; DE, deep infiltrating endometriosis; HRT, hormone replacement therapy; ICG, indocyanine green; MDT: multidisciplinary team; MIS, minimally invasive surgery; MRI, magnetic resonance imaging; TVUS, transvaginal ultrasound.

combined with NIR fluorescence imaging, which has been successfully used to demarcate the bladder and assess bladder wall integrity, particularly in complex surgeries (58).

When bladder endometriosis is suspected, particularly full-thickness lesions, preoperative planning should include consideration of partial cystectomy, involving multidisciplinary collaboration with urology (59).

Dense Adhesions and Obliterated Rectouterine Pouch

Dense adhesions involving the rectum and posterior uterus are commonly observed in patients with DE, particularly when the rectouterine pouch is obliterated (60). These anatomical distortions can represent a significant challenge during hysterectomy. As described by Tanaka et al for hysterectomy in cases with posterior cul-de-sac obliteration, after mobilizing the sigmoid colon and separating the bladder from the uterus, the lateral pararectal space should be developed and the ureter identified (60). Subsequently, the ureter is carefully isolated, the medial pararectal space is developed, and the hypogastric nerve plane is meticulously separated (60). Finally, the pouch of Douglas is reopened to provide further access (60).

In cases where endometriotic nodules are densely adherent to the rectum, multidisciplinary collaboration with colorectal surgery is often warranted to assess the extent of disease and determine the most appropriate surgical approach. Depending on the depth and circumferential involvement of the lesion, surgical options may also include rectal shaving (for superficial lesions that do not invade beyond the serosa), discoid excision (for full-thickness but localized lesions), or segmental resection with anastomosis (indicated in cases of bowel stenosis, multifocal disease, lesions > 3 cm or when more than 50% of the bowel wall circumference is involved) (29).

Ovarian Endometriomas and Adhesions

The presence of large endometriomas and adhesions involving the ovaries and pelvic sidewalls presents significant challenges during hysterectomy. These include distortion of adnexal anatomy and obscuration of critical structures such as the ureters and pelvic vasculature (61). This anatomical disruption can complicate both the performance of a hysterectomy and decisions regarding ovarian conservation or oophorectomy. When BSO is indicated, a meticulous dissection should begin laterally with mobilization of the adnexa at the level of the infundibulopelvic ligament, as this provides a more accessible entry point, especially in complex cases where midline anatomy may be distorted or obliterated (62). Precise identification and isolation of the ureter should precede any medial dissection (62). If ovarian preservation is planned, cystectomy should be performed with minimal use of bipolar electrosurgery to reduce thermal damage and preserve ovarian reserve. Indeed, two meta-analyses reported that hemostatic sealants and suturing result in a smaller reduction in anti-Müllerian hormone (AMH) levels compared to bipolar electrosurgery (63,64). However, in cases of extensive disease with dense adhesions, complete cystectomy may be technically challenging. In such situations, oophorectomy may become necessary (65). Therefore, it is essential to counsel all patients preoperatively about the potential need for oophorectomy, even when ovarian preservation is initially intended.

Intraoperative Hemorrhage and Vascular Injury

One of the significant intraoperative challenges during endometriosis-related hysterectomy is the increased risk of hemorrhage and vascular injury. It is primarily due to inflammation-induced angiogenesis and distortion of normal pelvic vascular anatomy associated with the disease (25). These pathological changes can obscure anatomical landmarks and displace or entrap major vascular structures. As a result, standard dissection planes may became unreliable, increasing the likelihood of inadvertent vascular injury and significant intraoperative bleeding (66). To mitigate these risks and enhance surgical safety, it is important to maintain a clear and dry surgical field, which facilitates accurate anatomical identification and precise dissection. The judicious use of advanced bipolar or ultrasonic devices is recommended for effective vessel sealing, minimizing the risk of vascular injury while ensuring adequate hemostasis (67). Early identification and control of major vascular pedicles, such as the infundibulopelvic ligaments and uterine arteries, are critical steps to reducing blood loss during the procedure (68). Moreover, preparation with hemostatic agents (for example, fibrin sealants or thrombin–gelatin matrices) and the implementation of clearly defined intraoperative transfusion protocols are imperative in cases where extensive surgical intervention is anticipated (69). In select complex cases, preoperative uterine artery embolization may be considered to reduce intraoperative blood loss, improve visualization, and optimize surgical outcomes (70).

