

# A narrative review of endometriosis surgery and infertility

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**Abstract:** Ectopic implantation of endometrial tissues outside of the endometrial layer is termed as endometriosis, which affects almost 10% of childbearing women, and the onset of pathogenesis goes back to the first menstrual bleeding. The frequency is increased to 25–50% in women diagnosed with infertility. The existence of endometriosis negatively effects fertility by many different pathways, but its surgical treatment may also decrease the potential for fertility. The goal of endometrioma surgery is to remove the cyst without tissue remnants and preserve the ovarian reserve as much as possible. In case of endometriosis if surgical intervention is a must for women with endometriosis, oocyte collection and embryo freezing before surgical intervention is recommended. Surgical intervention after fertility preservation in endometriosis minimizes the stress of the patient and surgeons feel safer during the surgical intervention. In patients with endometriosis, the choice of expectant management or surgical intervention should be individualized. In cases where the chance of spontaneous conception is high, surgery remains the primary option for appropriate treatment. Laparoscopic surgery is the preferred method for surgical removal of endometriotic lesions and surgery should be performed by skilled and specially trained surgeons. Deciding about the modality of endometriosis treatment is a controversial issue and preservation of fertility in women with endometriosis is fundamental. Each patient must be evaluated individually according to their symptoms, severity, age, expectations, and risks.

**Keywords:** Endometriosis; treatment of endometriosis; endometriosis surgery; infertility

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## Introduction

Ectopic implantation of endometrial tissues outside of the endometrial layer is termed as endometriosis, which affects almost 10% of childbearing women, and the onset of pathogenesis goes back to the first menstrual bleeding (1). Pain is the main symptom and endometriotic lesions may be localized inside or outside of the pelvis. Surgical management of endometriosis is a sum of decisions encompassing age, parity, fertility desire, symptoms, and quality of life (2). The goal for the treatment of endometriosis is to reduce the risk

of recurrence, increase the quality of life, and increase the chance of pregnancy (2).

Deciding about the modality of endometriosis treatment is a controversial issue and preservation of fertility in women with endometriosis is fundamental. In the context of infertility, the goal should be preserving the ovaries, tubes, and uterus during surgery. Surgeons usually find themselves in a difficult dilemma of either preserving the function and capacity of critical organs or further excising to achieve a disease-free state to decrease the risk of recurrence. Studies have reported the negative impact of surgical removal

of ovarian endometriosis on ovarian reserve, and further negative effects when performed bilaterally, which resulted in surgical abstinence and an increased number of oocyte retrievals for assisted reproductive technologies (ART). In case where both tubes are involved and destructed tubes removed during surgery, the only treatment option for pregnancy remains ART. In vitro fertilization (IVF) before surgery in women with hydrosalpinx carries the risk of IVF failure and should be carefully evaluated (3). The ovarian reserve is directly proportional to the pregnancy rate; therefore, endometriosis surgery should aim to minimize the loss of ovarian reserve (4). The severity and presenting symptoms of the disease may vary individually from puberty to menopause; hence, this requires specific and different medical or surgical approaches for every patient with endometriosis (5). Neighboring organ involvements in endometriosis in women with deeply infiltrating endometriosis (DIE) requires a multidisciplinary evaluation, and the priorities of the patient would lead the course of treatment at most (5).

We present the following article in accordance with the Narrative Review reporting checklist (available at <http://dx.doi.org/10.21037/gpm-20-55>).

## Methods

Database search is conducted through PubMed in 15th August 2020 by two authors. Articles published in English assessed in the regard of the following topics: 'endometriosis and ovarian reserve', 'endometriosis surgery and infertility', 'treatment of endometriosis and infertility', 'deep endometriosis surgery and fertility', 'endometriosis and obstetrics'. In total, 628 articles were assessed according to our mini review. With a detailed investigation, 58 of them were found relevant and are evaluated. Finally 30 articles were eligible and included for our mini review.

### *Endometriosis surgery in fertility desire*

For women seeking fertility solutions under the shadow of endometriosis, making the correct decision to treat is not simple and many issues in the decision-making process are controversial. In this circumstance, a thorough evaluation of the patient, the extent of endometriosis, ovarian reserve testing, and long-term consequences of surgical interventions should be taken into account. On the other hand, endometriosis without intervention caused harm to the ovarian reserve, equal to that of surgical

removal. If surgical intervention is a must for women with endometriosis, oocyte collection and embryo freezing before surgical intervention is recommended (6). Surgical intervention after fertility preservation in endometriosis minimizes the stress of the patient and surgeons feel safer during the surgical intervention. This approach also allows the patient attain spontaneous pregnancy within 6 months after surgery, if the fallopian tubes are patent and endometriotic foci are cleared carefully.

