

Application of Fertility Sparing Techniques in Women Suffering From Chocolate CYST and Management of Ovarian Endometriotic CYST

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Abstract: Endometriosis (en-doe-me-tree-O-sis) is a common and challenging condition of reproductive-aged women that carries a high individual and societal cost. The many molecular dissimilarities between endometriosis lesions and eutopic endometrium create difficulties in the development of new drug therapies and treatments. Surgery remains the gold standard for definitive diagnosis, but it must be weighed against the risks of surgical morbidity and potential decreases in ovarian reserve, especially in the case of endometriomas. Safe and effective fertility sparing techniques are discussed within this article for various presentations of endometriosis. Medical therapy is suppressive rather than curative, and regimens that are long-term and affordable with minimal side effects are recommended. Recurrences are common and often rapid when medical therapy is discontinued. Endometriosis in the setting of infertility is reviewed and appropriate management is discussed, including when and whether surgery is warranted in this at-risk population. In patients with chronic pain, central sensitization and myofascial pain are integral components of a multidisciplinary approach. Endometriosis is associated with an increased risk of epithelial ovarian cancer; however, the risk is low and currently no preventive screening is recommended. Hormone therapy for symptomatic women with postsurgical menopause should not be delayed as a result of concerns for malignancy or recurrence of endometriosis.

Keywords: Ovarian Endometriosis cyst (OMA), fertility sparing, management, fertility, ovarian reserve assessments.

INTRODUCTION

1. Endometriosis/ Chocolate Cyst:

Endometriosis is a common gynaecological disease with a high socio-economic impact, affecting 176 million women worldwide and approximately 10% of women of reproductive age [1]. It is a chronic, estrogen-dependent condition which is defined by the presence of endometrial glands and stroma outside

the uterine cavity, mostly in the ovaries and pelvic peritoneum. Women with endometriosis may be asymptomatic or experience different types of pain, including dysmenorrhea, chronic pelvic pain or dyspareunia [2–4]. Endometriosis may be classified in three subtypes: superficial peritoneal endometriosis, ovarian endometrioma (OMA), and deep infiltrating endometriosis [5].

Superficial Peritoneal Endometriosis (SPE): This is the most common type. The lesions are found on the peritoneum (the thin layer lining the pelvic cavity). These are usually small, flat, or raised patches on the surface of organs or tissues.

Ovarian Endometriomas (Chocolate Cysts): Endometriomas are cysts that form on the ovaries and are filled with old, dark blood, often referred to as "chocolate cysts." They can cause severe pain and potentially affect fertility.

Deeply Infiltrating Endometriosis (DIE): This occurs when endometrial-like tissue penetrates more than 5 mm into the tissues beneath the surface, such as the bladder, bowel, rectovaginal septum, or uterosacral ligaments. It is considered the most severe form and can cause significant pain and complications.

Each type may vary in severity and symptoms, and diagnosis typically requires imaging or surgical evaluation.

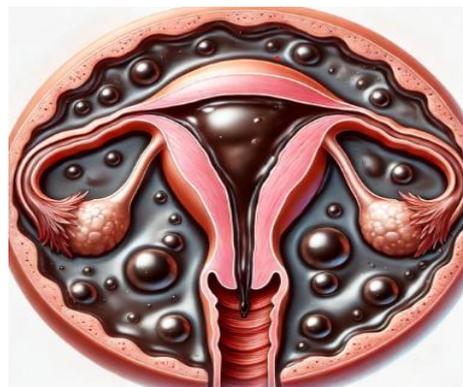


Fig.1 Chocolate Cyst.

2. Symptoms:

- Painful periods. Pelvic pain and cramping may start before a menstrual period and last for days into it. You also may have lower back and stomach pain. Another name for painful periods is dysmenorrhea.
- Pain with sex. Pain during or after sex is common with endometriosis.
- Pain with bowel movements or urination. You're most likely to have these symptoms before or during a menstrual period.
- Excessive bleeding. Sometimes, you may have heavy menstrual periods or bleeding between periods.
- Infertility. For some people, endometriosis is first found during tests for infertility treatment.
- Other symptoms. You may have fatigue, diarrhoea, constipation, bloating or nausea. These symptoms are more common before or during menstrual periods. [6]

3. Causes:

The exact cause of endometriosis isn't clear. But some possible causes include:

