Review Article

Clinical evaluation and management of endometriosis: 2024 guideline for Korean patients from the Korean Society of Endometriosis

Hyun Joo Lee, DEGREE[1]*, Sang-Hee Yoon, DEGREE[2]*, Jae Hoon Lee, DEGREE[3], Youn-Jee Chung, DEGREE[4], So Yun Park, DEGREE[5], Sung Woo Kim, DEGREE[6], Yeon Hee Hong, DEGREE[7], Sung Eun Kim, DEGREE[8], Youjin Kim, DEGREE[9], Sungwook Chun, MD, PhD[10], Yong Jin Na, MD, PhD[11]

Department of Obstetrics and Gynecology, [1]Pusan National University Hospital Biomedical Research Institute, Pusan National University School of Medicine, Busan, [2]Inje University Sanggye Paik Hospital, Seoul, [3]Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, [4]Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, [5]Ewha Womans University College of Medicine, Seoul, [6]Seoul National University College of Medicine, Seoul, [7]Seoul National University Bundang Hospital, Seongnam, [8]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, [9]Chungnam National University Hospital, Chungnam National University School of Medicine, Daejeon, [10]Inje University Haeundae Paik Hospital, Inje University College of Medicine, Busan, [11]Pusan National University Yangsan Hospital, Pusan National University School of Medicine, Yangsan, Korea

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Corresponding author: Sungwook Chun, MD, PhD

Department of Obstetrics and Gynecology, Inje University Haeundae Paik Hospital, Inje University College of Medicine, 875 Haeun-daero, Haeundae-gu, Busan 48108, Korea

E-mail: wooki1974@empal.com

https://orcid.org/

Corresponding author: Yong Jin Na, MD, PhD

Department of Obstetrics and Gynecology, Pusan National University Yangsan Hospital, Pusan National University School of Medicine, 20 Geumo-ro, Mulgeum-eup, Yangsan 50612, Korea

E-mail: yjna@pusan.ac.kr

https://orcid.org/

*These authors contributed equally and share first authorship.

ABSTRACT

Endometriosis, a prevalent but debilitating condition affecting women, poses significant challenges in diagnosis and management. The current 2024 guideline, developed by the Korean Society of Endometriosis (KSE), builds upon the 2018 KSE guideline. This guideline aims to provide customized recommendations tailored to Korea's unique clinical aspects and medical environment, and addresses key areas such as diagnosis, medical and surgical management, considerations for special populations, and its complex relationship with cancer.

Keywords: Endometriosis; Guideline; Diagnosis; Management; Cancer

Introduction

Endometriosis, a prevalent but debilitating condition affecting women, poses significant challenges in diagnosis and management. Although international guidelines exist, the unique clinical presentations and healthcare landscape in Korea necessitate tailored recommendations. The current 2024 guideline, developed by the Korean Society of Endometriosis (KSE), builds upon the 2018 KSE guideline and incorporates the latest evidence-based research and expert consensus to provide clinicians with comprehensive, up-to-date guidance [1]. This guideline addresses key areas such as diagnosis, medical and surgical management, considerations for special populations, and its complex relationship with cancer. The recommendations are categorized based on the strength of evidence using the GRADE framework, and the details are described in Table 1.

Diagnosis

Detailed history taking and physical examination are crucial to prevent delayed diagnosis, as patients may endure the disease for years before diagnosis [2,3]. Imaging studies, such as pelvic ultrasound and magnetic resonance imaging (MRI), are also notably accurate for endometriosis diagnosis. Therefore, international societies, including the European Society for Reproductive Medicine, have recommended that ovarian endometrioma and deep endometriosis (DE) be diagnosed solely upon imaging findings, excluding diagnostic laparoscopy [4].

1. Symptoms and signs

Endometriosis should be suspected in women of childbearing age presenting with gynecological symptoms, including menstrual pain, pelvic pain, dyspareunia, fatigue, and infertility (grade D) [5]. Endometriosis should be considered in women of childbearing age with dyschezia, dysuria, painful rectal bleeding or hematuria, periodic swelling/pain at the surgical site, and cough/hemoptysis/chest pain/shoulder pain/catamenial pneumothorax (grade D) [5].