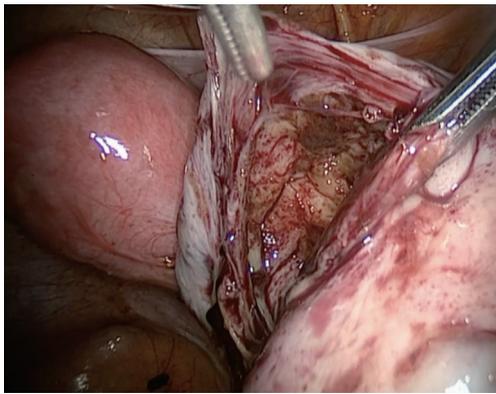
The impact of endometriosis on ovarian reserve has been discussed for years and is still a matter of controversy. It was reported that the presence of moderate to severe endometriosis significantly reduces serum anti-Mullerian hormone (AMH) levels when compared to women without the disease (7). It is not only the adhesion formation and mechanical events that reduce the ovarian reserve, but also the immunomodulation in the pelvic region. Moreover, endometriotic lesions dysregulate the genes for HOXA10-11, integrins, glycolidins, and B-catenin (8,9). Endometriosis, and particularly endometrioma, may alter the homeobox of the endometrium, which may have a serious impact on endometrial implantation (10). Considering this information, surgical removal of endometriotic lesions may be of benefit for the fertility outcomes of patients as well.

### *Endometriosis surgery and abnormal placental implantation*

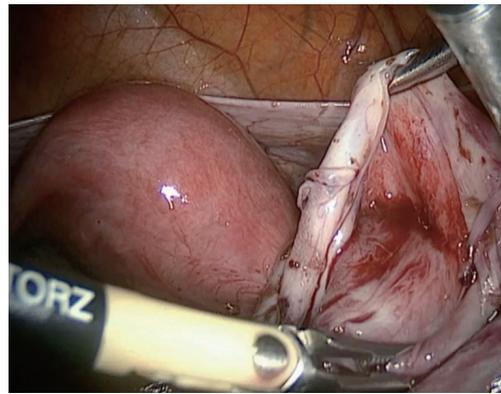
Endometriosis, and particularly DIE, is known risk factor for abnormal placental implantation (11). IVF itself, when multiple embryos are transferred, may augment abnormal placentation; thus, IVF in patients with endometriosis should be handled carefully and multifetal gestation needs to be avoided. Extensive surgery for endometriosis and pregnancy (either spontaneous or by ART) is another important issue that carries high surgical risks during cesarean section. Surgical risk augments, when severe bleeding due to placental invasion abnormalities associated with cesarean section and a cesarean hysterectomy, are a necessity (12).

### *Endometriosis surgery in endometrioma*

The presence and/or removal of endometrioma in women with infertility both have the potential harm to the ovarian reserve. Benaglia *et al.* studied the impact of endometrioma in two consecutive IVF cycles of 29 women retrospectively and reported that endometrioma related-ovarian responsiveness



**Figure 1** Cyst wall of endometrioma (UK's archive).



**Figure 2** Stripping the wall of endometrioma (UK's archive).

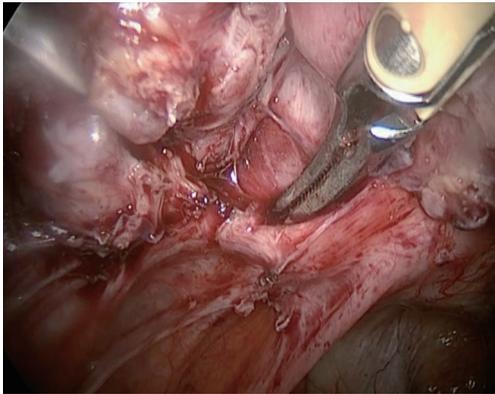
were not observed. In this study, patients with pregnancies were excluded (13). In an observational study, Santulli *et al.* studied the impact of ovarian endometrioma on infertility and reported that the presence of ovarian endometrioma was not a risk factor for infertility, but previous surgery for endometriosis was reported as a risk factor (14). Surgical removal of the ovarian cyst wall actually means the removal of ovarian cortex. The goal of endometrioma surgery is to remove the cyst without tissue remnants and preserve the ovarian reserve as much as possible (Video 1) (15,16). Two techniques used to remove endometrioma were compared in terms of disease recurrence and ovarian cystectomy was found to be superior to the ablation technique (Figures 1,2) (17). In an Endometriosis Treatment Italian Club position statement published in 2019, it was highly suggested to not remove endometriomas smaller than 4 cm so as to increase the probability of conception in patients who were referred for IVF (18). Although it was shown that serum AMH was lower in women who have ovarian endometrioma, after surgery for ovarian endometriotic cysts, it also decreased (19). Moreover, in that statement, it was also strongly suggested that women who were not planning to conceive immediately must not be left without long-term treatment of estrogen-progestins or progestins after surgery for endometriomas (18). On the other hand, Kasapoglu *et al.* showed in their study that women who had endometriomas larger than 3 cm in at least one ovary had lower AMH levels than the normal population, and at the 6-month follow-up without surgery, it was shown that it was associated with a faster decline in AMH levels than in healthy women (20).