- Retrograde menstruation: This is when menstrual blood flows back through the fallopian tubes and into the pelvic cavity instead of out of the body. The blood contains endometrial cells from the inner lining of the uterus. These cells may stick to the pelvic walls and surfaces of pelvic organs. There, they might grow and continue to thicken and bleed over the course of each menstrual cycle.
- Transformed peritoneal cells: Experts suggest that hormones or immune factors might help transform cells that line the inner side of the abdomen, called peritoneal cells, into cells that are like those that line the inside of the uterus.
- Embryonic cell changes: Hormones such as estrogen may transform embryonic cells in the earliest stages of development into endometrial-like cell growths during puberty.
- Surgical scar complication: Endometrial cells may attach to scar tissue from a cut made during surgery to the stomach area, such as a C-section.
- Endometrial cell transport: The blood vessels or tissue fluid system may move endometrial cells to other parts of the body.
- Immune system condition: A problem with the immune system may make the body unable to recognize and destroy endometriosis tissue. [6]

4. Diagnosis:

Doctors may suspect endometriosis based on your history or physical exam, and may use these tools to diagnose endometriosis:

- Laparoscope: In this procedure, a doctor makes a small cut in the abdomen and inserts a thin tube with a light and a camera. This allows the doctor to look at the tissues in and around the uterus, and check for signs of endometrial tissue growth.
- Biopsy: If the doctor finds suspicious tissue, he or she may use a small device to scrape off a few cells and send them to the laboratory. A pathologist examines the tissues under a microscope. Biopsy is required for definitive diagnosis of endometriosis.
- Ultrasound: This procedure uses sound waves to view organs. Transvaginal ultrasounds use a small wand inserted into the vagina to see the uterus, pelvic area and reproductive organs.
- MRI: This non-invasive scan uses magnetic waves to look at organs and tissues inside the body. [7]

5. Management:

5.1 Conservative Management:

1. Observation and Monitoring: Regular follow-up with ultrasound to monitor the size and changes in the endometrioma. Recommended for small, asymptomatic endometriomas or in women planning future fertility treatments.

2. Pain Management: Nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen or naproxen to alleviate pelvic pain and discomfort.

3. Hormonal Therapy: Aimed at suppressing ovarian function and reducing estrogen production (which fuels endometriosis growth).

- Oral contraceptive pills (OCPs): Continuous or cyclic use to reduce cyst growth and pain.
- Progestins: Such as medroxyprogesterone acetate or dienogest to shrink endometriotic tissue.
- GnRH agonists/antagonists: Suppress ovarian hormone production, inducing a temporary menopausal state.
- Aromatase inhibitors: To reduce estrogen levels and endometrioma growth (less commonly used). [8]

5.2 Medical Management:

There are numerous current medical treatments for the management of endometriosis symptoms. All of these treatments should be considered suppressive rather than curative. Medical therapy will not increase fecundity or resolve endometriomas or deeply infiltrating disease. Because the effectiveness of medical options for reducing symptoms is comparable, selection of an optimal regimen is based on multiple factors including patient age, patient

preference, reproductive plans, pain severity, and degree of disease. Additional factors include treatment cost and intended duration as well as treatment risks, side effect profiles, and accessibility. The main objective of medical management is to prevent recurrence and reduce symptoms, thereby eliminating the need for repeat surgery or prolonging the time between surgeries.

