

Surgery for endometriosis: beyond medical therapies

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Endometriosis-associated pelvic pain and subfertility may be managed medically in many cases; however, the surgical management of this insidious disease remains a necessary part of the treatment algorithm. Laparoscopy for diagnosis alone is rarely indicated with the advancements in preoperative imaging. When surgery is performed, the ideal goal would be a therapeutic and effective surgical intervention based on the preoperative evaluation. Surgery for women with pain due to endometriosis may be indicated in patients who cannot or do not wish to take medical therapies; acute surgical or pain events; deep endometriosis; during concomitant management of other gynecologic disorders; and patients seeking fertility with pain. The role of surgery for endometriosis-related subfertility may be considered in those with hydrosalpinges undergoing IVF; management of ovarian endometriomas in specific circumstances; and when a patient requests surgery as an alternative to assisted reproductive technology (ART). Surgery for ovarian endometriomas requires special attention due to the risk of potential harm on future fertility. Finally, a combined approach of surgery followed by postoperative medical therapy offers the best long-term outcomes for recurrence of disease and symptoms. A patient-centered approach and a goal-oriented approach are essential when determining the options for care in this population. (Fertil Steril® 2017; ■:■-■. ©2017 by American Society for Reproductive Medicine.)

Key Words: Endometriosis, laparoscopy, infertility, pelvic pain, ovarian endometrioma

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WHEN IS SURGERY INDICATED FOR THE TREATMENT OF ENDOMETRIOSIS?

The management of endometriosis-associated pelvic pain and subfertility has seen and will continue to see advancements in care options available for providers and their patients. The medical and surgical management schism is largely an issue of the past and most recognize the importance of an integrated approach for patients presenting with endometriosis-related health issues. However, there are circumstances in which surgical intervention is required, preferred, or requested. The aim of this article is to describe the role of surgery in endometriosis-related care.

SURGERY FOR DIAGNOSIS Diagnostic Laparoscopy Should be Replaced with a “See and Treat” Approach

Surgery has been heralded as the gold standard for the diagnosis of endometriosis as it provides a histologic evaluation of excised specimens. This is further supported by the lack of a definitive noninvasive test for endometriosis despite the ongoing work being conducted globally (1). As a result, should diagnostic laparoscopy remain the optimal route for diagnosis?

Laparoscopy for diagnostic purposes alone has several limitations that should challenge this antiquated practice. Although one cannot argue the value of having a histologic tissue

diagnosis, the following scenarios challenge routine diagnostic laparoscopy.

Unrecognized endometriosis lesions.

Lesions with an atypical appearance may not be recognized by the surgeon or may be very small/subtle and thus preclude pathologic specimen retrieval. Deep lesions below adhesions, which may be attributed to pelvic inflammation from previous surgery or infection, may be missed. Finally, adjacent organ involvement including intestinal, urinary tract, and deeper nerve involvement may be missed by a laparoscopic evaluation.

Excision specimens. Excision of peritoneal or deeper lesions at the time of diagnostic laparoscopy may not always be performed or possible. There are many reasons for this including specimens destroyed by crush or thermal injury at attempted removal and lack of skill set to excise relevant disease areas.

Surgical risks. The complications from diagnostic and operative gynecologic laparoscopy overall may be considered

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relatively low, but they are still an important consideration in deciding on the role of surgery (2). The experience of the surgeon, the patient's history and comorbidities, and the extent of disease are all factors that determine the risk of complications.

To optimize patient outcomes and to minimize exposure to multiple surgeries, at present the role of surgery would ideally be reserved for diagnostic confirmation AND simultaneous treatment. The benefits of a "see and treat" approach offer women the opportunity to confirm the pathology and address the underlying condition all during one anesthesia. Ideally the one "perfect" surgery would also occur in the appropriate surgical setting with an experienced surgical team with the right equipment, time, and assistance for the level of disease expected. Although there are always going to be exceptions to the ideal setting (i.e., unexpected findings), which would result in halting a procedure and further planning, health care providers should strive for optimal surgical management based on a robust preoperative evaluation.