2. Diagnostic tools

1) Physical examination

Pelvic and abdominal examinations should be performed in all patients with suspected endometriosis. This examination can be conducted at any point during the menstrual cycle (grade D) [6]. Painful nodules near the rectum, vagina, or fornix during a physical examination may indicate DE (grade C). Palpation of an ovarian mass during pelvic examination in women with suspected endometriosis suggests an ovarian endometrioma (grade C). Endometriosis cannot be excluded in women with suspected endometriosis, even with normal physical examination results. Additional tests, mostly based on imaging, should be considered (grade B) [7].

2) Biomarkers

There is insufficient evidence regarding the use of biomarkers from endometrial tissue, blood, menstrual blood, and uterine fluids for diagnosing endometriosis (grade A) [8]. Further research is

needed on biomarkers for endometriosis recurrence (grade C).

3) Imaging studies and approaches thereafter

For suspected endometriosis, transvaginal or transrectal ultrasound is recommended as the initial step to confirm or exclude ovarian endometrioma (grade A) [9]. For signs or symptoms of endometriosis, transvaginal or transrectal ultrasound may help confirm or exclude DE involving the sigmoid colon and rectum (grade A) [10]. If DE is suspected, especially involving the ureters, bladder, or intestines, additional imaging such as MRI should be considered (grade D). Even if imaging studies, such as pelvic ultrasound and MRI, appear normal, endometriosis cannot be excluded (grade D). In women with suspected endometriosis, empirical medical treatment, such as gonadotropin-releasing hormone (GnRH) agonists, progestins, and combined oral contraceptives (COC), may be initiated following imaging, regardless of imaging confirmation of endometriosis (grade D) [10]. After imaging studies are conducted on women with suspected endometriosis, diagnostic laparoscopy can be performed for lesion removal and pathological confirmation. Both empirical medical therapy and diagnostic laparoscopy are viable options for managing the condition. Currently, no evidence indicates which approach is more effective, and decisions can be made through patient discussion (grade D) [1].

3. Follow-up monitoring

Women with endometriosis, especially deep or ovarian cases, require close follow-up care (grade

D). Cancer antigen-125 (CA-125) exhibits low sensitivity but a high positive predictive value, making it a potential option for follow-up monitoring during treatment (grade D) [8].

Pelvic pain

Medical treatment

1. Nonsteroidal anti-inflammatory drugs (NSAIDs) and other analgesics

Women may be offered NSAIDs or other analgesics, alone or with other treatments, to reduce endometriosis-associated pain (grade C).

2. Hormone treatments

Hormone therapy is based on evidence that endometriosis is 'estrogen-dependent'. The most commonly prescribed drugs for endometriosis modify the hormonal environment by suppressing ovarian activity or acting directly on steroid receptors and enzymes in lesions [11]. These include progestogens, anti-progestogens, COC, GnRH agonists, GnRH antagonists, the levonorgestrel intrauterine system (LNG-IUS), and aromatase inhibitors such as letrozole [4]. Danazol and gestrinone are no longer recommended for endometriosis-associated pain owing to their severe side effects. In the clinical setting, the magnitude of the analgesic effect has been shown to be similar for all types of medical treatments, but inevitable side effects still exist [11]. Thus, the efficacy and side effect profiles of these therapies should be individualized.

1) COC

COCs are recommended to reduce endometriosis-associated dyspareunia, dysmenorrhea, and non-

menstrual pain (grade A) [12]. Women with endometriosis-associated dysmenorrhea can be offered the continuous use of COC (grade A) [13].

2) Progestogens (including progestogen-only contraceptives), anti-progestogens and danazol

Progestogens are recommended to reduce endometriosis-associated pain (grade A) [14]. Clinicians should take the different side-effect profiles of progestogens into account when prescribing them (grade D). LNG-IUS system or an etonogestrel-releasing subdermal implant is recommended to reduce endometriosis-associated pain (grade A) [15,16]. Danazol and gestrinone are no longer recommended as medical treatments for endometriosis-associated pain (grade C). Long-term treatment with dienogest should be individualized depending on the woman's pregnancy plan, disease recurrence, and side effects, without limiting the treatment period (grade D) [11,15,17-19]. When receiving long-term treatment with dienogest, a biannual bone mineral density (BMD) test may be helpful, as well as a breast examination at the same frequency as that for healthy women (grade D) [20-22].

