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PRACTICE ESSENTIALS

Fibroids: Growing management options for a prevalent problem

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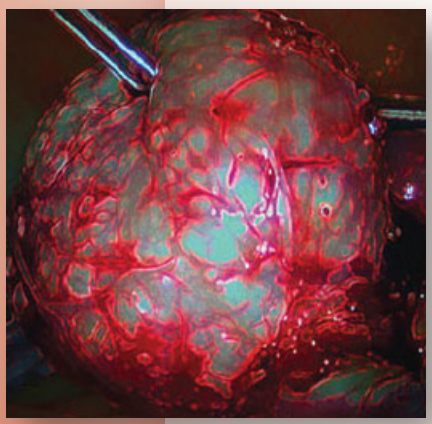

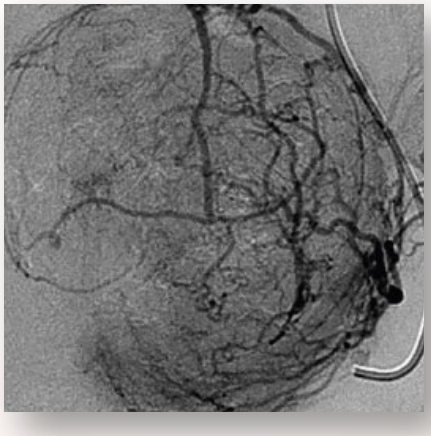

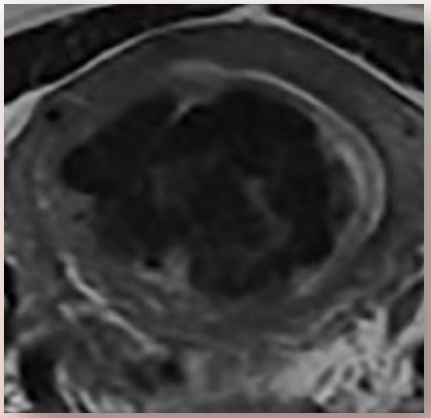

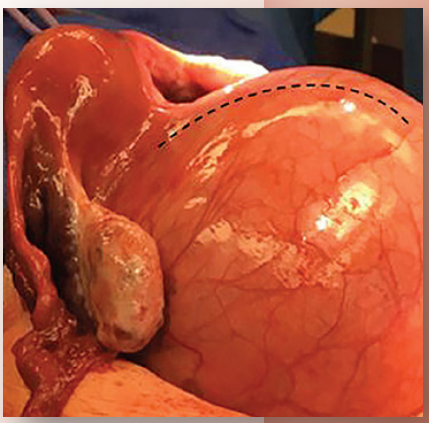

Fibroids: Growing management options for a prevalent problem

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OBG MANAGEMENT

Fibroid management: Expanded options help to optimize patient outcomes

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Fibroids are the most common tumor in women; in fact, they occur in up to 70% of females.[1] They are most often diagnosed in women aged 30 to 50 years.[2] Most fibroids are caused by a somatic mutation in one of 5 myocyte genes that results in clonal expansion of the mutated cell, giving rise to a fibroid tumor.[3] Estrogen and progesterone increase the frequency of myocyte mitosis and may be a driver of both key mutations and clonal expansion following a critical mutation. Compared to normal myometrium, cells in a fibroid are often hyper-responsive to estrogen and progesterone.[4,5] Suppression of estrogen and progesterone levels triggers quiescence in fibroid cells and a decrease in fibroid volume. Among women with fibroids the most common bothersome symptoms are heavy or prolonged menstrual bleeding, pelvic pain or bladder/bowel symptoms caused by the fibroid mass, and for some women fertility problems.

In the 1970s, I was taught that the surgical interventions to treat fibroids were limited to abdominal or vaginal hysterectomy and abdominal myomectomy. The hormonal treatments were estrogen-progestin contraceptives or depot medroxyprogesterone acetate, neither of which was approved by the US Food and Drug Administration (FDA) for the treatment of fibroids. Since that time, however, the surgical and medical options for treating fibroids have expanded greatly, giving women many options that can be tailored to their unique clinical situation.

Current surgical options include laparoscopic or vaginal hysterectomy, laparoscopic or hysteroscopic myomectomy, uterine artery embolization, endometrial ablation, focused ultrasound surgery, and radiofrequency ablation. Current hormone therapy options approved by the FDA for the treatment of heavy menstrual bleeding caused by fibroids include elagolix and relugolix combination therapy. Depot leuprolide acetate is also FDA approved for preoperative treatment of anemia caused by fibroids. In addition, levonorgestrel-releasing intrauterine devices (LNG-IUDs) and tranexamic acid are FDA approved for the treatment of heavy menstrual bleeding.

In this e-book, focused on the treatment of fibroids, leading experts provide clinical pearls on how to best use these treatments in your clinical practice to optimize your patient's health outcomes. Dr. Mark Trolice provides an overview of the management options for fibroids. Drs. Andrea Lukes and Tara Haelle highlight the two new hormonal treatments—elagolix and relugolix combination therapy—and Dr. Amy Garcia provides expert advice on the relative efficacy of the LNG-IUD and endometrial ablation for the treatment of heavy menstrual bleeding caused by fibroids. The surgical management of fibroids are discussed by expert surgeons with decades of experience: Drs. William Parker, Tiffany Sia, Hye-Chun Hur, and Charles Miller. And, finally, clinical pearls based on patient cases are provided by Drs. Joseph S. Sanfillippo, Linda D. Bradley, Ted L. Anderson, Morgan Booher, Mitchell Edelson, David Jaspan, and Jay Goldberg.

Among all clinicians, obstetrician-gynecologists are the best trained and most experienced in the treatment of fibroids. We alone can provide the full range of surgical and medical treatments of this prevalent health problem. ■

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Ob.Gyn. News

Fibroids: Is surgery the only management approach?

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July 22, 2021

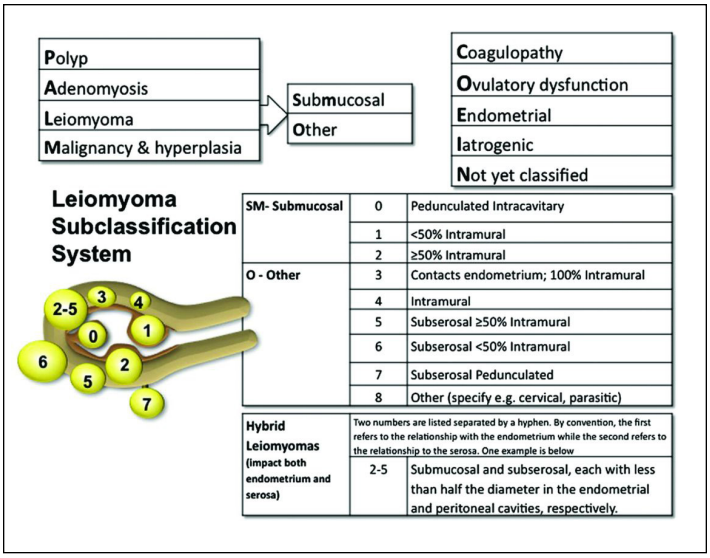
Two chronic gynecologic conditions notably affect a woman's quality of life (QoL), including fertility – one is endometriosis, and the other is a fibroid uterus. For a benign tumor, fibroids have an impressive prevalence found in approximately 50%-60% of women during their reproductive years. By menopause, it is estimated that 70% of women have a fibroid, yet the true incidence is unknown given that only 25% of women experience symptoms bothersome enough to warrant intervention. This month's article reviews the burden of fibroids and the latest management options that may potentially avoid surgery.

Background

Fibroids are monoclonal tumors of uterine smooth muscle that originate from the myometrium. Risk factors include family history, being premenopausal, increasing time since last delivery, obesity, and hypertension (ACOG Practice Bulletin no. 228 Jun 2021: Obstet Gynecol. 2021 Jun 1;137[6]:e100-e15) but oral hormonal contraception, depot medroxyprogesterone acetate (MPA), and increased parity reduce the risk of fibroids. Compared with White women, Black women have a 2-3 times higher prevalence of fibroids, develop them at a younger age, and present with larger fibroids.

The FIGO leiomyoma classification is the agreed upon system for identifying fibroid location. Symptoms are all too familiar to gynecologists, with life-threatening hemorrhage with severe anemia being the most feared, particularly for FIGO types 1-5. Transvaginal ultrasound is the simplest imaging tool for evaluation.

The chart illustrates the International Federation of Gynecology and Obstetrics (FIGO) classification system for fibroid location.



Adapted from Int J Gynecol Obstet. 2011;113:3-13.

Fibroids and fertility

Fibroids can impair fertility in several ways: alteration of local anatomy, including the detrimental effects of abnormal uterine bleeding; functional changes by increasing uterine contractions and impairing endometrium and myometrial blood supply; and changes to the local hormonal environment that could impair egg/sperm transport, or embryo implantation (*Hum Reprod Update*. 2017;22:665-86).

Prior to consideration of surgery, saline infusion sonogram can determine the degree of impact on the endometrium, which is most applicable to the infertility patient, but can also allow guidance toward the appropriate surgical approach.

Treatment options – medical

Management of fibroids is based on a woman's age, desire for fertility, symptoms, and location of the fibroid(s). Expectant observation of a woman with fibroids may be a reasonable approach, provided the lack of symptoms impairing QoL and of anemia. Typically, there is no change in fibroid size during the short term, considered less than 1 year. Regarding fertility, studies are heterogeneous so there is no definitive conclusion that fibroids impair natural fertility (*Reprod Biomed Online*. 2021;43:100-10). Spontaneous regression, defined by a reduction in fibroid volume of greater than 20%, has been noted to occur in 7.0% of fibroids (*Curr Obstet Gynecol Rep*. 2018;7[3]:117-21).