Class	Mechanism of Pain Relief	Drug	Dose	Side Effects
Estrogen-progestin combinations	<ul style="list-style-type: none"> • Ovulation inhibition • Decidualization or atrophy of lesions 	<ul style="list-style-type: none"> • Monophasic estrogen-progestin* 	Continuous orally daily	Breakthrough bleeding, breast tenderness, nausea, headaches, mood changes
Progestins	<ul style="list-style-type: none"> • Decidualization or atrophy of lesions • Inhibition of angiogenesis • Suppression of matrix metalloproteinase-facilitated growth and implantation of ectopic endometrium 	<ul style="list-style-type: none"> • Depo Provera* • Etonogestrel-releasing implant • Norethindrone acetate* • Levonorgestrel-releasing IUS • Medroxyprogesterone acetate • Dienogest[†] • Leuprolide depot** • Goserelin** • Nafarelin** 	<ul style="list-style-type: none"> • 104 mg SC every 3 mo • 1 for 3 y • 5 mg daily • 1 for 5 y • 30 mg orally for 6 mo, then 100 mg IM every 22 wk for 2 mo, then 200 mg IM monthly for 4 mo • 2 mg daily 	Acne, weight gain, mood changes, headache, breakthrough bleeding, breast tenderness, lipid abnormalities (norethindrone)
GnRH agonists	Inhibition of gonadotropin secretion and subsequent downregulation of ovarian steroidogenesis	<ul style="list-style-type: none"> • Danazol* 	<ul style="list-style-type: none"> • 3.75 mg IM monthly (11.25 mg IM every 3 mo) • 3.6 mg SC monthly (10.8 mg IM every 3 mo) • 200 micrograms intranasally twice daily 	Decreased bone density, atrophic vaginitis, hot flashes, headache, joint pain
Androgenic steroids	<ul style="list-style-type: none"> • Inhibition of pituitary gonadotropin secretion • Local growth inhibitor • Inhibition of estrogenic enzymes 	<ul style="list-style-type: none"> • Danazol* 	<ul style="list-style-type: none"> 100–400 mg orally twice daily 100 mg vaginally daily 	Hair loss, weight gain, acne, hirsutism
Antiandrogens	Competitively inhibition of the androgen receptor	<ul style="list-style-type: none"> • Cyproterone acetate[†] 	12.5 mg orally daily	Hair loss, breast tenderness, weight gain
GnRH antagonists	Inhibition of gonadotropin secretion and subsequent downregulation of ovarian steroidogenesis	<ul style="list-style-type: none"> • Elagolix 	150 mg orally daily	Hot flushes, lipid abnormalities, decreased bone density
Aromatase inhibitors	Local blockade of enzymatic (aromatase) conversion of androgens to estrogens	<ul style="list-style-type: none"> • Letrozole • Anastrozole 	<ul style="list-style-type: none"> • 2.5 mg orally daily • 1 mg orally daily 	Hot flushes, headaches, decreased bone density
Selective progesterone receptor modulators	Inhibition of ovulation, agonist or antagonist at progesterone receptor	<ul style="list-style-type: none"> • Mifepristone • Ulipristal acetate 	<ul style="list-style-type: none"> • 50 mg orally daily • 15 mg orally every other day 	Spotting, cramping, dizziness, headache, nausea

SC, subcutaneously; IUS, intrauterine system; IM, intramuscularly; GnRH, gonadotropin-releasing hormone.
 * U.S. Food and Drug Administration–approved for endometriosis.
[†] Used as monotherapy outside the United States.
^{**} With add-back, that is, 5 mg norethindrone acetate daily plus 800 international units vitamin D daily plus 1.25 g calcium daily.

Table 1: Medical Therapies for Endometriosis [9]

5.3 Surgical Management:

➤ Laparotomy:

A laparotomy for endometriosis is an open surgical procedure in which a large incision is made in the abdominal wall to access and treat severe or complex cases of endometriosis. It allows the surgeon to directly visualize and remove endometriotic lesions,

adhesions, or cysts (endometriomas) and repair any damage to nearby organs such as the bowel, bladder, or ureters. This procedure is typically performed when less invasive options, like laparoscopy, are not sufficient to manage the condition. It is usually indicated for advanced endometriosis, deeply infiltrating disease, or when vital organs are affected, and the goal is to alleviate symptoms, restore organ function, or improve fertility.

➤ Hysterectomy:

Hysterectomy, the surgical removal of the uterus, is sometimes used to treat endometriosis and pelvic pain. The procedure may be particularly important for those who also have adenomyosis in which the endometrial lining grows into the muscular wall of the uterus or fibroids. Either condition can cause pelvic pain during menstruation as well as heavy or irregular bleeding. Your surgeon excises any endometriosis found during the hysterectomy, as untreated endometriosis may continue to cause significant symptoms after hysterectomy.

Most of the time, it is not necessary to remove the ovaries, which is done via a procedure called an oophorectomy. After a hysterectomy, your period stops, but only removal of the ovaries causes the body to enter menopause. This can lead to symptoms of menopause, including hot flashes and bone density loss, no matter your age. Your doctor will help you decide whether this surgery is appropriate for you and, if so, develop a plan to help you manage the symptoms of menopause.