3) GnRH agonist

GnRH agonists are recommended to reduce endometriosis-associated pain, although evidence is limited regarding dosage or treatment duration (grade A) [23]. GnRH agonists are prescribed as second-line treatment (i.e., if COC or progestogens have been ineffective) due to their side-effect profile (grade B) [21]. Clinicians should consider prescribing add-back therapy alongside GnRH agonists to prevent bone loss and hypoestrogenic symptoms (grade A) [24].

4) GnRH antagonist

GnRH antagonists can be considered for reducing endometriosis-associated pain, although evidence is limited regarding the dosage or treatment duration (grade C) [25-27]. GnRH antagonists are prescribed as second-line treatment (i.e., if COC or progestogens have been ineffective) owing to their side-effect profile (grade D) [5].

5) Aromatase inhibitor

For endometriosis-associated pain refractory to other medical or surgical treatments, aromatase inhibitors are recommended. Aromatase inhibitors may be prescribed along with COC, progestogens, GnRH agonists, or GnRH antagonists (grade B) [28].

3. Non-medical treatment

Experts recommend that clinicians discuss non-medical strategies, such as acupuncture, physiotherapy, electrotherapy, psychological interventions, dietary interventions, and Chinese medicine, to address the quality of life and psychological well-being of women with endometriotic symptoms. However, clinicians should acknowledge that no recommendations can be made for any specific non-medical intervention to reduce pain or improve quality-of-life measures in women with endometriosis, since the potential benefits and harms are unclear (grade D) [29].

Surgical treatment

Surgical intervention may be considered for the reduction of endometriosis-associated pain (grade A). Excising endometriotic lesions is more effective than draining or ablating them in terms of pain and symptom reduction, as well as recurrence prevention (grade B).

Laparoscopy is recommended as the standard surgical method [30]. Compared to laparotomy, laparoscopic surgery has advantages, such as reduced pain, shorter hospitalization, and cosmetic aspects [31]. Compared to laparotomy, it also has the same effect on endometriosis pain [32]. Regarding robotic surgery, there was no difference in surgical results, but the robotic approach showed longer operation time compared to conventional laparoscopic surgery in certain situations [33]. Further studies are required to evaluate the cost-effectiveness of various surgical techniques.

1. Ovarian endometrioma

Cystectomy is more effective than drainage or ablation in reducing recurrence rates and endometriosis-associated pain during the surgical treatment of ovarian endometriomas (grade B). Minimizing ovarian damage is crucial during surgical intervention for ovarian endometriomas (grade A). Preoperative assessment of Anti-Müllerian hormone levels should be considered in cases of large, recurrent, or bilateral endometriomas in women who desire future pregnancy due to the increased risk of ovarian damage (grade D).

Surgical removal of large ovarian endometriomas (3 cm+) is more effective than drainage or electrocoagulation for alleviating symptoms and preventing recurrence [34-36]. In addition,

histological diagnosis is possible when a cystectomy is performed [35].

2. DE

Surgical excision of DE can reduce endometriosis-associated pain and improve the quality of life (grade B) [37,38]. Clinicians should consider referrals to tertiary care institutions to minimize complications during surgery, which often requires multidisciplinary expertise (grade D).

3. Hysterectomy

Considering hysterectomy for severe, treatment-resistant endometriosis pain in women who do not wish to conceive or if other uterine pathologies exist is a viable treatment option (grade D). Following hysterectomy and bilateral oophorectomy for the treatment of endometriosis, continuous combined estrogen-progestogen hormone therapy (HT) is recommended for the management of menopausal symptoms (grade C). Tibolone may be considered as a second-line option for patients who are unable to use continuous combined estrogen-progestogen HT (grade D).