Endometrioma recurrence is directly related to the resumption of menstrual bleeding after surgery and the postponement of menstruation after surgery decreases the recurrence after surgery (21). Those women who wish to

become pregnant later following surgery are recommended to use continuous oral contraceptive pills (OCPs) to prevent the recurrence of endometriomas. Overall pregnancy rates after endometriosis surgery have been reported as over 50% in literature (22).

#### ***Endometriosis surgery in DIE***

DIE is a histologically benign but behaviorally malignant disease, which invades neighboring organs and produces severe symptoms that affect the quality of life of the women involved. Uterosacral ligaments, posterior vaginal wall, bladder, ureters, rectum, rectosigmoid junction, ileum, and appendix are anatomical locations affected by DIE, and the lesions are frequently multifocal. Although rare, scar endometriosis, thoracic or diaphragmatic endometriosis, or nerve involvements by endometriosis may cause cyclic or chronic extra-pelvic pain symptoms, which require precise mapping for a targeted surgery to achieve the pain relief (23,24). For those who have bowel endometriosis, laparoscopic surgery increases the chance of spontaneous pregnancy (25). Pregnancy rates usually reach 50% after surgery. The European Society of Human Reproduction and Embryology guidelines are not actually directing, since the level of evidence to recommend a certain treatment approach was lacking in most studies, and therefore, the final report released reported that surgical removal of DIE nodules prior to ART treatment in women with endometriosis-related infertility was not well-established with regards to fertility preservation (26). For proper restoration of pelvic anatomy and adequate surgical removal of endometriotic lesions, the World Endometriosis Society recommends laparoscopic surgery in the hands of skilled



**Figure 3** Deep infiltrating nodule in left ovarian fossa, above the left uterosacral ligament (UK's archive).

or dedicated surgeons who have been trained specifically for this disease. Such a dedication has two targets: one is the complete removal of the lesions and the other is the restoration of fertility (*Figures 3,4*) (Video 2) (27).

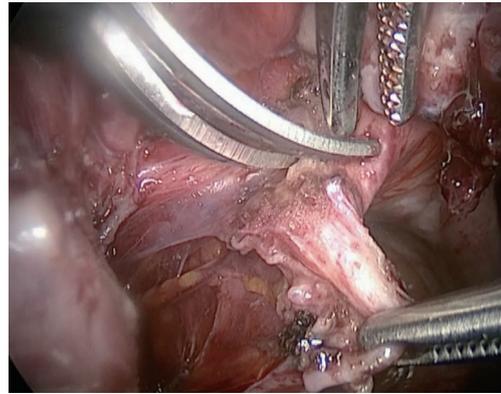
In patients with endometriosis, the choice of expectant management or surgical intervention should be individualized. In cases where the chance of spontaneous conception is high, surgery remains the primary option for appropriate treatment. Laparoscopic surgery is the preferred method for surgical removal of endometriotic lesions and surgery should be performed by skilled and specially trained surgeons (28).

Endometriosis and its symptoms are rarely seen after menopause, but endometriotic implants may not have disappeared, and they have a propensity to recur long after menopause. Among women who must have surgery, those over the age of 39 should have radical surgery to remove both ovaries, which can reduce the risk of recurrence; however, the potential risk of premature surgical menopause must be evaluated individually as well (29).

One important issue is the ongoing debate on surgical or medical treatment for endometriosis. It looks like the battle is between well-known speakers who promote the use of medications, while neglecting the benefits of surgical procedures, and talented surgeons who always emphasize the benefit of surgical removal of the lesions with limited knowledge of medical approaches (30).

## Conclusions

In conclusion, an individualized approach to each patient with endometriosis and infertility, and a thorough evaluation



**Figure 4** Excision of the deep infiltrating nodule (UK's archive).

before decision making are strongly recommended. Surgery for patients with a high chance of natural conception is the primary option, while for those who have low chance of spontaneous conception, IVF should be the priority. For those women whose endometriosis history proves a severe disease, and whose previous surgeries and AMH levels were low, oocyte collection and embryo cryopreservation before surgical intervention is recommended. If surgical intervention is adequate and cryopreserved embryos are present, then long-term suppression with continuous OCPs is recommended. If the fallopian tubes are patent and there is no male factor, patients may be allowed to have spontaneous conception after appropriate surgery.

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