When fertility is not desired, medical management of fibroids is the initial conservative approach. GnRH agonists have been utilized for temporary relief of menometrorrhagia because of fibroids

and to reduce their volume, particularly preoperatively. However, extended treatment can induce bone mineral density loss. Add-back therapy (tibolone, raloxifene, estriol, and ipriflavone) is of value in reducing bone loss while MPA and tibolone may manage vasomotor symptoms. More recently, the use of a GnRH antagonist (elagolix) along with add-back therapy has been approved for up to 24 months by the US Food and Drug Administration and has demonstrated a more than 50% amenorrhea rate at 12 months (*Obstet Gynecol*. 2020;135:1313-26).

Progesterone plays an important role in fibroid growth, but the mechanism is unclear. Although not FDA approved, selective progesterone receptor modulators (SPRM) act directly on fibroid size reduction at the level of the pituitary to induce amenorrhea through inhibition of ovulation. Also, more than one course of SPRMs can provide benefit for bleeding control and volume reduction. The SPRM ulipristal acetate for four courses of 3 months demonstrated 73.5% of patients experienced a fibroid volume reduction of greater than 25% and were amenorrheic (*Fertil Steril*. 2017;108:416-25). GnRH agonists or SPRMs may benefit women if the fibroid is larger than 3 cm or anemia exists, thereby precluding immediate surgery.

Other medication options include the levonorgestrel IUD, combined hormonal contraceptives, and tranexamic acid – all of which have limited data on effective results of treating abnormal uterine bleeding.

Treatment options – surgical

Fibroids are the most common reason for hysterectomy as they are the contributing indication in approximately one-third of surgeries. When future fertility is desired, current surgical options include hysteroscopic and laparoscopic (including robotic) myomectomy. Hysteroscopy is the standard approach for FIGO type 1 fibroids and can also manage some type 2 fibroids provided they are less than 3 cm and the latter is greater than 5 mm from the serosa. Type 2 fibroids may benefit from a "two-step" removal to allow the myometrium to contract and extrude the fibroid. In light of the risk of fluid overload with nonelectrolyte solutions that enable the use of monopolar cautery, many procedures are now performed with bipolar cautery or morcellators.

Laparoscopy (including robotic) has outcomes similar to those of laparotomy although the risk of uterine rupture with the former requires careful attention to thorough closure of the myometrial defect. Robotic myomectomy has outcomes similar to those of standard laparoscopy with less blood loss, but operating times may be prolonged (*Best Pract Res Clin Obstet Gynaecol*. 2018;46:113-9).

The rate of myomectomy is reported to be 9.2 per 10,000 woman-years in Black women and 1.3 per 10,000 woman years in White women (*Fertil Steril*. 2017;108:416-25). The rate of recurrence after myomectomy can be as great as 60% when patients are followed up to 5 years. Intramural fibroids greater than 2.85 cm and not distorting the uterine cavity may decrease in vitro fertilization (IVF) success (*Fertil Steril*. 2014;101:716-21).

Noninvasive treatment modalities

Uterine artery embolization (UAE) is the most popular minimally invasive alternative to surgical myomectomy. Risks include postembolization syndrome (pain, fever, nausea, leukocytosis, and occasionally malaise), infection, and damage to fertility. Rarely, loss of ovarian function can occur, particularly in women above age 45. Because of the disruption of uterine blood flow, UAE increases the risk of accelerating ovarian aging and infertility as well as atrophic endometrium. In addition, pregnancy complications are increased including miscarriage, preterm labor, and postpartum hemorrhage. There is debate regarding the need for cesarean section at time of delivery given the potential for weakening of the uterine wall following UAE.

High-intensity focused ultrasound (HIFU) is guided by ultrasound or MRI and involves a high-energy-density ultrasound wave passing through the skin. The wave is absorbed and transformed into heat, causing the tissue protein to coagulate, and to be absorbed by the body. The procedure is scarless, carries a minimal risk of infection, and offers less pain compared with traditional approaches. However, HIFU is time consuming, and skin burns and unintentional tissue injury are a risk. A meta-analysis demonstrated improved symptoms of fibroids at 6 and 12 months (*J Min Invasive Gynecol*. 2021 in press).

Ultrasound-guided microwave ablation (MWA) uses an ablative electrode that is directly inserted into the target tissue via transcutaneous or transcervical approach via ultrasound guidance using microwave to produce heat for tissue coagulation necrosis. The advantages of MWA compared with HIFU and RFA are a higher tissue temperature, larger ablation volume, shorter operating time, less pain and no adverse major events (*J Min Invasive Gynecol*. 2021, in press).

Conclusion

The current literature cannot conclude that fibroids reduce the likelihood of achieving pregnancy with or without fertility treatment, based on a specific size, number, or location (not including submucosal or cavity-distorting intramural fibroids). Definitive evidence on the efficacy of myomectomy to improve fertility remains limited. Hysteroscopic myomectomy presumably improves pregnancy rates, but there is uncertainty as to its role in reducing miscarriage. Novel nonsurgical modalities are available and are expected to continue being developed but clarity on fertility outcomes is needed.

The author reports no conflicts of interests.

OBG MANAGEMENT

How effective is elagolix treatment in women with fibroids and HMB?

Expert commentary on: Simon JA, Al-Hendy A, Archer DF, et al. Elagolix treatment for up to 12 months in women with heavy menstrual bleeding and uterine leiomyomas. Obstet Gynecol. 2020;135:1313-1326.

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Elagolix with hormonal add-back therapy (estradiol/norethindrone) was effective: 87.9% of participants who received combination therapy met both primary endpoints: 1) percentage of women with less than 80 mL menstrual blood loss during the final month, and 2) a 50% or greater reduction in menstrual blood loss from baseline to final month. Treatment was for up to 12 months as an extension of 1 of 2 randomized, double-blinded, placebo-controlled studies using elagolix.

Uterine fibroids are common (occurring in up to 80% of reproductive-age women),[1,2] and often associated with heavy menstrual bleeding (HMB). There are surgical and medical options, but typically medical options are used for short periods of time. Elagolix with hormonal add-back therapy was recently approved (May 29, 2020) by the US Food and Drug Administration (FDA) for treatment of HMB in women with uterine fibroids for up to 24 months.

Elagolix is an oral, nonpeptide gonadotropin-releasing hormone antagonist that results in a dose-dependent reduction of gonadotropins and ovarian sex hormones. There are now 2 approved products containing elagolix, with different indications:

- Orilissa. Elagolix was approved in 2018 by the FDA for moderate to severe pain associated with endometriosis. For that indication there are 2 dose options of elagolix (150 mg for up to 2 years and 200 mg for up to 6 months) and *there is no hormonal add-back therapy*.
- Oriahnn. Elagolix and hormonal add-back therapy was approved in 2020 for HMB associated with uterine fibroids for up to 24 months. The total daily dose of elagolix is 600 mg (elagolix 300 mg in the morning with estradiol 1 mg/norethindrone acetate 0.5 mg and then in the evening elagolix 300 mg and no hormonal add-back).

This new class of drug, GnRH antagonist, is an important one for women's health, and emerging science will continue to expand its potential uses, such as in reproductive health, as well as long-term efficacy and safety. The difference in daily dose of elagolix for endometriosis (150 mg for 24 months) compared with HMB associated with fibroids (600 mg for 24 months) is why the hormonal add-back therapy is important and allows for protection of bone density.

This is an important manuscript because it highlights a medical option for women with HMB associated with fibroids, which can be used for a long period of time. Further, the improvement in bleeding is both impressive and maintained in the extension study. Approximately 90% of women show improvement in their menstrual bleeding associated with fibroids.

The question of what to do after 24 months of therapy with elagolix and hormonal add-back therapy is an important one, but providers should recognize that the limiting factor with this elagolix and hormonal add-back therapy is bone mineral density (BMD). We will only learn more and more moving forward if this is a clinically meaningful reason for stopping treatment at 24 months. The FDA takes a strict view of safety, and providers must weigh this with the benefit of therapy.

One other highlight between the 2 approved medications is that Orilissa does not have a black box warning, given that there is no hormonal add-back therapy. Oriahnn does have a warning, regarding thromboembolic disorders and vascular events:

- Estrogen and progestin combinations, including Oriahnn, increase the risk of thrombotic or thromboembolic disorders, especially in women at increased risk for these events.
- Oriahnn is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women over 35 years of age who smoke or women with uncontrolled hypertension.

Details about the study

The study by Simon et al is an extension study (UF-EXTEND), in that women could participate if they had completed 1 of the 2 pivotal studies on elagolix. The pivotal studies (Elaris UF1 and UF2) were both randomized, double-blinded, placebo-controlled studies with up to 6 months of therapy; for UF-EXTEND, however, participants were randomly assigned to either combined elagolix and hormone replacement therapy or elagolix alone for an additional 6 months of therapy. Although it was known that all participants would receive elagolix in UF-EXTEND, those who received

hormonal add-back therapy were blinded. All women were then followed up for an additional 12 months after treatment ended.

The efficacy of elagolix was measured by the objective alkaline hematin method for menstrual blood loss with the a priori coprimary endpoints. The elagolix and hormonal add-back therapy group showed objective improvement in menstrual blood loss at 12 months in 87.9% of women in the extension study (89.4% in the elagolix alone group). This compares with 72.2% improvement at 6 months of treatment in the UF1 and UF2 studies for those taking elagolix and hormonal add-back therapy. These findings illustrate maintenance of the efficacy seen within the 6-month pivotal studies using elagolix over an extended amount of time.