The decision to perform bilateral oophorectomy with hysterectomy should be carefully considered. Thorough patient discussions should be held before surgery, explaining that the probability of pain persisting after hysterectomy is about 15% and that there is a 3-5% risk of worsening pain or developing new symptoms [39]. Pain after hysterectomy may be due to ovarian remnant syndrome.

4. Adjuvant medication before and after surgery

Preoperative hormonal treatment, compared to surgery alone, is not recommended for pain management in women with endometriosis, as it does not provide significant benefits on the pain and/or recurrence reduction rate in the postoperative period (grade A) [40]. Postoperative hormonal treatment includes short-term (less than 6 months) and long-term (6 months or more) treatment, and long-term treatment aims to prevent recurrence (grade D). In women who are not planning to become pregnant, postoperative hormonal treatment may be considered for the management of endometriosis-associated pain (grade C) [40].

Infertility: assisted-reproductive techniques (ART)

1. Intrauterine insemination (IUI) after superovulation

In women with minimal or mild endometriosis-related infertility, IUI with superovulation can be performed (grade B) [1, 41]. IUI with superovulation could be considered in severe endometriosis-related infertility, although its effectiveness is unproven (grade B) [42].

2. ART

ART can be performed in women with endometriosis-related infertility, especially when fallopian tube function is poor, male factor infertility exists, or other infertility treatments fail (grade B) [43]. Surgery is not recommended to increase the live birth rate before ART in patients with minimal or

mild endometriosis (grade A) [44,45]. Performing surgery before ART in women with ovarian endometrioma may negatively affect the ovarian reserve. However, surgery to relieve endometriosis-related pain or increase access to follicles should be considered (grade A). Surgery to remove DE before ART should be decided based on pain and patient preference, as research on whether surgery improves fertility is lacking (grade B) [46]. There is insufficient evidence to support the long-term use of gonadotropin-releasing hormone agonists to increase live birth rates before ART (grade A) [47,48]. There is insufficient evidence regarding whether long-term use of COCs or progesterone before ART increases the live birth rate (grade B) [49]. Since there is no difference in live birth rates depending on the type of gonadotropin-releasing hormone analog used during superovulation for ART, the choice of gonadotropin-releasing hormone analog can be determined based on patient and physician preference (grade B) [50,51]. ART does not worsen symptoms or cause recurrence of endometriosis (grade A) [52]. In women with endometriomas in the ovaries, the risk of ovarian abscesses after oocyte retrieval is very low; however, antibiotics can be used for prevention (grade B) [53].

3. Preservation of fertility in patients with endometriosis

There is insufficient evidence regarding the indications, benefits, and safety of fertility preservation in women with moderate-to-severe endometriosis. However, healthcare professionals should provide thorough counseling to patients regarding fertility preservation (grade B) [54]. Women with bilateral endometriomas or those with recurrent endometriomas after surgery may consider fertility

preservation before surgery for endometriomas (grade C) [55-57]. Women who do not wish to or cannot undergo ovarian stimulation for oocyte retrieval or those who require the removal of ovaries may consider ovarian tissue cryopreservation (grade C) [56,57].

Infertility: surgical, medical, and non-medical treatments

Endometriosis can induce infertility through various mechanisms, and studies on treatments for endometriosis-associated infertility, including medical, surgical, and non-medical therapies, have been conducted to enhance natural conception rates [58-60].

1. Surgical treatment

For mild–revised American Society for Reproductive Medicine (rASRM) stage I/II-endometriosis-associated infertility, surgery may be considered to increase natural conception rates. Concerning pregnancy rates, laparoscopic surgery is superior to diagnostic laparoscopy (grade A) [58-60]. In severe-rASRM stage III/IV-endometriosis, laparoscopic surgery demonstrates higher natural conception rates than expectant management (grade A) [61,62]. There is no definitive evidence that laparoscopic surgery improves fertility in DE. However, among patients experiencing clinical symptoms such as dyschezia who desire pregnancy, it can be considered a treatment option (grade D) [58-62]. When deciding on surgery, factors such as the presence of pain, patient's age, surgical history, presence of other infertility factors, and ovarian reserve should be considered (grade D). To increase natural conception rates, ovarian cystectomy may be considered over other surgical

methods, such as drainage or ablation (grade A) [63-65]. It is important to be cautious, as ovarian reserve may diminish during surgery, potentially impacting future pregnancy rates (grade B) [66]. The endometriosis fertility index can be used to counsel patients regarding the possibility of natural conception without the need for ART after surgery for endometriosis (grade D) [67].