➤ Ovarian Cystectomy:

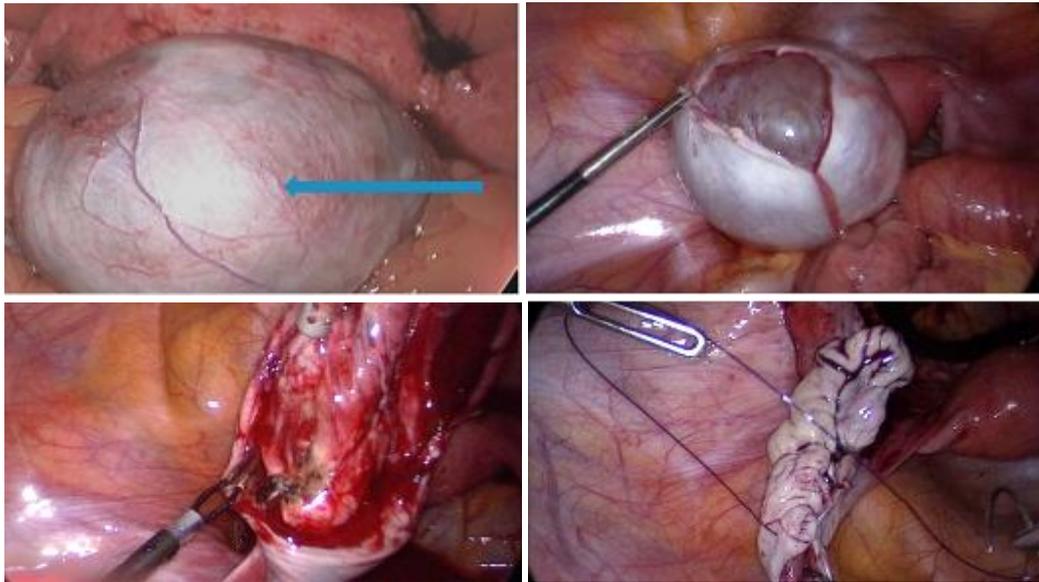


Fig. 2,3,4,5 Ovarian cystectomy. 1 – Chocolate cyst. 2 – dissect the cyst wall from the ovarian parenchyma. 3 & 4 – achieve haemostasis by targeted coagulation and/or suturing and then reconstruct the ovary. [16]

6. Fertility-Sparing Techniques:

6.1 Oocyte Cryopreservation:

Oocyte cryopreservation is a technique that involves the freezing and preservation of oocytes at low temperatures. These frozen oocytes can be used later when the patient decides to pursue reproductive desire. Initially developed for patients undergoing gonadotoxic therapies, this method has been employed for social freezing and fertility preservation in women with endometriosis [10]. Compared to embryo cryopreservation, oocyte cryopreservation allows for the preservation of unfertilized eggs, enabling the choice of partner in the future. Since the first successful birth achieved with this technique in 1986 [11], oocyte cryopreservation has undergone significant advancements over three decades. It has been consistently utilized in clinical settings for the past ten years. Specifically, new

methods involving cryoprotectants and cryotools in conjunction with rapid cryopreservation techniques and fertilization through Intra cytoplasmic Sperm Injection (ICSI) have been developed [12].

6.2 Embryo Cryopreservation:

The accumulation of embryos for cryopreservation involves a COS protocol similar to that used for accumulating cryopreserved oocytes. However, in this case, it includes the fertilization of the oocytes with the seminal fluid from a male partner or a sperm donor. Including a third party, this procedure has ethical and legal implications for death or separation [13]. On the other hand, considering the highest cumulative pregnancy rate with an increase in the number of a patient's oocytes and embryos, it should be noted that a lower percentage of oocytes survive the cryopreservation techniques and subsequent thawing for use compared to embryos [14].

6.3 Ovarian Tissue Cryopreservation:

Ovarian tissue cryopreservation (OTCP) is utilized for FP in oncological patients who need to initiate high-risk gonadotoxic therapies (chemotherapy or radiotherapy) and cannot delay treatment to undergo COS. OTCP offers benefits not only to individuals with oncological conditions but also to girls and women facing benign diseases like β -thalassemia and autoimmune disorders necessitating bone marrow transplantation, as well as benign ovarian conditions like endometriosis, requiring procedures like oophorectomy with a risk of premature ovarian insufficiency [15]. However, OTCP may be a valuable option for patients who cannot undergo COS and require urgent surgery, such as because of occlusive bowel endometriosis and hydronephrosis. OTCP requires two surgical procedures: the first to harvest the ovarian tissue and the second for transplantation. In addition, it harms ovarian reserve, has higher morbidity than oocyte or embryo cryopreservation, and can potentially promote the development of post-surgical adhesions.