The safety of elagolix also was demonstrated in UF-EXTEND. The 3 most common adverse events were similar to those found in Elaris UF1 and UF2 and included hot flushes, headache, and nausea. In the elagolix and hormonal add-back therapy group during the extension study, the percentage with hot flushes was 7%, headache 6%, and nausea 4%. These are small percentages, which is encouraging for providers and women with HMB associated with fibroids.

Effects on bone density

Bone density was evaluated at baseline in the UF1 and UF2 studies, through treatment, and then 12 months after the extended treatment was stopped. The hormonal add-back therapy of estradiol 1 mg/norethindrone acetate 0.5 mg significantly protected bone density. Some women did not have a decrease in bone density, but for those who did the average was less than 5% for the lumbar spine. The lumbar spine is considered the most reactive, so this illustrates the safety that combined therapy offers women with HMB and fibroids.

The lumbar spine is considered the most reactive, so this site is often used as the main focus with BMD studies. As Simon et al show, the lumbar spine mean BMD percent change from baseline for the elagolix with add-back therapy was -1.5% (95% confidence interval [CI], -1.9 to -1.0) in women who received up to 12 months of treatment at month 6 in the extension study. After stopping elagolix with add-back therapy, at 6 months the elagolix with add-back therapy had a Z-score of -0.6% (95% CI, -1.1 to -0.1). This shows a trend toward baseline, or a recovery within a short time from stopping medication.

Study strengths and limitations

Strengths of this study include its overall design; efficacy endpoints, which were all established a priori; the fact that measurement of menstrual blood loss was done with the objective alkaline hematin method; and the statistical analysis, which is thorough and well presented. This extension study allowed further evaluation of efficacy and safety for elagolix. Although the authors point out that there may be some selection bias in an extension study, the fact that so many women elected to continue into the extended study is a positive reflection of the treatment.

As providers learn of new therapies for management of HMB associated with fibroids, it is important to consider who will benefit the most. In my opinion, any woman with heavy periods associated with fibroids could be a candidate for elagolix with add-back therapy. This treatment is highly effective, well tolerated, and safe. My approach to management includes educating a woman on all potential therapies and this new option of elagolix and add-back therapy is an important one. The decision for an individual woman on how to manage heavy periods associated with fibroids should consider her contraceptive needs, medical issues, and the risk and benefit of individual therapies.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Elagolix and hormonal add-back therapy offer a long-term medical option for women with HMB associated with fibroids that is both effective and safe.

Dr. Lukes reports being the Principal Investigator for Abbvie, Myovant, and Obseva; a consultant for Abbvie, Myovant, and Antev; a speaker for Abbvie; a member of the Liberty Steering Committee for Myovant; and an investigator for Abbvie, Myovant, Obseva, Merck, Bayer, Sequoia, Ferring, and Sebela.

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Ob.Gyn. News

Relugolix combo effective for uterine fibroids through 1 year

Tara Haelle

October 23, 2020

A combination therapy using the experimental drug relugolix was effective in treating pain and heavy bleeding from uterine fibroids for a full year, according to findings from a long-term extension study of the phase 3, open-label LIBERTY trials.

The drug was also well tolerated, with retention of bone mineral density and no new adverse events, said Ayman Al-Hendy, MD, PhD, who presented the results October 17 at the virtual American Society for Reproductive Medicine 2020 Scientific Congress.

"Relugolix combination therapy represents a potential long-term treatment for women with heavy menstrual bleeding associated with uterine fibroids," said Al-Hendy, a gynecologist and endoscopic surgeon at the University of Chicago.

Dr. Al-Hendy, who consults for the company that makes the drug, on October 20 presented results showing improvement in quality of life with relugolix therapy.

"The fact that this longer-term study shows continued, persistent results at a year really gives us confidence that we'll be able to use these drugs as a long-term therapy to treat fibroids," Hugh S. Taylor, MD, president-elect of ASRM, said in an interview. Dr. Taylor, a professor and chair of ob.gyn. and reproductive sciences at Yale University, New Haven, Conn., was not involved in the study.

"A drug like this is so necessary," Dr. Taylor continued. "We don't have any other drugs on the market approved for long-term use."

Relugolix is an oral gonadotropin-releasing hormone (GnRH) receptor antagonist under investigation for long-term management of uterine fibroids. The once-daily combination therapy includes 40 mg relugolix, 1 mg estradiol, and 0.5 mg norethindrone acetate.

A combination of relugolix—a gonadotropin-releasing hormone receptor antagonist—estradiol (an estrogen), and norethindrone acetate (a progestin), was US Food and Drug Administration (FDA)-approved in 2021 for 24-month use for the management of heavy menstrual bleeding associated with uterine leiomyomas in premenopausal women. The FDA labeling indicates that more-than-24-month-use may result in bone loss that may not be reversible.

Reference

1. Myfembree [package insert]. Brisbane, CA: Myovant Sciences, Inc. May 2021.

Extension study shows prolonged benefits

The extension trial enrolled women aged 18-50 years who were experiencing heavy menstrual bleeding from uterine fibroids and who completed the 24-week phase 3, double-blind, placebo-controlled LIBERTY 1 or 2 trials. Heavy menstrual bleeding was defined as bleeding in which at least 80 mL of blood was lost per cycle for two cycles or 160 mL was lost during one cycle. Ultrasound imaging was used to confirm the presence of fibroids.

In LIBERTY 1 and 2, women were randomly assigned to receive relugolix combination therapy, placebo, or relugolix alone for 12 weeks followed by combination therapy for the remaining 12 weeks (delayed group). Those trials found that relugolix combination therapy was effective through 6 months in reducing menstrual blood loss and pain in women with uterine fibroids without loss of bone mineral density. LIBERTY 3 extended the trial to 52 weeks, with all participants receiving relugolix combination therapy.

As in the earlier trials, the primary endpoint was reduced menstrual blood loss. By the end of the study, women needed to have at least a 50% reduction in blood loss from the initial study's baseline while maintaining a blood loss of <80 mL. The investigators also evaluated the mean percentage of menstrual blood loss reduction, amenorrhea rate, and improvements in anemia as secondary endpoints and assessed changes in bone mineral density.

The extension study enrolled 78% (n = 477) of the 610 women who completed the initial study; of those, 363 women completed the extension study.

Among the 163 women who began with relugolix combination therapy in the first two trials, 87.7% met the primary endpoint in a per-protocol analysis through week 52. The proportion of responders in the extension study was 75.6% among the group that formerly received placebo (n = 164) and 79.9% in the delayed group (n = 149).

The overall average reduction in menstrual blood volume was 89.9%. Most of the women experienced amenorrhea at the end of the year: 70.6% in the relugolix group, 57.9% in the group that formerly received placebo, and 68.5% in the delayed group.

Reductions in uterine volume and uterine fibroid volume were also sustained from week 24 to week 52. For the relugolix combination therapy group, the mean loss of uterine fibroid volume from

baseline was 13.5% at week 24 and 18.3% at week 52. Similarly, the delayed group's average loss in fibroid volume was 28.1% at week 24 and 33.9% at week 52. The placebo group, which only had a 7% loss in fibroid volume at week 24, had an 18.4% loss in volume from baseline at week 52.

Among patients with anemia, defined as hemoglobin concentrations of <10.5 g/dL at baseline, 59% of those in the original relugolix group saw an improvement of at least 2 g/dL hemoglobin. The women's improvement in pain symptoms also continued through week 52, with a 51.3-point reduction in scores on the bleeding pain and discomfort scale from baseline to the end of the study.

Adverse events were the same in the extension study and in the initial study. Those most commonly reported were headache and hot flashes. No serious safety signals occurred. The average reduction in bone mineral density was 0.80% at week 52, indicating no concerning loss.

A new drug class to treat uterine fibroids

Relugolix is one of three GnRH antagonists being studied for the long-term treatment of fibroids. The US Food and Drug Administration approved the combination of elagolix, estradiol, and norethindrone acetate (Oriahnn) in May. Linzagolix, another GnRH antagonist, is currently in clinical trials.

"We'll have a whole class of new drugs that are likely to fulfill this long sought-after goal of reducing the need for surgery for fibroids and doing it without a lot of side effects," Dr. Taylor said. "The quality-of-life improvements seen here, the lack of significant adverse effects – none that were surprising in long term – the relatively low reduction in bone mineral density in a year are all very exciting [and suggest] that this will be a safe and effective long-term treatment."

Significant improvement in quality of life

In the presentation on quality of life with relugolix therapy, Dr. Al-Hendy shared results regarding the severity of women's symptoms as well as health-related quality of life, as determined on the basis of the Uterine Fibroid Symptom and Health-Related Quality of Life (UFS-QoL) questionnaire at baseline, week 12, and week 24 in LIBERTY 1 and 2. Higher UFS-QoL scores correlate with more severe symptoms. With the subscale of health-related quality of life, higher scores indicate a better quality of life.

The substudy enrolled 253 patients who received relugolix combination therapy and 256 patients who received placebo. The average menstrual blood loss was 243 mL in the relugolix group and 215 mL in the placebo group at baseline. Mean fibroid volume was the same in both groups at baseline, 73 cm^3.

The proportion of Black patients was similar in both groups: 48% of the relugolix group and 54% of the placebo group.

The severity of women's symptoms dropped from a baseline UFS-QoL score of 57 to 22.4 at 6 months among those who received relugolix combination therapy. In the placebo group, the initial score of 59.6 only dropped to 46.9 ($P < .0001$, for –21.4 difference in change).