2. Medical treatment

In women with endometriosis-related infertility, the use of ovarian suppression therapy, such as GnRH agonists, progesterone, or COCs, is not recommended for improving fertility (grade A) [68-70]. Hormonal suppression therapy following surgery for endometriosis is not recommended for increasing pregnancy rates (grade A) [68]. Women who do not immediately attempt pregnancy after surgery or those who seek pain relief or aim to prevent recurrence may consider hormonal therapy following surgery for endometriosis (grade B) [69]. Using letrozole for purposes other than ovulation induction, as well as other anti-inflammatory medications, is not recommended for improving natural pregnancy rates in infertile women with endometriosis (grade A) [70]. The provision of specific nutrients or the application of non-medical alternative therapies is not recommended for infertile women with endometriosis (grade D).

3. Non-medical treatment

There is no reliable evidence supporting the efficacy of non-medical methods, such as diet, Chinese medicine, electrotherapy, acupuncture, physiotherapy, exercise, and psychological interventions, to

increase the likelihood of pregnancy in women with endometriosis; therefore, they are not recommended.

Endometriosis in special populations

1. Endometriosis in pregnancy

Pregnancy does not always suppress the progression of endometriosis, and it is not recommended to encourage pregnancy for the treatment of endometriosis (grade C) [71,72]. Surgery should be considered if endometriosis is suspected to be atypical or if malignancy cannot be excluded (grade B). Women with endometriosis may experience an increased risk of miscarriage and ectopic pregnancy during the first trimester (grade B) [73-75]. Complications related to endometriosis in the second and third trimesters include gestational diabetes, gestational hypertension, small for gestational age, premature rupture of membranes, preterm labor, placenta previa, placental abruption, cesarean section, and miscarriage (grade B) [73-75]. Women with endometriosis before pregnancy can be managed with regular prenatal care unless they have high-risk endometriosis (adenomyosis, ART pregnancies, and DE). However, clinicians should be aware of potential complications (grade D). Close observation is necessary even after childbirth (grade C).

2. Endometriosis in adolescence

1) Diagnosis

Detailed history-taking, including age at menarche, menstrual cycle, family history, and presence of

reproductive tract anomalies, is necessary for diagnosing endometriosis during adolescence (grade B) [76-78]. Endometriosis during adolescence should be considered if chronic or acyclic pelvic pain is accompanied by nausea, dysmenorrhea, gastrointestinal disturbances, dysuria, or dyspareunia (grade B) [79]. Transvaginal ultrasonography is effective for diagnosing endometriosis, but if not feasible, transabdominal, transrectal, or transperineal ultrasonography or pelvic MRI may be considered (grade B) [79]. Diagnosing endometriosis in adolescents using biomarkers such as CA-125 is not recommended (grade C) [80]. Diagnostic laparoscopy may be considered for adolescents with suspected endometriosis who are negative on imaging or do not respond to medical therapy (grade C) [81].

2) Treatment

If endometriosis is suspected, NSAIDs can be considered as the first-line treatment to control pain (grade B) [82]. If there is no response to NSAIDs for pain associated with endometriosis, COCs or progestins should be prescribed. However, it is important to note that some progestins may cause BMD loss (grade B) [83,84]. If COCs or progestin therapy fails, GnRH agonists with add-back therapy may be considered (grade C) [85]. Treatment may be considered to control related symptoms in adolescents with endometriosis, but high recurrence rates should be taken into account (grade C) [86,87]. If surgery is necessary, it should be performed by a skilled specialist using laparoscopy, and all lesions should be removed if possible (grade D) [88,89].