Conversion to Laparotomy

In endometriosis-related hysterectomy, intraoperative challenges may occasionally preclude safe laparoscopic completion. Extensive pelvic adhesions, deep infiltrating disease involving critical structures, or restricted anatomical access can compromise the safety and feasibility of a minimally invasive approach (71,72). In such cases, conversion to laparotomy may be necessary. Preoperative counseling is therefore essential and should explicitly address the potential need for surgical conversion.

A summary of key operative challenges, contributing factors, and mitigation strategies is presented in Table 4.

Outcomes, Complications, and Long-term Management

The surgical management of endometriosis, particularly in cases requiring hysterectomy, demands careful consideration of both immediate outcomes and long-term implications for patient health and quality of life (QoL). A thorough understanding of potential complications, along with the development of individualized strategies for long-term management, is essential to optimize patient care.

Surgical Outcomes and Symptom Relief

Multiple studies have demonstrated significant reductions in pain symptoms following hysterectomy, particularly when performed in conjunction with excision of endometriotic lesions. In a Swedish registry-based study, 84% of women reported satisfaction and significant pain relief (76). A multicenter cohort further showed greater improvement in noncyclical pain and dyspareunia when hysterectomy was added to lesion excision (77). Although hysterectomy may provide definitive symptom relief in carefully selected patients, it should not be considered a universal solution for endometriosis. Conservative strategies remain appropriate in several situations, including young patients with active fertility desire, early-stage disease responsive to medical therapy, or cases where pain is driven by central sensitization rather than active pelvic disease (78). In addition, the psychological impact of definitive surgery must be considered, as loss of fertility may lead to emotional distress or postoperative regret in some women, particularly when preoperative counseling is insufficient (79). Therefore, shared decision-making, reproductive counseling, and individualized risk-benefit assessment are essential components of surgical planning,

Table 4. Surgical Challenges and Risk Mitigation Strategies in Hysterectomy for Endometriosis (29,35,73-75)

Intraoperative challenge	Associated risk	Mitigation strategy
Dense pelvic adhesions	Ureteral, bowel, or vascular injury	Early retroperitoneal entry and ureterolysis; Sharp adhesiolysis; Early identification of anatomical landmarks; Define conversion threshold; MDT support when required
Hypervascular field/heavy bleeding	Hemorrhage; transfusion; poor visualization	Prompt vascular pedicle control; Use of vessel-sealing devices and hemostatic agents; Establishment of standardized transfusion protocols for complex cases
Intraoperative bleeding	Dense vascular adhesions; neovascularization from chronic inflammation	Prompt vascular pedicle control; Use of vessel-sealing devices and hemostatic agents; Standardized transfusion protocols for complex cases
Bladder adhesions/ureteric involvement	Thermal, traction, or devascularization injury	Early identification of vesicouterine fold and ureters; Sharp or reverse vesicouterine dissection; Consider preoperative ureteral stenting or retrograde ICG; Intraoperative assessment of bladder integrity (ICG, methylene blue, or cystoscopy); Multidisciplinary collaboration with urology
Bowel infiltration (DE)	Perforation; leak; need for resection	Preoperative bowel preparation protocol (institutional standard); Lateral approach to the rectovaginal space via pararectal spaces; Sharp dissection; Multidisciplinary planning with colorectal surgery to evaluate the extent of resection needed

DE: deep infiltrating endometriosis; ICG: indocyanine green MDT: Multidisciplinary team.

consistent with principles of patient-centered care.

Ovarian conservation is associated with markedly higher recurrence and reoperation rates, approximately sixfold and eightfold, respectively, compared to hysterectomy with BSO (40). However, BSO precipitates premature menopause, resulting in an elevated risk of long-term complications related to prolonged hypoestrogenism (80,81).

QoL frequently improves significantly following hysterectomy (or other surgical procedures) for endometriosis, as measured using validated instruments such as the Endometriosis Health Profile-30 (EHP-30) and the Short Form-36 Health Survey (SF-36) (82). For instance, a prospective study of 102 women demonstrated marked reductions in EHP-30 scores across core domains (such as pain, emotional well-being, control/powerlessness, and social support) at 3 and 6 months postoperatively (all $P < 0.0001$) (83). Moreover, these QoL improvements have been shown to persist long-term. In one cohort study, significant improvements across all five EHP-30 domains were sustained for up to 6.8 years following surgery ($P < 0.001$) (84). A prospective observational study conducted by Guo et al also reported meaningful improvements in QoL subscale scores, including pain, emotional well-being, and self-image ($P \leq 0.002$) (85).