At present, there is a greater focus on advanced imaging for endometriosis and the management of deep and ovarian endometriosis has seen a fundamental shift in practice (3, 4). The use of imaging to help diagnose and plan surgical intervention is critical to the management of women with signs and symptoms suggestive of endometriosis.

SURGERY IN ENDOMETRIOSIS-ASSOCIATED PELVIC PAIN: WHEN IS IT NECESSARY?

The role of surgery in pelvic pain requires careful consideration and should be individualized based on the patient's presenting complaint and findings on evaluation. Chronic pain is complex and often involves multiple factors beyond simply a diagnosis of endometriosis (5). Abnormal exaggerated pain responses from the central nervous system (central sensitization) further complicate the management of the patient with pain. Surgery for endometriosis may be an appropriate intervention, but it should ideally only be used when its therapeutic benefit outweighs the risks. Patient-centered care would prioritize pain reduction and improvement of quality of life versus optimal "debulking" of disease that may not offer those benefits or may lead to harm. For the present discussion we will consider endometriosis-associated pelvic pain (EAPP) as pain symptoms attributed to endometriosis in the absence of other causes or central sensitization.

A general statement of the benefits of surgery for EAPP at present is very difficult to define due to the limited evidence available through randomized control trials, the varying disease presentations (i.e., deep, ovarian, extrapelvic, and superficial), and the differing surgical approaches and skill sets (6, 7). Based on the Cochrane review by Duffy et al. (7), "moderate quality evidence" suggests that the surgical management of mild and moderate endometriosis reduces overall pain, yet there were limited comparisons to medical therapies and poor reporting on adverse events. However, as Hirsch et al. (8) point out in their 2016 systematic review, there is significant variation in outcome reporting in

endometriosis trials prohibiting larger generalization of outcomes. Becker et al. (9), on behalf of the World Endometriosis Research Foundation collaborative, have published guidance on basic data that should be gathered for surgical endometriosis research. Despite the need for clarity in the literature and further higher quality evidence, surgery continues to have a significant role in managing EAPP.

SURGERY MAY BE CONSIDERED IN THE FOLLOWING SCENARIOS

Patients Who Decline, Do Not Respond to, Do Not Tolerate, or Have Contraindications to Medical Therapy

Medical management for EAPP has its benefits but unfortunately there is no single medical treatment that will work in all patients (10). At present, medical management of endometriosis is restricted to hormonal suppression and once medications are discontinued, in the reproductive aged woman, the pain symptoms will return (6, 11). Medical treatment itself has limitations due to an incomplete response or intolerable side effects such as irregular menstrual bleeding, headache, or mood changes (12). Therefore, surgery may be required in women who decline long-term therapy, experience significant side effects, or have contraindications to medical therapy.

Another important aspect to consider for surgical interventions for EAPP is patient choice. Patients may elect to undergo surgical management for many reasons such as declining medical options, requesting surgical confirmation, or perceived failure of therapy. This is an important consideration that many surgeons will face.

It is important to counsel patients regarding the benefits and limitations of surgical intervention. Although there is an overall improvement in pain symptoms, there is a risk of pain recurrence or persistence. As a result, repeat surgical intervention, in women who decline or cannot use medical therapies, may be necessary. A 2010 review by Berlanda et al. (13) suggested that repeat surgery may have the same results as primary surgery for EAPP; however, with up to 50% recurrence of pain at 5 years, there may be many women in need of repeat intervention.

Acute Surgical or Pain Event

An urgent admission for severe pain in women of reproductive age is part and parcel of gynecology emergency care. When there is not a clear diagnosis of the underlying etiology, a presumed adnexal event (i.e., torsion), or ruptured hemorrhagic ovarian cyst in an unstable patient, surgery may be indicated. At times the underlying finding may be endometriosis related (ruptured ovarian endometrioma) or endometriosis may be found concomitantly. In these circumstances it is important to consider documenting the findings, managing the issue at the time, and planning for elective care whether it be long-term medical or surgery in the future.