- In Vitro Fertilization (IVF): If fertility is affected due to severe endometriosis or repeated cyst formation, IVF may be recommended. IVF can bypass any issues caused by endometriomas, such as tubal blockages or decreased ovarian function. IVF may involve ovarian stimulation to produce eggs, which are then fertilized in the lab and implanted into the uterus.
- Egg Freezing: For women with a significant risk of ovarian damage due to multiple surgeries or large cysts, egg freezing may be considered. This technique allows women to preserve their eggs for future use, even if their ovarian function is impaired later on due to cysts or surgery.

6.4 Assisted Reproductive Technologies (ART):

6.5 Oral Contraceptives:

OCs suppress ovulation, reducing the cyclical hormonal changes (particularly estrogen production) that stimulate the growth of endometriotic tissue, including endometriomas. OCs can help preserve fertility by reducing ovarian damage from inflammation caused by endometriomas.

7. Lifestyle Modification:

PATIENT COUSSELLING OF CHOCOLATE CYST	
DIET AND NUTRITION	LIFESTYLE MODIFICATION
Eat Anti-inflammatory Foods. Include fruits, vegetables, whole grains, nuts, seeds, and fatty fish (rich in omega-3).	Practice mindfulness, meditation, or deep breathing exercises. Consider therapy or counselling if stress is a significant factor.
Reduce Red Meat and Trans Fats. These may promote inflammation and worsen symptoms.	Maintain a consistent sleep schedule and aim for 7-9 hours of restful sleep per night.
Consider vitamin D, omega-3 fatty acids, and magnesium to reduce pain and inflammation.	Maintaining a healthy weight can help regulate estrogen levels, reducing the progression of endometriosis.
Avoid High-Estrogen Foods. Limit soy and unfermented soy products that mimic estrogen.	Consider complementary therapies like acupuncture or heat therapy (e.g., heating pads) to relieve pain.
Limit sugar, refined carbs, red meat, and dairy (high in saturated fats).	Avoid smoking, as it can exacerbate endometriosis and lower fertility
Focus on whole, unprocessed foods.	Limit intake of Alcohol, as it may increase estrogen levels and inflammation
Include foods rich in fibre, antioxidants.	Stay hydrated to reduce bloating and improve digestion, as gastrointestinal symptoms are common in endometriosis.
Stay hydrated (8-10 glasses of water daily).	Join endometriosis support groups for emotional support and shared experiences.
EXERCISE	YOGA
Regular Exercise Reduces inflammation, stress, and estrogen levels. Pelvic floor strengthening exercises.	Child's Pose (Balasana), Cat-Cow Pose (Marjaryasana-Bitilasana), Bridge Pose (Setu Bandhasana), Cobra Pose (Bhujangasana), Supine Twist (Supta Matsyendrasana), Butterfly Pose (Baddha Konasana)

Engage in moderate aerobic exercise (e.g., walking, swimming) and yoga for 30 minutes, 3-5 times a week.	Alternate nostril breathing (Nadi Shodhana).
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CONCLUSIONS

OMAs are present in 17–44% of young women with endometriosis, and may be diagnosed with high accuracy by means of transvaginal sonography. Management options for OMAs include expectant management, medical treatment, surgical treatment, in vitro fertilization (IVF) in case of infertility-associated endometriosis, or a combination of the above. The choice of management depends on many clinical parameters that should be taken into consideration, the first of which is the main presenting symptoms and the OMA size. Surgery was considered in the recent past as the gold standard treatment in case of ovarian OMAs, in particular for cysts larger than 3 cm. Recently, however, evidence has been accumulating as to a possible detrimental role of excisional surgery of the OMA on the ovarian reserve. Therefore, in more recent years, a shift towards more conservative approaches to ovarian OMAs are being followed, probably with less referral to surgery, and more patients amenable to medical therapy. As to fertility sparing techniques, prevention of ovaries or eggs as IVF or egg freezing may help to reserve. As a consequence, also delaying surgery may damage the ovarian reserve. Therefore, when discussing the available management options with the patient with an ovarian OMA, the clinician is today faced with the dilemma whether to opt for surgery or to resort to medical therapy, and the issue of preserving the ovarian reserve has become pivotal in research and academic discussion. The aim of the present review is to evaluate the current evidence on the conservative management of ovarian OMAs, with particular focus on the issue of the ovarian reserve.

Acknowledgement: None

Source of Funding: None

Conflict of Interest: The authors declare no conflict of interest

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