3) Fertility preservation

Adolescents with endometriosis should be informed that endometriomas and the impact of surgery can decrease ovarian reserve, which may affect future fertility (grade D).

3. Endometriosis after menopause

Endometriosis is steroid-dependent; therefore, its progression decreases after menopause [90]. However, some of these women continue to experience endometriosis-related symptoms even after menopause [91]. Understanding whether endometriosis remains active after menopause and its association with health issues is crucial for making careful decisions regarding treatment.

1) Treatment

Endometriotic symptoms may persist even after menopause (grade C) [90,91]. Treatment for endometriosis may still be necessary after menopause if needed (grade B). Any pelvic masses should be carefully evaluated and addressed, as they may be cancerous (grade C).

2) Menopausal symptom management in women with a history of endometriosis

In menopausal women who have undergone hysterectomy for endometriosis and experience vasomotor symptoms, progestogens should be combined with estrogen therapy, considering the higher risk of malignant transformation (grade C) [92,93]. Tibolone may be considered a second-line agent for patients who find it difficult to continue with combined estrogen-progestogen continuous HT (grade D) [92-94]. For women with a history of endometriosis who have undergone

surgical menopause at a young age, continuous combined estrogen-progestogen HT is recommended until the natural age of menopause (grade D) [95,96].

Endometriosis in special situations

1. Asymptomatic endometriosis

No electrocauterization is required for endometriosis discovered incidentally during surgery (grade B). It is not necessary to administer medication to patients with incidentally diagnosed endometriosis (grade C) [97]. Surgical removal of a >4 cm asymptomatic endometrioma may be carefully considered due to the potential risk of ovarian cancer, although the association is not definitively established (grade D) [97-99]. Patients with asymptomatic endometriosis should be informed about their condition (grade D). For patients with asymptomatic endometriosis, periodic ultrasound examinations can be performed (grade C) [100].

2. Recurrent endometriosis

When operating on patients with endometrioma, ovarian cystectomy should be performed instead of drainage or electrocauterization to prevent endometriosis-related dysmenorrhea, dyspareunia, or pelvic pain. However, the possibility of decreased ovarian reserve during surgery must be considered (grade B) [101]. For secondary prevention of endometriosis-related dysmenorrhea after surgery, LNG-IUS (52 mg) or COCs should be prescribed for at least 18-24 months (grade B) [102]. Hormone

therapy (dienogest, GnRH agonist, and COC) or surgery can be used to treat pain in patients with recurrent endometriosis (grade B) [103]. If there are no immediate plans for pregnancy after surgery for endometrioma, long-term hormone therapy can be considered to prevent the recurrence of endometrioma and endometriosis-related symptoms (grade B) [104]. Long-term hormonal therapy after surgery can be considered to prevent the recurrence of DE (grade B) [105]. There was no significant decrease in BMD with long-term use of dienogest for recurrence prevention other than age-related changes (grade B) [106]. As ART is not considered to increase the recurrence of endometriosis, it can be performed when necessary in women with DE (grade B) [106]. For women who want to get pregnant, a second surgery for recurring endometriosis should be a last resort (grade B).

3. Primary prevention of endometriosis

The intake of vitamin D, omega-3, dairy products, and alcohol abstinence may help reduce the risk of endometriosis (grade C) [51,107-110]. The usefulness of COCs for the primary prevention of endometriosis is still uncertain (grade C) [111].

4. Extrapelvic endometriosis

Endometriosis primarily affects the pelvic organs, yet approximately 5% of cases are extrapelvic. The gastrointestinal tract and urinary system are the most frequent sites of extrapelvic endometriosis and are managed as extensions of pelvic endometriosis [112]. In contrast, abdominal wall

endometriosis and thoracic endometriosis can be easily overlooked if physicians do not suspect endometriosis and there is no established standard treatment protocol. Abdominal wall endometriosis is associated with a history of abdominal surgery [113-115]. Its most prevalent form arises from cesarean section, whereas occurrences in the umbilicus or perineum incision sites are rare. Thoracic endometriosis is classified as catamenial pneumothorax or hemothorax, which occurs in the pleura and presents with symptoms of pneumothorax or hemothorax. Catamenial hemoptysis invades the lung parenchyma and appears as hemoptysis or pulmonary nodules on imaging studies [116,117]. Although these are similar, they are presumed to have distinct etiologies [115-118].

