

ROUNDTABLE

Endometriosis: Expert perspectives on medical and surgical management

Challenging to manage, endometriosis requires a thorough understanding of the disease process, first- and second-line therapies, and multidisciplinary care

Expert panel featuring Arnold P. Advincula, MD; Douglas N. Brown, MD; and Hye-Chun Hur, MD, MPH

ndometriosis is one of the more daunting diagnoses that gynecologists treat. In this roundtable discussion, moderated by OBG MANAGEMENT Board Member Arnold P. Advincula, MD, 2 leading surgeons discuss endometriosis diagnosis as well as medical and surgical management.

First-time evaluation

Arnold P. Advincula, MD: When a patient presents to your practice for the first time and you suspect endometriosis, what considerations tailor your evaluation, and what does that evaluation involve?

Hye-Chun Hur, MD, MPH: The diagnosis is contingent on a patient's presenting profile. How symptomatic is she? How old is she? What are her reproductive goals? The gold standard for diagnosis is a histologic diagnosis, which is surgical. Depending on the age profile, however, and how close she is to menopause, the patient may be managed medically. Even women in the young reproductive age group may be managed medically if symptoms are responsive to medical treatment.

Douglas N. Brown, MD: I agree. When a patient presents without a laparoscopy, or a tissue diagnosis, but the symptoms are consistent with likely endometriosis (depending on where she is in her reproductive cycle and

Take-home points

- Endometriosis management involves fluidity of care. Treatment approaches will change throughout a patient's reproductive life, depending on the patient's presenting symptoms and reproductive goals.
- Inform the patient of the disease process and how it may affect her menstrual pain symptoms and family planning.
- Educate patients so they may effectively participate in the management discussion. Hear the voice of the patient to make a tailored plan of care for each individual.
- Endometriosis can be a complex medical problem. Use a comprehensive multidisciplinary approach when appropriate.

what her goals are), I think treating with a first-line therapy—hormonal treatments such as progestin-only oral contraceptive pills—is acceptable. I usually conduct a treatment trial period of 3 to 6 months to see if she obtains any symptom relief.

If that first-line treatment fails, generally you can move to a second-line treatment.

I have a discussion in which I either offer a second-line treatment, such as medroxyprogesterone (Depo-Provera) or leuprolide acetate (Lupron Depot), or get a tissue diagnosis, if possible, by performing laparoscopy. If first-line or even second-line therapy fails,



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OBG Management Expert Panel



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> you need to consider doing a diagnostic laparoscopy to confirm or deny the diagnosis.

> **Dr. Advincula:** Are there any points in the evaluation of a patient who visits your practice for the first time where you would immediately offer a surgical approach, as opposed to starting with medical management?

> **Dr. Hur:** A large percentage of my patients undergo surgical evaluation, as surgical diagnosis is the gold standard. If you look at the literature, even among surgeons, the accuracy of visual diagnosis is not great.^{1,2} I target individuals who are either not responsive to medical treatment or who have never tried medical treatment but are trying to conceive, so they are not medical candidates, or individuals who genuinely want a diagnosis for surgical management-sometimes even before first-line medical treatment.

> **Dr. Brown:** Your examination sometimes also dictates your approach. A patient may never have had a laparoscopy or hormone

therapy, but if you find uterosacral ligament nodularity, extreme pain on examination, and suspicious findings on ultrasound or otherwise, a diagnostic laparoscopy may be warranted to confirm the diagnosis.

Endometrioma management

Dr. Advincula: Let's jump ahead. You have decided to proceed with laparoscopy and you encounter an endometrioma. What is your management strategy, particularly in a fertility-desiring patient?

Dr. Hur: Even if a woman has not undergone first-line medical treatment, if she is trying to conceive or presents with infertility, it's a different balancing act for approaching the patient. When a woman presents, either with an ultrasound finding or an intraoperative finding of an endometrioma, I am a strong advocate of treating symptomatic disease, which means complete cyst excision. Good clinical data suggest that reproductive outcomes are improved for spontaneous pregnancy rates when you excise an endometrioma.3-6

Dr. Advincula: What are the risks of excision of an endometrioma cyst that patients need to know about?