However, interpretation of these outcomes must be cautious due to limitations in the available evidence. These include the predominance of observational studies, selection bias, and heterogeneity in surgical techniques, extent of excision, and definitions of surgical success. Follow-up duration also varies considerably across studies, and recurrence is inconsistently defined, often based on symptom return rather than imaging or surgical confirmation. Furthermore, many studies do not adequately stratify outcomes by disease phenotype (e.g., DE vs. ovarian endometriosis), patient age, or hormonal status, which may confound long-term quality-of-life and recurrence assessments.

Beyond clinical outcomes and QoL improvement, the economic implications of complex endometriosis surgery also warrant consideration. Minimally invasive approaches, including conventional laparoscopy and robotic-assisted surgery, are generally associated with shorter hospital stays, faster postoperative recovery, and earlier return to daily activities, which may partially offset higher procedural costs (42,43,66). Robotic-assisted surgery, while offering technical advantages in selected anatomically complex cases, is consistently associated with increased direct costs related to equipment, maintenance, and operative time (42,45). Therefore, surgical route selection should balance disease complexity, expected clinical benefit, surgeon expertise, institutional resources, and cost-effectiveness, particularly within publicly funded healthcare systems and high-volume referral centers (35,46).

Perioperative Complications

Hysterectomy performed in advanced endometriosis cases, particularly in DE, is associated with a significantly higher risk of intraoperative and postoperative complications compared to standard hysterectomy (29). DE is a significant risk factor due to its frequent involvement of multiple pelvic compartments and adjacent organs (29,35,86). Previous abdominal and pelvic surgeries further increase surgical complexity by contributing to dense adhesions, which complicate dissection, increase the risk of iatrogenic injury, and prolong operative time (87).

Intraoperative hemorrhage is a significant complication, often resulting from vascular involvement or dissection in areas with neovascularized adhesions (71,74). The urinary bladder, ureters, rectosigmoid colon, and pelvic autonomic nerves are particularly susceptible to injury, especially in the presence of dense fibrosis that obliterates anatomical planes (86). These potential complications underscore the need for meticulous surgical technique and a comprehensive understanding of pelvic anatomy.

Nerve-sparing techniques have become an integral part of advanced laparoscopic gynecologic surgery, aiming to reduce postoperative neurological sequelae (88). However, they require advanced surgical expertise and detailed knowledge of pelvic neuroanatomy, given the steep learning curve (88). Neurologic injury after complex hysterectomy is a serious but rare complication, and is more likely to occur in cases involving severe endometriosis or requiring extensive adhesiolysis (89). Direct transection, thermal injury from energy devices, or ischemia due to devascularization can potentially occur (88). Involvement of the inferior hypogastric plexus can lead to bladder retention or incontinence, constipation, and sexual dysfunction (86).

Additional postoperative complications impacting recovery and long-term outcomes include surgical-site infections, hematoma formation in the pelvic cavity or at the vaginal cuff, including cases complicated by secondary infection, urinary tract injuries or dysfunction, bowel complications such as ileus or fistula formation, adhesion recurrence and delayed wound healing (90–93). These complications are particularly associated with extensive tissue dissection, impaired vascularization due to fibrosis, and patient-related risk factors such as smoking, diabetes, or obesity (93).

Hormonal Management and Surgical Menopause

BSO is often considered during hysterectomy for endometriosis to suppress estrogen production and reduce the risk of disease recurrence, particularly in severe, refractory cases with ovarian involvement (38,49). However, BSO induces surgical menopause, which entails both immediate and long-term consequences, notably vasomotor symptoms, urogenital atrophy, bone mineral density decline, increased cardiovascular risk, and potential neurocognitive impairment (77,94). Therefore, the decision to perform concurrent BSO should be individualized, based on disease severity, patient age, symptomatology, fertility desires, and long-term health risks.