Deep Endometriosis

The most severe and morbid form of endometriosis is the deep invasive type, which may result in significant organ compromise including genitourinary tract obstruction, renal compromise, or bowel obstruction. Invasive lesions may be limited to the pelvis; however, evaluation of extrapelvic disease may be required when symptoms dictate (i.e., catamenial pneumothorax). Although medical therapy may be effective in many cases, the surgical approach is often required in expert hands complemented by an experienced institution (14).

The approach to deep endometriosis has been increasingly described in the literature and demonstrates improved imaging, experience, and surgical techniques. As an example, Abrão et al. (15) published an expert-guided consensus article in 2015 outlining the clinical factors to consider for deep endometriosis infiltrating the rectosigmoid colon. Ferrero et al. (16) provide an overview of deep endometriosis and options for management for pain. A systematic approach in experienced hands for these complex cases also relies on expert guided imaging to plan appropriately (3). Guerriero et al. (4) recently published the International Deep Endometriosis Analysis group framework on advanced ultrasound for deep endometriosis as a guide for improved imaging in this field. Ultimately, when surgery is indicated, women with deep endometriosis are best served in centers with the appropriate tools to evaluate, excise, and manage this complex condition.

Concomitant Management of Disease

In patients undergoing surgery for conditions other than endometriosis, there may be an opportunistic or concomitant management option. Patients with symptoms due to conditions, such as uterine fibroids, may often have endometriosis present and perhaps some of the symptoms may be attributed to this finding (i.e., dysmenorrhea in uterine fibroids) (17). Consideration for concomitant management should be part of the discussion. The corollary of this is the finding of incidental endometriosis in an asymptomatic woman. The appropriateness of surgical excision of these lesions, as well as the extent of surgical excision, should be carefully considered, as the benefit may not outweigh risks.

Ovarian Endometrioma with a Suspicion of Concomitant Malignancy

The complex adnexal mass requires surgical management when the differential diagnosis includes malignancy. As such, ovarian endometriomas may present a difficult diagnosis in some women and especially in women at risk of malignancy based on family or personal history. An appropriate evaluation of complex masses is encouraged in women with endometriosis to determine an overall risk assessment (18). Although most women with endometriosis and ovarian endometriomas have a benign condition, there is an ever-growing area of study of the relationship between endometriosis and epithelial ovarian cancer that may lead patients and surgeons toward a histologic diagnosis (19). A detailed discussion of the approach to the ovarian endometrioma is outlined.

Pelvic Pain and Desire to Conceive

Because most medical management options, with the exception of analgesics, prevent pregnancy, surgery may be the only option for treatment in this subgroup. A thoughtful discussion, which considers fertility options versus surgical intervention, is very important in this population. Balancing pain symptoms with the potential risk of harm to the reproductive organs is a common conundrum in this clinical sphere. However, in cases where pain significantly affects one's quality of life and results in an inability to function, then the priority is to help the individual resolve these issues first. In some cases the benefits of surgery may be realized through improved pain control and through improved pregnancy rates (PRs) (7). However, if fertility issues persist after surgical management, then appropriate evaluation and intervention will be required.

THE ROLE OF SURGERY FOR ENDOMETRIOSIS-RELATED SUBFERTILITY

In the absence of pain, the role of surgical management of endometriosis for subfertility is considered next. Is there a role of enhancing fertility in women with endometriosis through surgical management or improving outcomes of fertility therapies such as IVF?

Mild-to-Moderate Endometriosis

Endometriosis has a number of effects that can individually or collectively affect fertility, such as chronic inflammation with a proinflammatory biochemical milieu, pelvic adhesions that disrupt anatomy and affect oocyte or embryo transport, and diminished ovarian reserve (20). Surgical treatment of disease may theoretically improve the environment for successful conception. The most recent Cochrane review on this topic by Duffy et al. (7) suggests that laparoscopic treatment of mild and moderate endometriosis increases live birth and ongoing PRs.