Health-related quality of life increased from 38.3 to 76.6 among those who received relugolix. In the placebo group, it increased from 35.7 to 48.2 ($P < .0001$, for 24.5 difference). Subscales of health-related quality of life – including concern, control, activities, energy/mood, self-consciousness, and sexual function – also all improved significantly in the relugolix group, compared with the placebo group ($P < .0001$).

"This is a condition we see all the time that's easily diagnosed, and we have first-line drugs we've been using to treat them, but none are good long-term fixes," Dr. Taylor said. The current first-line treatments, oral contraceptives, can stabilize bleeding, "but they don't make the fibroids shrink, they don't stop the bleeding, women continue to have breakthrough bleeding, and the fibroids can continue to grow."

He said most of the estimated 600,000 hysterectomies performed in the United States each year are for uterine fibroids.

"It's a major surgery that no one wants to go through if they don't have to," Dr. Taylor said. "Here we have a drug that really has potential to stop the growth of the fibroids, that can stop the bleeding or dramatically improve it, and, really, for the first time, directly impact the fibroids and give us a long-term alternative."

The studies were funded by Myovant Sciences. Dr. Al-Hendy reported consulting for AbbVie, Bayer, and Myovant Sciences, and he owns a patent for novel diagnostics and therapeutics for uterine sarcoma. Dr. Taylor has disclosed no relevant financial relationships.

A version of this article originally appeared on Medscape.com.

OBG MANAGEMENT

For heavy menstrual bleeding, are long-term outcomes similar for treatment with the LNG-IUS and radiofrequency endometrial ablation?

Expert commentary on: Beelen P, van den Brink MJ, Herman MC, et al. Levonorgestrel-releasing intrauterine system versus endometrial ablation for heavy menstrual bleeding. Am J Obstet Gynecol. 2021;224:187.e1-187.e10.

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Both LNG-IUS and radiofrequency endometrial ablation interventions led to a large decrease in menstrual blood loss with similar quality of life (QoL) and satisfaction scores at 2 years postintervention, according to a randomized clinical trial (RCT) from the Netherlands. The investigators evaluated bleeding reduction, need for reintervention, and QoL for women who received either the Mirena levonorgestrel intrauterine system (LNG-IUS) 52 mg or endometrial ablation with the NovaSure device for primary treatment of heavy menstrual bleeding (HMB).

Counseling patients regarding treatment of HMB requires a realistic discussion about the risks of intervention and the expected outcomes. In addition to decreasing menstrual blood loss, treatment benefits of the LNG-IUS include a reversible form of intervention, minimal discomfort with placement in an office environment with an awake patient, and a reliable form of contraception. Abnormal uterine bleeding (AUB) and progesterone-related adverse effects historically have been associated with LNG-IUS use and can lead to patient desires for device removal or additional intervention.

Similarly, in addition to endometrial ablation (EA) decreasing menstrual blood loss, its benefits include avoiding a hysterectomy with an outpatient procedure. Endometrial ablation does require a desire for no future pregnancies while using a reliable form of contraception. Risks of EA include failure to improve HMB or worsening pelvic pain that requires additional intervention, such as hysterectomy. Historically, clinical data suggest failure is more likely for women less than 40 years of age or with adenomyosis at the time of ablation.

Results of a long-term RCT by Beelen and colleagues may aid gynecologists in counseling patients on the risks and benefits of these 2 treatment options.

Details of the study

Performed between 2012 and 2016, this multicenter RCT evaluated primary intervention of the LNG-IUS in 132 women versus EA in 138 women. The women were older than age 34, did not want a future pregnancy, and had other etiologies of AUB eliminated. The primary outcome was blood loss after 24 months as assessed with a Pictorial Blood Loss Assessment Chart (PBAC) score.

Secondary outcomes included controlled bleeding, defined as a PBAC score not exceeding 75 points; complications and reinterventions within 24 months; amenorrhea; spotting; dysmenorrhea; presence of clots; duration of blood loss; satisfaction with treatment; QoL; and sexual function.

The statistical null hypothesis of the trial was noninferiority of LNG-IUS treatment compared with EA treatment.

Results. Regarding the primary outcome, the mean PBAC score at 2 years was 64.8 for the LNG-IUS treatment group and 14.2 for the EA group. Importantly, however, the authors could not demonstrate noninferiority of the LNG-IUS compared with EA as a primary intervention for HMB.

For the secondary outcomes, there was no significant difference between groups, with both groups having a significant decrease in HMB at 3 months with PBAC scores that did not exceed 75 points: 60% in the LNG-IUS group and 83% in the EA group. In the LNG-IUS group, 35% of women received additional medical or surgical intervention versus 20% in the EA group.

Study strengths and limitations

Strengths of this study include its multicenter design, with 26 hospitals, and the long-term follow-up of 24 months. During the follow-up period, women were allowed to receive a reintervention

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Counseling patients regarding the LNG-IUS and EA for management of HMB requires a discussion balanced by information regarding the risks and the foreseeable benefits of these interventions. This study suggests that long-term primary and secondary outcomes are similar. Therefore, in choosing between the 2, a patient may rely more on her values, her age, and her consideration of future pregnancy and uterine preservation.

as clinically indicated; thus, outcomes reflect results that are not from only a single designated intervention. For example, of the women in the LNG-IUS group, 34 received a surgical intervention, 31 (24%) underwent EA, and 9 (7%) underwent a hysterectomy. However, 6 of the 9 who underwent hysterectomy had a preceding EA, and these 6 women are not reported as surgical intervention of EA since the original designation for intervention was the LNG-IUS.

Notably, the patients and physicians were not blinded to the intervention, and the study excluded patients who wanted a future pregnancy.

Dr. Garcia reports serving as a consultant to Karl Storz Endoscopy, Minerva Surgical, and UVision 360.

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OBG MANAGEMENT

Abdominal myomectomy: Patient and surgical technique considerations

Myomectomy is appropriate for many women with uterine fibroids. Here, guidance on abdominal myomectomy, including intraoperative technique, controlling blood loss, and postoperative care.

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CASE Woman with fibroids seeks alternative to hysterectomy
A 42-year-old woman (G2P2) presents to the office for evaluation of heavy menstrual bleeding and known uterine fibroids. Physical examination reveals a 16-week-sized uterus, and ultrasonography shows at least 6 fibroids, 2 of which impinge on the uterine cavity. She does not want to have any more children, but she wishes to avoid a hysterectomy.

Abdominal myomectomy: A good option for many women

Abdominal myomectomy is an underutilized procedure. With fibroids as the indication for surgery, 197,000 hysterectomies were performed in the United States in 2010, compared with approximately 40,000 myomectomies.[1,2] Moreover, the rates of both laparoscopic and abdominal myomectomy have decreased following the controversial morcellation advisory issued by the US Food and Drug Administration.[3]

The differences in the hysterectomy and myomectomy rates might be explained by the many myths ascribed to myomectomy. Such myths include the beliefs that myomectomy, when compared with hysterectomy, is associated with greater risk of visceral injury, more blood loss, poor uterine healing, and high risk of fibroid recurrence, and that myomectomy is unlikely to improve patient symptoms.

Studies show, however, that these beliefs are wrong. The risk of needing treatment for new fibroid growth following myomectomy is low.[4] Hysterectomy, compared with myomectomy for similar size uteri, is actually associated with a greater risk of injury to the bowel, bladder, and ureters and with a greater risk of operative hemorrhage. Furthermore, hysterectomy (without oophorectomy) can be associated with early menopause in approximately 10% of women, while myomectomy does not alter ovarian hormones. Another myth debunked: Fibroids do not "degenerate" into leiomyosarcomas, and the risk of leiomyosarcoma in premenopausal women with presumed uterine fibroids is extremely low.[5,6]

For women who have serious medical problems (severe anemia, ureteral obstruction) due to uterine fibroids, surgery usually is necessary. In addition, women may request surgery for fibroid-associated quality-of-life concerns, such as heavy menstrual bleeding, infertility, pelvic pressure, urinary frequency, or incontinence. In one prospective study, the authors found that when women were assessed 6 months after undergoing myomectomy, 75% reported experiencing a significant decrease in bothersome symptoms.[7]

Myomectomy may be considered even for women with large uterine fibroids who desire uterine conservation. In a systematic review of the perioperative morbidity associated with abdominal myomectomy compared with abdominal hysterectomy for fibroids, which included 1,520 women with uterine size up to 16 to 18 weeks, no difference was found in major morbidity rates.[8] Investigators who studied 91 women with uterine size ranging from 16 to 36 weeks who underwent abdominal myomectomy reported 1 bowel injury, 1 bladder injury, and 1 reoperation for bowel obstruction; no women had conversion to hysterectomy.[9]

Since ObGyn residency training emphasizes hysterectomy techniques, many residents receive only limited exposure to myomectomy procedures. Increased exposure to and comfort with myomectomy surgical technique would encourage more gynecologists to offer this option to their patients who desire uterine conservation, including those who do not desire future childbearing.

Imaging techniques are essential in the preoperative evaluation

For women with fibroid-related symptoms who desire surgery with uterine preservation, determining the myomectomy approach (abdominal, laparoscopic/robotic, hysteroscopic) depends on accurate assessment of the size, number, and position of the fibroids. If abdominal myomectomy is planned because of uterine size, the presence of numerous fibroids, or patient choice, transvaginal/transabdominal ultrasonography usually is adequate for anticipating what will be found during surgery. Sonography is readily available and is the least costly imaging technique that can

help differentiate fibroids from other pelvic pathology. Although small fibroids may not be seen on sonography, they can be palpated and removed at the time of open surgery.