Dr. Brown: Current standard of care is cystectomy, stripping the cyst wall away from the ovarian cortex. There is some concern that the stripping process, depending on how long the endometrioma has been present within the ovary, can cause some destruction to the underlying oocytes and perhaps impact that ovary's ability to produce viable eggs.

Some studies, from France in particular, have investigated different energy sources, such as plasma energy, that make it possible to remove part of the cyst and then use the plasma energy to vaporize the rest of the cyst wall that may be lying on the cortex. Researchers looked at anti-Müllerian hormone levels, and there does seem to be a difference in terms of how you remove the cyst.7-9 This energy source is not available to everyone; it's similar to laser but does not have as much penetration. Standard of care is still ovarian stripping.

The conversation with the patient—if she is already infertile and this cyst is a problem—

TABLE US Food and Drug Administration-approved drug classes for endometriosis treatment

Drug	Adverse effects
Danazol	Hair loss, weight gain, acne, hirsutism
Monophasic estrogen-progestin	Breakthrough bleeding, breast tenderness, nausea, headaches, mood changes
Goserelin Leuprolide depot	Decreased bone density, atrophic vaginitis, hot flashes, headache, joint pain
Nafarelin	
Depo-Provera Norethindrone acetate	Acne, weight gain, mood changes, headache, breakthrough bleeding, breast tenderness, lipid abnormalities (norethindrone)
	Danazol Monophasic estrogen-progestin Goserelin Leuprolide depot Nafarelin Depo-Provera

Source: Falcone T, Flyckt R. Clinical management of endometriosis [published online ahead of print February 5, 2018]. Obstet Gynecol. doi:10.1097/AOG.0000000000002469.

would be that it likely needs to be removed. There is a chance that she may need assisted reproduction; she might not be able to get pregnant on her own due either to the presence of the endometrioma or to the surgical process of removing it and stripping.

Dr. Advincula: How soon after surgery can a patient start to pursue trying to get pregnant? **Dr. Hur:** I think there is no time restraint outside of recovery. As long as the patient has a routine postoperative course, she can try to conceive, spontaneously or with assisted reproduction. Some data suggest, however, that ovarian reserve is diminished immediately after surgery. 10-12 If you look at the spontaneous clinical pregnancy outcomes, they are comparable 3 to 6 months postsurgery.^{4,12-14}

Dr. Brown: I agree. Time is of the essence with a lot of patients, many of whom present after age 35.

Dr. Hur: It's also important to highlight that there are 2 presentations with endometrioma: the symptomatic patient and the asymptomatic patient. In the asymptomatic patient, her age, reproductive goals, and the bilaterality (whether it is present on both sides or on one side) of the endometrioma are important in deciding on a patient-centered surgical plan. For someone with a smaller cyst, unilateral presentation, and maybe older age at presentation, it may or may not impact assisted reproductive outcomes.

If the patient is not symptomatic and she is older with bilateral endometriomas less than 4 cm, some data suggest that patient might be better served in a conservative fashion. 6,15-17 Then, once she is done with assisted reproduction, we might be more aggressive surgically by treating the finding that would not resolve spontaneously without surgical management. It is important to highlight that endometriomas do not resolve on their own; they require surgical management.

Endometriosis management for the patient not seeking fertility

Dr. Advincula: Let's now consider a patient on whom you have performed laparoscopy not only to diagnose and confirm the evidence of endometriosis but also to treat endometriosis, an endometrioma, and potentially deeply infiltrative disease. But this person is not trying to get pregnant. Postoperatively, what is your approach?