Hormone replacement therapy (HRT) plays a central role in managing the sequelae of surgical menopause, especially in premenopausal women undergoing BSO. Although evidence remains limited, current recommendations support the use of combined estrogen-progestogen therapy over unopposed estrogen, even in women post-hysterectomy, to mitigate the risk of endometriosis recurrence (4,95). Estrogen-only regimens are generally avoided due to concerns regarding malignant transformation of residual endometriotic lesions (95). Alternatives such as tibolone may offer a safe and effective option, particularly in patients for whom standard combined estrogen–progestogen therapy is contraindicated or poorly tolerated. Recent evidence suggests that tibolone provides effective relief of menopausal symptoms while maintaining a low risk of endometriosis recurrence, making it a valuable alternative in selected patients with a history of endometriosis following BSO (95,96). While evidence-based guidelines on the optimal timing of HRT initiation postoperatively are lacking, early initiation is typically recommended to alleviate menopausal symptoms and mitigate long-term complications of hypoestrogenism (97). Continuation is generally recommended until the average age of natural menopause to reduce the risk of estrogen deficiency-related comorbidities (4).

Fertility Considerations and Reproductive Counseling

The decision to undergo a hysterectomy for the management of endometriosis carries significant implications for a woman's fertility. In patients desiring future conception, medical management or conservative surgery may be preferred, depending on disease severity, reproductive potential, and patient priorities.

Among premenopausal women scheduled for hysterectomy, those who expressed a desire for future childbearing exhibited significantly higher levels of anxiety, depression, and postoperative regret, both preoperatively and up to two years after surgery, highlighting the importance of comprehensive preoperative counseling and the consideration of fertility-sparing alternatives (98,99). Such counseling should include referral to a reproductive endocrinologist or fertility specialist when appropriate. Endometriosis itself and surgical management can compromise ovarian reserve, and fertility preservation strategies (such as oocyte or embryo cryopreservation) should be discussed before surgery in high-risk cases (100).

Long-term Follow-up and Multidisciplinary Care

Following hysterectomy for endometriosis, particularly in complex cases, structured, individualized long-term follow-up is essential to monitor recovery, evaluate symptom resolution, detect potential complications, assess HRT when applicable, and identify signs of disease recurrence. A retrospective cohort study following conservative laparoscopic surgery for endometriosis utilized a structured follow-up schedule in which patients underwent gynecological examinations, symptom assessments, and TVUS at 3, 6, and 12 months, followed by annual evaluations thereafter (83,84). Although this protocol was applied in the context of fertility-preserving surgery, similar principles can be adapted for post-hysterectomy surveillance. In such cases, however, an initial postoperative consultation should occur earlier, typically within 4-6 weeks after surgery, to assess wound healing, evaluate early complications, and initiate or adjust HRT.

Despite definitive surgical intervention, some patients may experience persistent pelvic pain, which may result from central sensitization, pelvic floor dysfunction, or residual/recurrent disease. Central sensitization has been identified as a robust predictor of ongoing pain at six months post-hysterectomy (101). Management typically requires a multimodal approach. This may include analgesia with NSAID, neuromodulating agents (tricyclic antidepressants, serotonin and norepinephrine reuptake inhibitors), anticonvulsants (gabapentin, pregabalin), and hormonal suppression when residual endometriosis is suspected, particularly in cases of ovarian conservation or DE (4,102,103). Combined hormonal contraceptives or GnRH agonists/antagonists initiated early in the postoperative period may help suppress residual lesions and reduce recurrence risk (103,104). Adjunctive therapies such as pelvic floor physical therapy, acupuncture, and cognitive behavioral therapy may also have benefits in pelvic pain management (105,106). Persistent or worsening pain beyond the expected recovery period warrants reevaluation to exclude structural causes and guide further intervention.

The psychological impact of endometriosis and its surgical management, including hysterectomy and surgical menopause, is profound and often underrecognized. Depression, anxiety, and reduced health-related QoL are well-documented in this population (98). Providing access to psychological support services, including counseling and support groups, is essential to address the emotional burden associated (99). A multidisciplinary care model is imperative, particularly in the management of severe endometriosis. A systematic review by Fang et al on multidisciplinary care for pelvic pain and endometriosis found that, although high-quality evidence is limited, integrated models show promise for improving patient-centered outcomes (107). Implementing such collaborative approaches ensures coordinated care that addresses the full spectrum of medical, surgical, and psychosocial needs for these women.