If submucous fibroids need to be better defined, saline-infusion sonography can be performed. However, if laparoscopic/robotic myomectomy (which precludes accurate palpation during surgery) is being considered, magnetic resonance imaging (MRI) allows the best assessment of the size, number, and position of the fibroids.[10] When adenomyosis is considered in the differential diagnosis, MRI is an accurate way to determine its presence and helps in planning the best surgical procedure and approach.

Correct anemia before surgery

Women with fibroids may have anemia requiring correction before surgery to reduce the need for intraoperative or postoperative blood transfusion. Mild iron deficiency anemia can be treated prior to surgery with oral elemental iron 150 to 200 mg per day. Vitamin C 1,000 mg per day helps to increase intestinal iron absorption. Three weeks of treatment with oral iron can increase hemoglobin concentration by 2 g/dL.

For more severe anemia or rapid correction of anemia, intravenous (IV) iron sucrose infusions, 200 mg infused over 2 hours and given 3 times per week for 3 weeks, can increase hemoglobin by 3 g/dL.[11] In our ObGyn practice, hematologists manage iron infusions.

FIGURE 1 Ilioinguinal nerve at the lateral border of the rectus muscle

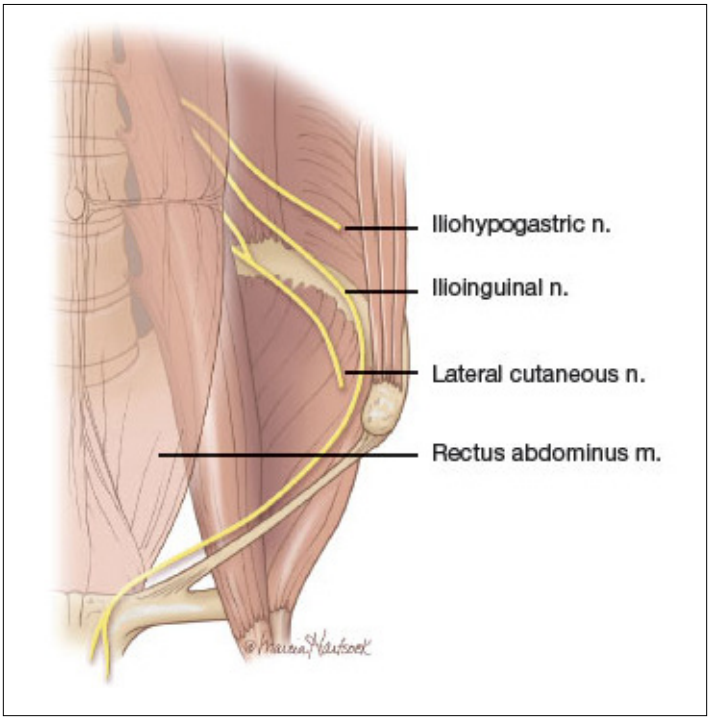

ILLUSTRATION: MARCIA HARTSOCK FOR OBG MANAGEMENT

Abdominal incision technique

Even a large uterus with multiple fibroids usually can be managed through use of a transverse lower abdominal incision. Prior to reaching the lateral borders of the rectus abdominis, curve the fascial incision cephalad to avoid injury to the ileoinguinal nerves (**FIGURE 1**). Detaching the midline rectus fascia (linea alba) from the anterior abdominal wall, starting at the pubic symphysis and continuing up to the umbilicus, frees the rectus muscles and allows them to be easily separated (see **VIDEO 1**). Since fascia is not elastic, these 2 steps are important to allow more room to deliver the uterus through the incision.

Delivery of the uterus through the incision isolates the surgical field from the bowel, bladder, ureters, and pelvic nerves. Once the uterus is delivered, inspect and palpate it for fibroids. Identify the fundus and the position of the uterine cavity by locating both uterine cornua and imagining a straight line between them. It may be necessary to explore the endometrial cavity to look for and remove submucous fibroids. Then plan the necessary uterine incisions for removing all fibroids (see **VIDEO 2**).

4 approaches to managing intraoperative blood loss

In my practice, we employ misoprostol, tranexamic acid, vasopressin, and a uterine and ovarian vessel tourniquet to manage intraoperative blood loss.[12] Although no data exist to show that using these methods together is advantageous, they have different mechanisms of action and no negative interactions.

Misoprostol 400 µg inserted vaginally 2 hours before surgery induces myometrial contraction and compression of the uterine vessels. This agent can reduce blood loss by 98 mL per case.[12]

Tranexamic acid, an antifibrinolytic, is given IV piggyback at the start of surgery at a dose of 10 mg/kg; it can reduce blood loss by 243 mL per case.[12]

Vasopressin 20 U in 100 mL normal saline, injected below the vascular pseudocapsule, causes vasoconstriction of capillaries and small arterioles and venules and can reduce blood loss by 246 mL per case.[12] Intravascular injection should be avoided because rare cases of bradycardia and cardiovascular collapse have been reported.[13] Using vasopressin to decrease blood loss during myomectomy is an off-label use of this drug.

Place a tourniquet around the lower uterine segment, including the infundibular pelvic ligaments. Tourniquet use is the most effective way to decrease blood loss during myomectomy, since it can reduce blood loss by 1,870 mL.[12] For women who wish to preserve fertility, take care to ensure that the tourniquet does not compromise the tubes. For women who are certain they do not want to preserve fertility, discuss the possibility of performing bilateral salpingectomy to decrease the risk of subsequent tubal ("ovarian") cancer.

Some surgeons incise the broad ligaments bilaterally and

pass the tourniquet through the broad ligaments to avoid compromising blood flow to the ovaries. Occluding the utero-ovarian ligaments with bulldog clamps to control collateral blood flow from the ovarian artery has been described, but the clamps can tear these often enlarged and fragile uterine veins during manipulation of the uterus. Release the tourniquet every 15 to 30 minutes to allow reperfusion of the ovaries. In women with ovarian torsion lasting hours to days, the ovary has been found to resist hypoxia and recover function.[14] Antral follicle counts of detorsed and contralateral normal ovaries following a mean of 13 hours of hypoxia are similar 3 months following detorsion.[15]

Consider blood salvage. For women with multiple or very large fibroids, consider using a salvage-type autologous blood transfusion device, which has been shown to reduce the need for heterologous blood transfusion.[16] This device suctions blood from the operative field, mixes it with heparinized saline, and stores the blood in a canister (**FIGURE 2**). If the patient requires blood reinfusion, the stored blood is washed with saline, filtered, centrifuged, and given back to the patient intravenously. Blood salvage, or cell salvage, avoids the risks of infection and transfusion reaction, and the oxygen transport capacity of salvaged red blood cells is equal to or better than that of stored allogeneic red cells.

FIGURE 2 **A salvage-type autologous blood transfusion device reduces the need for transfusion**

Pictured, Cell Saver 5 Autologous Blood Recovery System, Haemonetics

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Additional surgical considerations

Previous teaching suggested that proper placement of the uterine incisions was an important factor in limiting blood loss. Some authors suggested that vertical uterine incisions would avoid injury to the ascending uterine vessels should inadvertent extension of the incision occur. Other authors proposed horizontal uterine incisions to avoid severing the arcuate vessels that branch off from the ascending uterine arteries and run transversely across the uterus. However, since fibroids distort the normal vascular architecture, it is not possible to entirely avoid severing vessels in the myometrium (**FIGURE 3**, page 15).[17] Uterine incisions can therefore be made as needed based on the position of the fibroids and the need to avoid inadvertent extension to the ascending uterine vessels or cornua.[17]

Fibroid anatomy and vascularity. Fibroids are entirely encased within the dense blood supply of a pseudocapsule (**FIGURE 4**, page 15),[18] and no distinct "vascular pedicle" exists at the base of the fibroid.[19] It is therefore important to extend the uterine incisions down through the entire pseudocapsule until the fibroid is clearly visible. This will identify a less vascular surgical plane, which is deeper than commonly recognized. Once the fibroid is reached, the pseudocapsule can be "wiped away" using a dry laparotomy sponge (see **VIDEO 3**). Staying under the pseudocapsule reduces bleeding and may preserve the tissue growth factors and neurotransmitters that are thought to promote wound healing.[20]

Adhesion prevention. Limiting the number of uterine incisions has been suggested as a way to reduce the risk of postoperative pelvic adhesions. To extract fibroids that are distant from an incision, however, tunnels must be created within the myometrium, and this makes hemostasis within these defects difficult. In that blood increases the risk of adhesion formation, tunneling may be counterproductive. If tunneling incisions are avoided and hemostasis is secured immediately, the risk of adhesion formation should be lessened.

Therefore, make incisions directly over the fibroids. Remove only easily accessed fibroids and promptly close the defects to secure hemostasis. Multiple uterine incisions may be needed; adhesion barriers may help limit adhesion formation.[21]

On final removal of the tourniquet, carefully inspect for bleeding and perform any necessary re-suturing. We place a pain pump (ON-Q* Pain Relief System, Halyard Health, Inc) for pain management and close the abdominal incision in the standard manner.

Postoperative care: Manage pain, restore function

The pain pump infuser, attached to one soaker catheter above and one below the fascia, provides continuous infusion of bupivacaine to the incision at 4 mL per hour for 4 days. The pain pump greatly reduces the need for postoperative opioids.[22] Use of a patient-controlled analgesia pump, with its associated adverse effects (sedation, need for oxygen saturation monitoring, slowing of bowel function) can thus be avoided. The patient's residual pain is controlled with oral oxycodone or hydrocodone and scheduled nonsteroidal anti-inflammatory drugs.