Dr. Brown: Suppressive therapy for this patient could be first-line or second-line therapy, such as a Lupron Depot or Depo-Provera. We keep the patient on suppressive therapy (whatever treatments work for her), until she's ready to get pregnant; then we take her off. Hopefully she gets pregnant. After she delivers, we reinitiate suppressive therapy. I will follow these women throughout their reproductive cycle, and I think having a team of physicians who are all on the same page can help this patient manage her disease through her reproductive years.

"If the patient is not symptomatic and she is older with bilateral endometriomas less than 4 cm, some data suggest that patient might be better served in a conservative fashion."

-Hye-Chun Hur, MD, MPH

Surgical technique: Excision versus ablation

Hye-Chun Hur, MD, MPH: I am a strong advocate of excision of endometriosis. I believe that it's essential to excise for 2 very important reasons. One reason is for diagnosis. Accurately diagnosing endometriosis through visualization alone is poor, even among gynecologic surgeons. It is very important to have an accurate diagnosis of endometriosis, since the diagnosis will then dictate the treatment for the rest of a patient's reproductive life.

The second reason that excision is essential is because you just do not know how much disease there is "behind the scenes." When you start to excise, you begin to appreciate the depth of the disease, and often fibrosis or inflammation is present even behind the endometriosis implant that is visualized.

Douglas N. Brown, MD: I approach endometriosis in the same way that an oncologist would approach cancer. I call it cytoreduction-reducing the disease. There is this iceberg phenomenon, where the tip of the iceberg is seen in the water, but you have no idea how deep it actually goes. That is very much deep, infiltrative endometriosis. Performing an ablation on the top does almost nothing for the patient and may actually complicate the situation by causing scar tissue. If a patient has symptoms, I firmly believe that you must resect the disease, whether it is on the peritoneum, bladder, bowel, or near the ureter. Now, these are radical surgeries, and not every patient should have a radical surgery. It is very much based on the patient's pain complaints and issues at that time, but excision of endometriosis really, in my opinion, should be the standard of care.

Risks of excision of endometriosis

Dr. Brown: The risks of disease excision depend on whether a patient has ureteral disease, bladder disease, or bowel disease, suggested through a preoperative or another operative report or imaging. If this is the case, we have a preoperative discussion with the patient about, "To what extent do you want me to go to remove the disease from your pelvis? If I remove it from your peritoneum and your bladder, there is the chance that you'll have to go home with a Foley catheter for a few days. If the bowel is involved, do you want me to try to resect the disease or shave it off the bowel? If we get into a problem, are you okay with me resecting that bowel?" These are the issues that we have to discuss, because there are potential complications, although known.

> **Dr. Hur:** If a patient presented warranting surgical management once, and she is not menopausal, the likelihood that disease will recur is quite high. Understanding the nature and the pathology of the disease, hormonal suppression would be warranted. Suppression is not just for between pregnancies, it's until the patient reaches natural menopause. It's also in the hopes of suppressing the disease so she does not need recurrent surgeries.

> We typically do not operate unless patients have recurrence of symptoms that no longer respond to medical therapy. Our hope is to buy them more time closer to the age of natural menopause so that medical repercussions do not result in hysterectomy and ovary removal, which have other nongynecologic

manifestations, including negative impact on bone and cardiac health.

The role of the LNG-IUD

Dr. Advincula: Something that often comes up is the role of a levonorgestrel-releasing intrauterine device (LNG-IUD) as one therapy option, either preoperatively or postoperatively. What is your perspective?

Dr. Hur: I reserve the LNG-IUD as a secondline therapy for patients, predominantly because it allows direct delivery of the medication to the womb (rather than systemic exposure of the medication). For patients who experience adverse effects due to systemic exposure to first-line treatments, it might be a great option. However, I do not believe that it consistently suppresses the ovaries, which we understand feeds the pathology of the hormonal stimulation, and so typically I will reserve it as a second-line treatment.