1) Diagnosis of extrapelvic endometriosis

Endometriosis should be considered in women of childbearing age who have dyschezia, dysuria, painful rectal bleeding or hematuria, periodic swelling/pain at the surgical site, and cough/hemoptysis/chest pain/shoulder pain/catamenial pneumothorax (grade D). A multidisciplinary approach is recommended for diagnosing and treating suspected extrapelvic endometriosis (grade D).

2) Management of extrapelvic endometriosis

① Endometriosis of the abdominal wall

Surgical resection is preferred for endometriosis in the abdominal wall, umbilicus, perineum, and inguinal region. In cases where surgery is difficult, medical treatment can be considered, such as in

pelvic endometriosis (grade D) [119,120].

② Thoracic endometriosis

For thoracic endometriosis, surgical and medical treatments such as GnRH agonists, COCs, and progestins can be considered, and a multidisciplinary approach is necessary (grade D) [121]. Owing to the high recurrence rate of thoracic endometriosis, medical treatment is frequently initiated after surgical resection (grade D) [118,122].

Endometriosis and cancer

Endometriosis shares characteristics with cancer, including chronic inflammation, resistance to cell death, tissue invasion, and the presence of local and distant lesions [123,124]. Research is ongoing to understand its association with cancer and to develop early detection methods. Concerns arise regarding the cancer risk linked to hormone therapy and the uncertain effect of surgery on ovarian cancer risk in patients with endometriosis.

1. Malignant tumors associated with endometriosis

Endometriosis does not have a high overall cancer risk but is linked to ovarian, breast, and thyroid cancers, although the absolute increase in risk compared to the general population is minimal (grade A). Clinicians should inform women that endometriosis does not significantly increase the risk of ovarian, breast, or thyroid cancers (grade D). More data are needed to predict if

endometriosis will progress to cancer. Until clear risk factors for ovarian cancer in patients with endometriosis are identified, proactive measures, such as surgical oophorectomy, are not recommended (grade D).

1) Risk assessment by cancer type (Table 2)

Endometriosis is associated with a relatively increased ovarian cancer risk, particularly clear-cell and endometrioid carcinomas [125-127]. Two meta-analyses reported that the relative risk of cervical cancer is low in women with endometriosis [127,128]. Recent meta-analyses report that endometriosis increases the relative risk of breast cancer [128,129], particularly among individuals aged over 50 [130,131]. In a meta-analysis of five studies, endometriosis was reported to increase the thyroid cancer risk [128]. A meta-analysis of seven studies explored the link between endometriosis and melanoma and found no association, although only two studies concerning basal cell carcinoma were included, with an increased risk reported [128]. Additional research is required to fully understand these associations.

2) Comparison with the cancer incidence rate in the general population (Table 3)

Risk estimates derived from recent meta-analytic data indicating elevated risks for ovarian cancer (summary relative risks [SRR], 1.93), breast cancer (SRR, 1.04), and thyroid cancer (SRR, 1.39) among women with endometriosis demonstrate that while these relative risks are higher, the absolute risks remain notably low compared to the general population [128,132]. Clinicians are advised to reassure

women with endometriosis that despite the association with certain cancers, such as ovarian, breast, and thyroid cancer, their absolute cancer risk is minimal and akin to that of women without endometriosis [132].

3) Factors predicting progression to ovarian cancer

Factors predicting progression to ovarian cancer include the association of endometrioma with an increased risk, whereas superficial and DE show no such correlation [133]. Studies offer limited evidence regarding the predictive value of somatic mutations in DE in ovarian cancer [128]. Serum CA-125 testing or imaging, commonly used for ovarian malignancy surveillance in women with endometriosis, lacks clear efficacy according to randomized controlled trials [134,135]. In one study, the predictive risk factors for ovarian cancer in patients with endometriosis included increasing age, menopausal status, elevated CA-125 levels, large endometrioma (>9 cm), and long-term endometriosis (>5 years) [136]. However, further longitudinal analyses are necessary to confirm these predictions and establish definitive risk factors for ovarian cancer in this population.