In my practice, we use an enhanced recovery after surgery (ERAS) protocol designed to reduce postoperative surgical stress and expedite a return to baseline physiologic body functions.[23] Excellent well-researched, evidence-based studies support the effectiveness of ERAS in gynecologic and general surgery procedures.[24]

Pre-emptive, preoperative analgesia (gabapentin and celecoxib) and end-of-case IV acetaminophen are given to reduce the inflammatory response and the need for postoperative opioids. Once it is confirmed that the patient is hemodynamically stable, add ketorolac 30 mg IV every 6 hours on postoperative day 1. Nausea and vomiting prophylaxis includes ondansetron and dexamethasone at the end of surgery, avoidance of bowel edema with restriction of intraoperative and postoperative fluids (euvolemia), early oral feeding, and gum chewing. On the evening of surgery, the urinary catheter is removed to reduce the risk of bladder infection and facilitate ambulation. Encourage sitting at the bedside and early ambulation starting the evening of surgery to reduce risk of thromboembolism and to avoid skeletal muscle weakness and postoperative fatigue.

Most women are able to be discharged on postoperative day 2. They return to the office on postoperative day 5 for removal of the pain pump.

CASE Continued: Fibroids removed via abdominal myomectomy

We performed an abdominal myomectomy through a Pfannenstiel incision. Nine fibroids—3 of which were not seen on MRI—ranging in size from 1 to 7 cm were removed. Intravaginal misoprostol, IV tranexamic acid, subserosal vasopressin, and a uterine vessel tourniquet limited the intraoperative blood loss to 225 mL. After surgery, a pain pump and ERAS protocol allowed the patient to be discharged on postoperative day 2, and she returned to the office on day 5 for removal of the pain pump. Oral pain medication was continued on an as-needed basis.

Acknowledgement

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OBG Manag. 2017;29(4):22-24, 26-28.

FIGURE 3 Distortion of normal uterine vessels by fibroids[17]

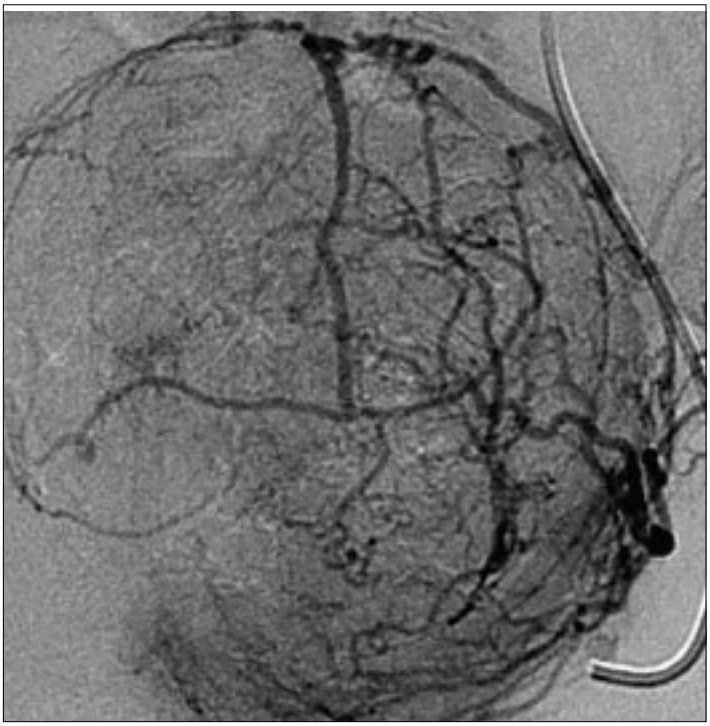

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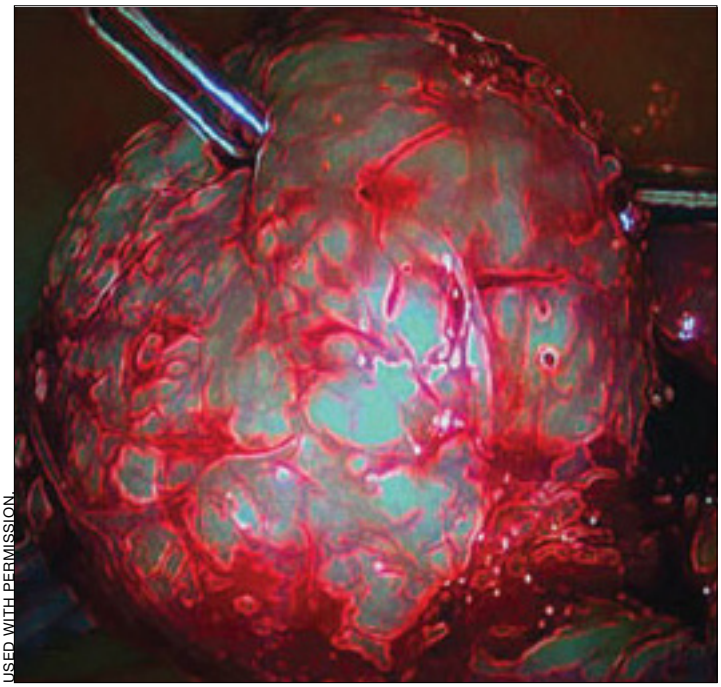
FIGURE 4 A pseudocapsule with a rich vascular network surrounds the fibroid[18]



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OBG MANAGEMENT

Laparoscopic myomectomy: Tips for patient selection and technique

Some women who want fibroids removed but the uterus preserved are candidates for laparoscopic myomectomy. This article explains patient selection and provides tips for addressing issues before, during, and after the procedure.

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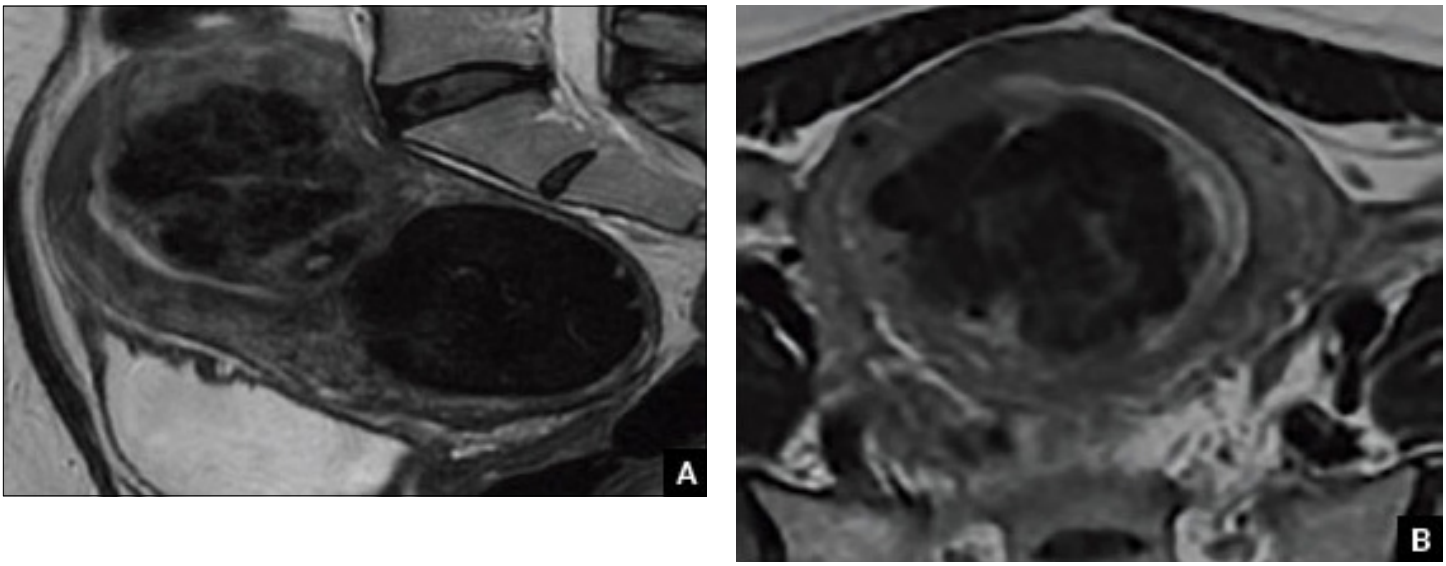
CASE Patient wants minimally invasive surgery for her fibroids, and no hysterectomy

A 44-year-old G1P1 woman comes to the office to discuss her uterine fibroids, heavy menstrual bleeding, and urinary frequency. Treatment with oral contraceptives has not been effective in reducing the bleeding. She now wants surgical treatment without a hysterectomy (the hysterectomy was recommended by her previous gynecologist). On examination, a 14-week-size irregular uterus is felt. Myomectomy is discussed, and the patient asks if minimally invasive surgery (MIS) is possible. Complete blood cell count testing shows a hemoglobin level of 9.4 g/dL. Pelvic magnetic resonance imaging (MRI) shows a 6-cm type 2 posterior fundal fibroid and a 6-cm type 5 posterior lower-uterine-segment fibroid (FIGURE 1). These 2 fibroids have regular contours, and enhancement is not increased with contrast, consistent with benign fibroids.

Determining that laparoscopic myomectomy is a good option

Fibroids may affect quality of life—they may cause heavy menstrual bleeding, pelvic pain or pressure, or urinary frequency or incontinence. For many women who want large or numerous fibroids removed but the uterus preserved, abdominal myomectomy is required. Smaller and less numerous fibroids usually can be managed laparoscopically or with robotic assistance.