Dr. Brown: I utilize the LNG-IUD in a similar fashion. I may have patients who have had a diagnostic laparoscopy somewhere else and were referred to me because they now have known stage 3 or 4 endometriosis without endometriomas. Those patients, if they are going to need suppressive therapy after surgery and are not ready to get pregnant, do very well with the LNG-IUD, and I will place it during surgery under anesthesia. If a patient has endometriomas seen at the time of surgery, we could still place an LNG-IUD at the time of surgery. We may need to add on an additional medication, however, like another oral progesterone. I do have patients that use both an IUD and either combined oral contraceptive pills and/or oral progestins. Those patients usually have complicated cases with very deep infiltrative disease.

Managing endometriosis involving the bowel

Dr. Advincula: Patients often are quite concerned when the words "endometriosis" and "bowel" come together. How do you manage disease that involves the bowel?

Dr. Hur: A lot of patients with endometriosis

have what I call neighboring disease—it's not limited just to the pelvis, but it involves the neighboring organs including the bowel and bladder. Patients can present with symptoms related to those adjacent organs. However, not all disease involving the bowel or bladder manifests with symptoms, and patients with symptoms may not have visible disease.

Typically, when a patient presents with symptoms of bowel involvement, where the bowel lumen is narrowed to more than 50% and/or she has functional manifestations (signs of obstruction that result in abnormal bowel function), we have serious conversations about a bowel resection. If she has full-thickness disease without significant bowel dysfunction-other than blood in her stool-sometimes we talk about more conservative treatment because of the longterm manifestations that a bowel resection could have.

Dr. Brown: I agree completely. It is important to have a good relationship with our colorectal surgeons. If I suspect that the patient has narrowing of the lumen of the large bowel or she actually has symptoms such as bloody diarrhea during menstruation-which is suggestive of deep, infiltrative and penetrative disease-I will often order a colonoscopy ahead of time to get confirmed biopsies. Then the patient discussion occurs with our colorectal surgeon, who operates with me jointly if we decide to proceed with a bowel resection. It's important to have subspecialty colleagues involved in this care, because a low anterior resection is a very big surgery and there can be down-the-stream complications.

The importance of multidisciplinary care

Dr. Advincula: What are your perspectives on a multidisciplinary or interdisciplinary approach to the patient with endometriosis? **Dr. Brown:** As I previously mentioned, it is important to develop a good relationship with colorectal surgery/urology. In addition, behavioral therapists may be involved in the care of patients with endometriosis, for a number of reasons. The disease process

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is fluid. It will change during the patient's reproductive years, and you need to manage it accordingly based on her symptoms. Sometimes the diagnosis is not made for 5 to 10 years, and that can lead to other issues: depression, fibromyalgia, or irritable bowel syndrome.

The patient may have multiple issues plus endometriosis. I think having specialists such as gastroenterologists and behavioral therapists on board, as well as colorectal and urological surgeons who can perform these complex surgeries, is very beneficial to the patient. That way, she benefits from the team's focus and is cared for from start to finish.

Dr. Hur: I like to call the abdomen a studio. It does not have separate compartments for each organ system. It's one big room, and often the neighboring organs are involved, including the bowel and bladder. I think Dr. Brown's observation-the multidisciplinary approach to a patient's comprehensive care—is critical. Like any surgery, preoperative planning and preoperative assessment are essential, and these steps should include the patient. The discussion should cover not only the surgical outcomes that the surgeons expect, but also what the patient expects to be improved. For example, for patients with extensive disease and bowel involvement, a bowel resection is not always the right approach because it can have potential long-term sequelae. Balancing the "Having specialists such as gastroenterologists and behavioral therapists on board, as well as colorectal and urological surgeons who can perform these complex surgeries, is very beneficial to the patient. That way, she benefits from the team's focus and is cared for from start to finish."

-Douglas N. Brown, MD

risks associated with surgery with the longterm benefits is an important part of the discussion.

Dr. Advincula: Those are both excellent perspectives. Endometriosis is a very complicated disease state, does require a multidisciplinary approach to management, and there are implications and strategies that involve both the medical approach to management and the surgical approach.

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