One must balance the risk of surgical intervention with the alternative options for enhancing fertility such as assisted reproductive technology (ART). This point is best illustrated among women who have repeat surgeries for endometriosis. It has been suggested that repeat surgery may benefit pain symptom yet resulting in reduced PRs (21).

Deep Endometriosis and Subfertility

Somigliana and Garcia-Velasco (22) published a thorough and frank review on the topic of managing deep endometriosis in patients with subfertility. The bottom line is that many case series report show excellent outcomes of surgical intervention; however, one must take these series in context of their own individual center and acknowledge the inherent biases of case series. At this point, the main reason to manage deep endometriosis surgically would be to alleviate pain or visceral obstruction in expert hands. Conservative "radical" excision is possible to retain the uterus and ovaries and should be the goal in those wishing to conceive.

The Management of Ovarian Endometriomas

A detailed discussion for the surgical management of endometriomas is outlined. However, the key indication for managing the “asymptomatic” ovarian endometrioma in patients with subfertility is to improve access for ART. The endometrioma size, location, and transvaginal access for retrieval may all have a factor in determining whether patients require surgery. In fact, Hamdan et al. (23), in their meta-analysis found that the outcome of IVF/intracytoplasmic sperm injection (ICSI) did not differ in women who had their endometriomas treated surgically versus no surgery.

Hydrosalpinges and IVF

Due to the anatomic disruption associated with endometriosis, one may develop concurrent unilateral or bilateral hydrosalpinges, and the inflammatory milieu of this condition diminishes IVF success rates. At present multiple studies have shown that removal or occlusion of the tubes, which does eliminate the possibility of natural conception, improves IVF outcomes (24).

Sociocultural and Religious Considerations

A patient’s sociocultural preferences and religious practices can strongly determine ART options. For example, Jewish Law, the Roman Catholic Church, and Islamic Law each have different views on the acceptability of different forms of ART (25). A frank and open discussion between the care provider and the patient is essential to determining an option that is acceptable. In some cases, surgery may be the only acceptable option.

Patient Choice versus Surgeon Choice

In a patient-centered environment the autonomy of the patient takes precedence and this part of the discussion must not be omitted. In an ideal setting where individuals have all contemporary options available, they should have the opportunity to choose between medical and surgical care alternatives.

The unfortunate truth of being able to individualize care based on patient choice is that not all medical and surgical options are available globally. For medical therapies the limitations may be cost, lack of approval of all medical therapies, cultural barriers (i.e., access to hormonal contraceptives), and provider biases. Surgical management has very similar challenges. Additional considerations include the availability of experienced surgeons, surgical wait lists, and the public versus private health care system dichotomy. The socioeconomic impact of choosing the right treatment for women cannot be underestimated at the global stage.

In summary, the following may be considered indications for surgery in patients with endometriosis-related subfertility without significant pain:

- Mild-to-moderate endometriosis
- Improving access for oocyte retrieval
- Treating hydrosalpinges to improve IVF outcomes

- Patient declines ART due to personal, cultural, or religious reasons
- Patient choice for surgery or unable to access interventions such as ART

SURGICAL MANAGEMENT OF OVARIAN ENDOMETRIOMAS

Surgical excision of an ovarian endometrioma in women wishing to preserve fertility or ovarian function has been shown to be effective in managing pain and has a lower recurrence risk than drainage and coagulation alone (26). However, the risk of affecting ovarian reserve after endometrioma surgery should be considered. The main question is: how much of an effect does the ovarian endometrioma impact underlying ovarian reserve just by being present versus how much of an impact does surgical intervention have on the remaining reserve or can it improve reserve?