Unlike existing guidelines and prior narrative reviews that focus primarily on medical therapy and general surgical indications, this review provides a surgically oriented, pathophysiology-based framework specifically tailored to the planning and execution of complex hysterectomy in endometriosis. Through the proposed Pathophysiology-Anchored Triage and Hysterectomy Strategy model (Figure 1), we integrate biological mechanisms, such as estrogen-dependent inflammation (30,31), fibrosis and nerve involvement driving deep infiltrative disease (70,101), KRAS/miRNA-associated invasive behavior (28–30), and progesterone resistance (34), with stepwise surgical decision-making including route selection, ureterolysis strategy, multidisciplinary involvement, and perioperative risk mitigation (70,87,88). This framework operationalizes disease biology into an actionable surgical pathway, moving beyond current guideline-based algorithms by addressing not only who might benefit from hysterectomy, but also how to plan and perform it safely and effectively in patients with advanced or refractory disease.

Intraoperative complexity remains a major determinant of outcomes in hysterectomy for endometriosis, particularly in cases of deep infiltrating disease. Technological innovation is supporting safer dissections; for example, real three-dimensional vision combined with near-infrared ICG imaging improves identification of deep lesions and ureteral course during complex pelvic surgery (108). However, hysterectomy must remain positioned within the therapeutic continuum of endometriosis care. Hormonal therapies such as dienogest and combined oral contraceptives remain evidence-based first-line management options (109), and surgery is reserved for carefully selected patients with treatment failure or contraindications. Preoperative evaluation is critical, and the identification of coexisting adenomyosis may guide treatment choice and help explain persistent symptoms despite medical therapy (110). Emerging translational research, including salivary microRNA profiling to detect progesterone resistance, may soon enable biologically informed stratification and earlier referral for surgery in non-responders (111). These developments reflect the evolution toward precision surgery, integrating imaging innovation, medical optimization, and molecular profiling to individualize hysterectomy decisions.

This review has several limitations that should be acknowledged. First, as a narrative review, it does not follow a systematic methodology and is subject to selection and interpretation bias. To mitigate these limitations, article selection emphasized recent systematic reviews, meta-analyses, international guidelines, and high-quality clinical studies, with original research included when particularly relevant to complex surgical decision-making. However, the heterogeneity of study designs, surgical techniques, and patient populations still limits the comparability of reported outcomes. Additionally, much of the current evidence on complex hysterectomy in endometriosis originates from high-volume tertiary referral centers, which may limit the generalizability of findings to lower-resource or lower-expertise settings. Finally, evidence specifically supporting pathophysiology-guided surgical planning is still evolving, and there remains a need for prospective multicenter studies to validate structured clinical decision-making frameworks and perioperative algorithms in this context.

Conclusions

Hysterectomy in the context of endometriosis represents a pivotal yet highly individualized decision, particularly for patients with refractory symptoms who have exhausted medical management. While hysterectomy with oophorectomy is associated with a lower risk of recurrence and reoperation, these benefits must be weighed against the consequences of surgical menopause and long-term health effects. Given the frequent complexity of these procedures, including involvement of adjacent organs, parametrial fibrosis, and obliterated tissue planes, optimal outcomes are best achieved in tertiary referral centers with expertise in endometriosis surgery, where multidisciplinary teams can manage bowel, urinary tract, and nerve involvement while minimizing intraoperative risk.

Future progress in this field will rely on the continued integration of pathophysiological insights with surgical expertise and technological innovation. Advances in precision imaging, such as high-resolution pelvic MRI with tractography and expert transvaginal sonography, are improving preoperative disease mapping and identification of DE compartments (112). Intraoperative navigation technologies, including fluorescence-guided ureterolysis and image-guided dissection, are enhancing anatomical safety in complex pelvic surgery (53). At the molecular level, biomarker research involving KRAS variants, microRNA signatures, and inflammatory cytokine profiles may enable biological stratification, recurrence prediction, and personalized surgical planning (28,113). In parallel, emerging artificial intelligence applications are being explored for automated lesion recognition, prediction of surgical complexity, selection of operative routes, and integration into multidisciplinary planning algorithms (114,115).

To validate these innovations, prospective multicenter studies evaluating long-term outcomes across different surgical strategies and endometriosis phenotypes are urgently needed. Ultimately, aligning surgical decision-making with the biological heterogeneity of endometriosis represents a key step toward personalized, durable, and high-quality care for affected individuals.

Authors' Contribution

Conceptualization: Tiago Meneses Alves, Hélder Ferreira.
Methodology: Tiago Meneses Alves, Hélder Ferreira.
Investigation: Tiago Meneses Alves, Hélder Ferreira.

Supervision: Hélder Ferreira.
Writing-original draft: Tiago Meneses Alves.
Writing-review and editing: Hélder Ferreira.

Conflict of Interests
Authors declare that they have no conflict of interests.

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