FIGURE 1 Pelvic MRI scans of uterine fibroids



Pelvic magnetic resonance imaging (MRI) scans show a 6-cm type 2 posterior fundal fibroid (A) and a 6-cm type 5 posterior lower-uterine-segment fibroid (B) in a 44-year-old woman.

A systematic review of 6 randomized, controlled trials comparing laparoscopic and open myomectomy in 576 patients found that, although laparoscopic myomectomy was associated with longer operative time (approximately 13 minutes), it was also linked to less operative blood loss, fewer overall complications, reduced postoperative pain, and faster recovery.[1] However, wide application of the laparoscopic approach may be limited by the size and number of fibroids that can be reasonably removed and by the surgical skill needed for fibroid excision and laparoscopic suturing.

Use imaging to assess fibroid size, location, and number

Four imaging modalities can be used for fibroids: transvaginal sonography (TVS), saline-infusion sonography (SIS), hysteroscopy, and MRI. TVS is the most readily available and least costly modality used to differentiate fibroids from other pelvic pathology; SIS provides contrast for the endometrial cavity and better defines submucous fibroids; and hysteroscopy detects visually apparent distortion of the cavity. MRI, however, provides the most complete evaluation of size, position, and number of fibroids.

A study comparing TVS, SIS, hysteroscopy, and MRI found that number and position of fibroids were best identified with MRI.[2] In addition, with MRI, the proximity of the fibroids and uterus to the bladder, rectum, and iliac bones can be evaluated. As tactility in laparoscopic and robot-assisted surgery is very limited, surgeons who use MRI to accurately assess fibroids preoperatively may be able to avoid missing them during the procedure.[3] MRI also can be used reliably to diagnose adenomyosis and may be able to help identify uterine sarcoma.

Tip. For all women considering laparoscopic or robot-assisted myomectomy, I order pelvic MRI with and without contrast. Having the radiologist limit the number of MRI sequences may reduce the cost and make it comparable to that of other imaging modalities. I request T2-weighted MRI scans in the coronal, sagittal, and axial planes; in addition, to determine distortion of the uterine cavity by submucous fibroids, I request scans in the planes parallel with and perpendicular to the uterine axis. One gadolinium-enhanced T1-weighted MRI scan is needed to evaluate perfusion.

Although radiologists are experts in image interpretation, they are unfamiliar with the treatments and surgical issues that gynecologists must consider. Reading MRI scans for fibroids is straightforward, and gynecologists who regularly treat women with fibroids should consider viewing images with a radiologist until they become proficient.

Surgeon and patient factors

Surgeons who have the experience and skill and know the size, number, and position of fibroids are able to select the appropriate candidates for laparoscopic myomectomy. Authors of a study of 2,050 laparoscopic myomectomies found that fibroids larger than 5 cm, removal of more than 3 fibroids, and broad ligament fibroids were more likely to be associated with major complications, including visceral injury, conversion to laparotomy, and bleeding requiring blood transfusion.[4]

In laparoscopic myomectomy, uterus reconstruction requires laparoscopic suturing. Although robot-assisted myomectomy may make laparoscopic suturing easier, the added cost, longer operative time, and unimproved outcomes must be considered too.

Trocar placement

Place the patient in the dorsal lithotomy position.

Tip. For most women, I do not use a uterine manipulator, as my assistant can manipulate the uterus with laparoscopic graspers.

Port placement should be based on the position and size of the fibroids to be removed. Laparoscopic suturing is more ergonomic with 2 ports placed on one side of the patient (**FIGURE 2**). For suture access, a 12-mm port is placed about 2 cm medial to the iliac crest and a 5-mm port is placed medial to the 12-mm port, near the level of the umbilicus. Lateral trocars should be placed high, above the superior aspect of the uterus, to make it easier to access the fibroids, and lateral to the inferior epigastric vessels, to avoid injuring those vessels. If the uterus is near or above the umbilicus, a left upper quadrant approach may be used, with the access ports placed above the umbilicus.

FIGURE 2 Port placement for laparoscopic myomectomy, based on position and size of fibroids to be removed

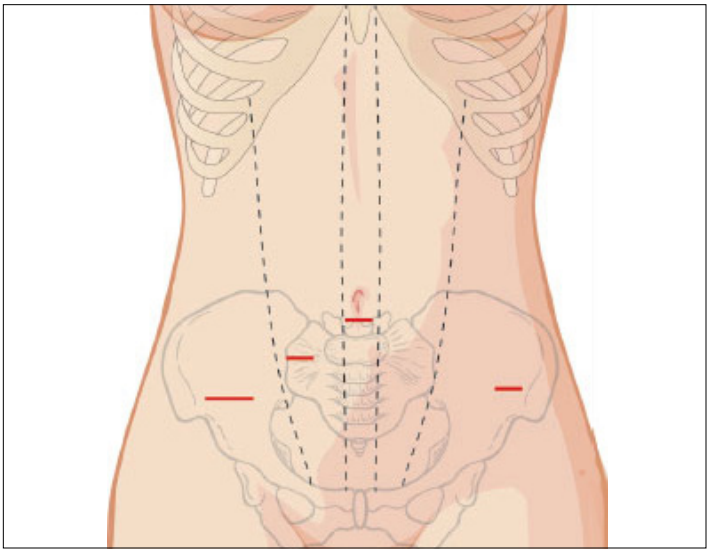


Illustration shows 2 ports placed on one side of the patient for suturing; a 12-mm port placed approximately 2 cm medial to the iliac crest for suture access; and a 5-mm port placed medial to the 12-mm port, near the level of the umbilicus, for fibroid removal.

Managing intraoperative blood loss

I use a combination of 3 agents to reduce intraoperative blood loss during laparoscopic myomectomy: preoperative misoprostol and tranexamic acid and intraoperative vasopressin. Although there are no data showing an advantage in using these drugs together, the agents have different mechanisms of action and no negative interactions.

Injected below the vascular pseudocapsule, 20 units of vasopressin in 100 mL of normal saline causes vasoconstriction of capillaries, small arterioles, and venules. Avoid intravascular injection given that bradycardia and cardiovascular collapse have been reported (rare cases). Loss of peripheral pulses, bradycardia, unmeasurable blood pressure, and cardiac complications have been reported after myometrial injection of ≥5 units of vasopressin.[5]

Although vasopressin is a powerful vasoconstrictor, these clinical findings are often interpreted as severe hypotension. However, evaluation of peripheral arterial blood flow by Doppler ultrasonography has revealed severe vasospasm and increased proximal blood pressure.[5] Keep this potential reaction in mind to avoid misinterpreting findings and treating a patient with vasopressors. Presence of palpable carotid pulses and maintenance of normal partial pressure of end-tidal carbon dioxide can help differentiate peripheral vasospasm from global hypotension.

Use of vasopressin to reduce blood loss during myomectomy is off-label. On occasion, I apply a tourniquet around the lower uterine segment, including the infundibular pelvic ligaments. I use a red Robinson catheter, throw 1 tie in front of the uterus, pull with graspers on both ends until it is tight, and then clamp the half-knot with a locking grasper.

Tip. Although a salvage-type autologous blood transfusion device may be used during laparoscopic or robot-assisted myomectomy, cases in which this device is considered for very large or multiple fibroids might be better managed with abdominal myomectomy.

Surgical technique

After injecting vasopressin, I use a high-frequency mechanical vibration scalpel to incise the myometrium directly over a prominent fibroid and carry the incision deeply until fibroid tissue is definite. Alternatively, a monopolar laparoscopic needle can be used in cut mode—which also limits damage to the myometrium.

Tip. The course of vessels over a fibroid is unpredictable, and we cannot be certain that any uterine incision will avoid bleeding. Therefore, I make transverse incisions, which allow more ergonomic laparoscopic suturing.

It is important to incise completely through the myometrium and through the pink-red pseudocapsule containing the vascular network surrounding the fibroid. This plane is often deeper than usually recognized and can be identified just over the white fibroid.

The fibroid is grasped with a tenaculum for traction, and countertraction is applied with a grasper on the myometrial edges. Once the fibroid is reached, graspers and the mechanical vibration scalpel are used to tease the pseudocapsule away from the fibroid (**VIDEO**).

Tip. Staying under the pseudocapsule reduces bleeding and may preserve the tissue's growth factors and neurotransmitters, which are thought to promote wound healing.6

Dissection with the mechanical vibration scalpel (or monopolar needle) should be performed under visual control to identify the tissue adhering to the fibroid, which is desiccated and then divided. The fibroid is dissected until free of the myometrium and is placed in the right lower abdomen. Small fibroids can be strung together on a long suture so none will be lost. Using bipolar paddles, desiccate large bleeding vessels in the myometrial defect sparingly, with care taken to avoid devascularizing the myometrium, which might compromise wound healing. Myometrial repair should be performed in accordance with the accepted surgical technique used in laparotomy.

Place delayed absorbable sutures in 2 or 3 layers, as needed, to reapproximate the myometrium and secure hemostasis.

Tip. I use 0 polydioxanone interrupted figure-of-8 sutures, but continuous running sutures with or without barbs also can be used. For the serosa, I use a continuous barbed suture in a baseball stitch, which buries both the raw edges of the serosa and the barbs for smooth closure (**FIGURE 3**, page 19). These closure methods have not been compared to see which provides superior wound healing or subsequent wound strength.