2. Cancer risk linked to the treatment of endometriosis

Clinicians should inform and reassure women with endometriosis regarding the risk of malignant tumors when using oral contraceptives for pain management or preventing recurrence (grade D) [3,137,138]. Complete removal of endometriosis and endometrioma-containing ovaries can reduce ovarian cancer risk. However, the treatment method must be decided considering the disadvantages

of surgery (surgery-related complications, pain, decreased ovarian function, etc.) (grade D) [139,140].

3. Monitoring to detect malignant tumors

Women with endometriosis should not undergo additional testing beyond the current cancer screening protocols (grade D). For individuals with additional risk factors, such as specific gene mutations or family history, cancer screening may be warranted following individualized guidelines (grade D).

Conclusion

The current 2024 guideline represents a significant advancement in the clinical evaluation and management of endometriosis for Korean patients. By integrating the latest research findings and expert consensus, this guideline offers comprehensive recommendations tailored to the specific needs of the Korean population. While acknowledging the limitations of existing evidence, this guideline emphasizes a patient-centered approach, advocating for shared decision-making and personalized treatment plans. Further research and collaboration in Korea will enhance endometriosis care and improve women's lives.

Conflict of interest

Ethical approval

Patient consent

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Table 1. Grading of recommendations [141]

Recommendation grade	**Definition**
A	Strong evidence base; at least one randomized controlled trial, systematic reviews, or meta-analysis
B	Moderate evidence base; at least one high quality non-randomized controlled trial, such as case-control or cohort studies
C	Limited evidence base; non-analytic studies such as cross-sectional studies, case reports or case series
D	Expert opinion

Table 2. Summary of selected major studies on the association between endometriosis and relative cancer risk

Study	Relative risk (95% CI)				
	2014	**2016**	**2019**	**2021**	**2022**
	Kim et al. [125] (2014)	**Wang et al. [126) (2016)**	**Li et al. [127] (2019)**	**Kvaskoff et al. [128] (2021)**	**Ye et al. [130] (2022)**
Ovarian cancer	1.26 (1.21±1.32)	1.42 (1.28±1.57)	1.96 (1.69±2.29)	1.93 (1.68±2.22)	
Clear-cell	2.61 (2.23±3.05)			3.44 (2.82±4.42)	
Endometrioid	1.76 (1.55±1.96)			2.33 (1.82±2.98)	
Endometrial cancer			1.18 (0.88±1.58)	1.23 (0.97±1.57)	1.66 (1.15±2.41)
Cervical cancer			0.67 (0.54±0.84)	0.68 (0.56±0.82)	
Breast cancer				1.04 (1.00±1.09)	1.08 (1.00±1.17)
Thyroid cancer				1.39 (1.24±1.57)	
Colon cancer				1.00 (0.87±1.16)	
Skin cancer					
Cutaneous melanoma				1.17 (0.97±1.41)	
Basal-cell carcinoma				1.18 (1.11±1.25)	
Lung cancer				0.94 (0.84±1.04)	
Stomach cancer				0.97 (0.81±1.18)	
Liver cancer				1.05 (0.77±1.44)	
Pancreatic cancer				0.96 (0.61±1.50)	
Bladder cancer				0.94 (0.76±1.14)	

Kidney cancer				1.20 (0.93±1.55)	

Values are presented as mean±standard deviation.

CI, confidence interval.

Table 3. Comparison of absolute risk of cancer incidence in a woman's lifetime between women with and without endometriosis

	Absolute risk of cancer in a woman's lifetime		**Increased risk in women with endometriosis**
	All women	**Women with endometriosis**	
Ovarian cancer	1.3	2.5	+1.2
Breast cancer	12.8	13.3	+0.5
Thyroid cancer	1.3	1.8	+0.5

Values are presented as number (%).