Several studies including a recent prospective cohort study by Goodman et al. (27) showed that women with endometriomas have a lower baseline antimüllerian hormone level compared with those women without endometrioma. Surgical excision of endometriomas further reduced antimüllerian hormone levels at 1 month and they did appear to recover at 6 months but only back to the baseline. Although this was the first study to use a control group that included patients without endometrioma but with endometriosis, other investigators (28–31) have found similar concerns with surgical management of endometriomas.

Factors that may predict greater impact of surgical endometrioma management on ovarian reserve have included age and bilateral ovarian cystectomy (32). Repeat endometrioma surgery may also risk further harm of ovarian tissue, as suggested in a recent small study by Muzii et al. (33).

Another important concept to contemplate when surgery is considered for ovarian endometriomas is the association of this type of disease with severe deep endometriosis, especially in patients with pain symptoms (34). As a result, the complexity of the surgical procedure is often beyond simple excision of the endometriotic cyst and may require more extensive dissection and an interdisciplinary approach. Suboptimal excision of ovarian disease in cases of an oophorectomy may lead to ovarian remnant and hence require further surgical or medical management (35).

In summary, the management of ovarian endometriomas for women with pain must also consider the individual’s plan for future fertility. For women wishing to conceive in the future, the surgeon must consider the following:

- Ovarian reserve may be lower in women with ovarian endometrioma compared with those women without
- Surgical excision of an endometrioma is ideal for pain but may lead to reduced ovarian reserve in the short term
- Bilateral, compared to unilateral, ovarian cystectomy for endometriomas may result in a greater negative effect on ovarian reserve
- Recurrent endometrioma excision may further reduce ovarian reserve compared with primary surgery

THE ROLE OF POSTOPERATIVE MEDICAL THERAPY

Medical and surgical therapies are complementary to one another and should be considered in all patients who present with endometriosis-associated symptoms. The main role of medical therapy after fertility-sparing endometriosis surgery in women with EAPP is to prevent the recurrence of symptoms and/or disease. There may be incomplete surgical excision in some cases and postoperative medical suppression acts as an adjuvant treatment for symptom control.

The type of medical therapy after surgery has varied, yet oral contraceptives (OCs) and progestin agents have shown benefit in preventing recurrence of symptoms compared with surgery alone (36). The use of the progestin intrauterine system has also been shown to be effective in long-term pain control in conjunction with surgery (6). Similar to other chronic conditions, endometriosis is best managed with long-term medical suppression, as opposed to intermittent short courses, as symptoms and disease may return after medication has been discontinued in reproductive aged women (37).

Recurrence of endometriomas is a major concern especially in patients with pain and wishing to preserve ovarian function. The recurrence rate for ovarian endometriomas after surgical excision may be as high as 50% at 5 years. The use of medical therapy, such as the combined hormonal contraceptives, is effective at reducing endometrioma recurrence and related pain (36, 38–40). However, long-term postoperative suppression is an obvious barrier to conception. In women wishing to conceive, the role of postoperative medical suppression is limited as it has not shown benefit in increasing PRs (6). Women with deep endometriosis should also receive the same medical approach after surgical management as those with superficial disease and ovarian endometriomas (41).

Finally, the management of endometriosis is the treatment of a chronic condition during the reproductive lifespan that requires a balanced approach based on a patient's symptoms, expectations, and desire for pregnancy. Surgery alone is unlikely to benefit our most affected patients and as such there is a need for combined medical and surgical management options.

In conclusion, the surgical management of endometriosis has and will continue to have a role despite advancing medical options. For women suffering with endometriosis-associated pelvic pain and/or endometriosis-associated subfertility, there are multiple considerations for surgical intervention. The patient presentation, findings on evaluation, response to therapies, and individual treatment preferences all play a role in determining the recommendations we, as health care providers, will offer. As in any complex medical condition the "truth" lies somewhere in the middle. Between the extremes of surgery-only versus medical-only approaches, there exists a careful balance of approaches centered on the patient's needs and desires.

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