Morcellating the fibroid

The fibroid can be morcellated with an electromechanical morcellator or a scalpel (hand morcellation). Either instrument can be used in contained or uncontained fashion. I insert an electromechanical morcellator through the right lower quadrant incision and morcellate tissue in the anterior midpelvis. Safety requires careful control of the rotating blade and scrutiny of the bowel, bladder, and major vessels. Our operating room has **4 rules for morcellator use:**

1. The blade is activated only under direct visualization.
2. Both the surgeon and the assistant must say "ready" before the blade is activated.
3. The hand holding the morcellator must remain still while tissue is being drawn into the device.
4. Any undue resistance from the tissue is cause to stop the blade. This precaution is taken because there is a tendency to drop the blade in an attempt to overcome the resistance.

Tip. I limit rotational forces and scattering of tissue by "pulsing" the blade on and off when morcellating softer tissue.

Various methods of *contained morcellation* (morcellation in a containment bag) have been described.[7] In one method, tissue is placed in a bag, the neck of the bag is brought through an enlarged umbilical incision, and the tissue is cut into small pieces until it is entirely removed. Another method is to use an

electromechanical morcellator with a specially designed containment bag inside the abdomen. The bag is introduced through a 12-mm port and unfurled inside the abdomen; the specimen is placed in the bag; the neck of the bag is brought out through the port; the bag is insufflated with carbon dioxide; the laparoscope, a 5-mm grasper, and the morcellator tip are passed into the bag; and morcellation is performed. Early studies of contained morcellation reported longer operating times, leaking bags, and visceral injuries. In 2016, the US Food and Drug Administration (FDA) cleared the PneumoLiner containment system but required that its manufacturer (Advanced Surgical Concepts) warn patients and health care providers that its bag has not been proved to reduce the risk of spreading cancer during morcellation procedures.[8]

Irrigation is important

During laparoscopic myomectomy, fibroid removal by myometrial dissection disperses tissue fragments, and the unprotected fibroid is usually stored in the abdomen until hemostasis is secured and suturing completed. Limiting the rotational forces that lead to further dispersement and irrigating copiously to remove tissue fragments help eliminate residual tissue.

The pelvis and the abdomen are irrigated with normal saline (approximately 3 L) and suctioned multiple times.

Tip. Alternating between the Trendelenburg and reverse Trendelenburg positions allows fluid to wash tissue down to the pelvis, where it is more easily seen and removed.

Careful inspection for tissue fragments and copious irrigation and suctioning are important in reducing the risk that tissue fragments will remain in the peritoneal cavity and parasitic fibroids will develop. In cases of occult leiomyosarcoma (LMS), this step may be particularly important.

Final steps

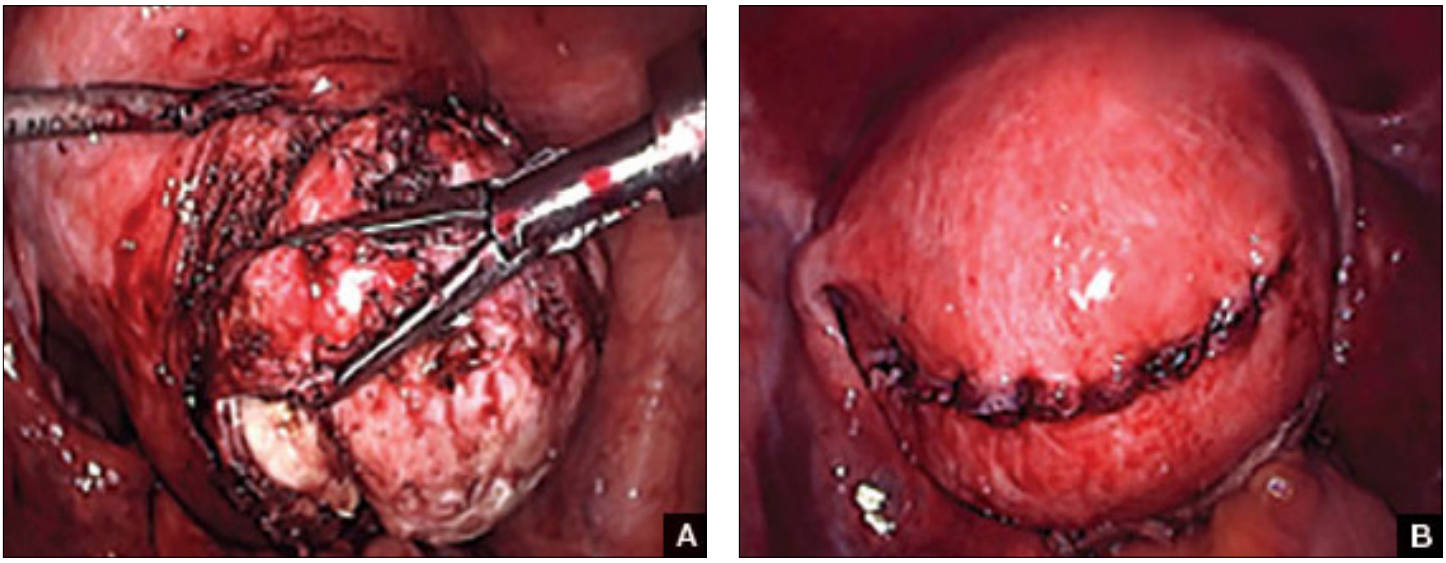
I place a knitted fabric of modified cellulose over the hysterotomy suture lines to reduce the incidence of adhesion formation. Once the procedure is complete, the local anesthetic bupivicaine is injected deep into the incision sites. Injecting anesthetic before making the incisions does not provide better pain relief; injecting after the procedure provides pain relief for 6 hours.[9]

Morcellation and risk of leiomyosarcoma

Given the need to prevent laparoscopic morcellators from inadvertently spreading tissue within the peritoneal cavity of women with occult LMS, the FDA issued a safety communication in 2014 warning against their use in the majority of women who undergo myomectomy or hysterectomy for fibroids.[10] However, Pritts and colleagues estimated the prevalence of LMS in women who had surgery for presumed uterine fibroids at about 1 in 2,000 (0.05%), significantly lower than the FDA's estimate of 1 in 350.[10,11] In 2015, a large population-based prospective registry study found 2 cases of occult LMS in 8,720 fibroid surgery patients (0.02%).[12]

Since LMS metastasizes through the bloodstream, there is no reliable evidence that morcellation influences survival or that electromechanical morcellation is inferior to vaginal or mini-laparotomy morcellation with a scalpel. According to recent

FIGURE 3 Laparoscopic removal of a fibroid



Laparoscopic removal of a fibroid with a mechanical vibration scalpel and tenaculum (A) and closure of the incision site with continuous barbed suture in a baseball stitch (B).

USED WITH PERMISSION.

publications, compared with MIS, open abdominal surgery is associated with more morbidity and mortality in women.[13] Since the FDA advisory was issued, the number of abdominal surgeries has increased, as has the number of related complications.[13]

I use electromechanical morcellation techniques for women who want MIS. All surgical procedures have potential risks, and patients' and physicians' understanding of risks forms the foundation of medical decision making. The possibility of occult LMS should be considered by women and their gynecologists, and proper informed consent, noting both the LMS risk and the increased risks of abdominal surgery, should be obtained.

Risk of uterine rupture after laparoscopic myomectomy

After abdominal myomectomy, uterine rupture during pregnancy or delivery is rare, according to reviews of delivery records of many thousands of women.[14] Operative techniques, instruments, and energy sources used during laparoscopic or robot-assisted myomectomy may differ from those used during laparotomy, and anecdotal communications suggest that uterine rupture may be more common after laparoscopic or robot-assisted myomectomy. A meta-analysis of 56 articles (3,685 pregnancies) published between 1970 and 2013 found 29 cases of uterine rupture after myomectomy, with no statistical difference in rupture risk between laparoscopic and abdominal myomectomy.[15] As most reports are case studies or small case series, the incidence of rupture cannot be reliably calculated.

There is no consensus regarding the factors that may increase the risk of uterine rupture after laparoscopic myomectomy. Three factors are postulated to interfere with myometrial wound healing and increase uterine rupture risk: failure to adequately suture myometrial defects, excessive use of monopolar or bipolar electrosurgery with devascularization of the myometrium, and lack of hemostasis with

Preoperative considerations for patients undergoing laparoscopic myomectomy

Condition	Management
Anemia	• Before surgery, increase hemoglobin levels with use of 1 of 3 treatments: – Intravenous iron[a,1] – Gonadotropin-releasing hormone agonist[b,2] – Ulipristal[c,3]
Postoperative nausea and vomiting	• The night before surgery, have the patient place a scopolamine patch behind her ear – Reduces risk
Surgical blood loss	• 2 hours before surgery, have the patient insert misoprostol 400 µg intravaginally – Induces myometrial contraction and compression of uterine vessels – Reduces surgical blood loss • On entry to operating room, piggyback IV tranexamic acid 10 mg/kg – Reduces bleeding
Pain and inflammatory reaction	• 30 minutes before surgery, give celecoxib 400 mg and gabapentin 1,200 mg orally, with sip of water – Provides preemptive pain relief – Celecoxib also decreases inflammatory reaction to surgery
Venous thromboembolism	• Use sequential compression devices in all cases – Risk is low to moderate
Surgical site infection	• Antibiotic prophylaxis typically not administered – Risk is low in laparoscopic procedures in which neither vagina nor bowel is entered

[a]Intravenous iron can increase hemoglobin levels by 1 to 2 g/dL within 1 week.

[b]According to a *Cochrane Review*, hemoglobin levels rose by 1.3 g/dL in women who had fibroids treated with a gonadotropin-releasing hormone agonist for 3 to 4 months.

[c]Taking ulipristal 5 mg/day for 13 weeks increased hemoglobin levels by 4 g/dL in women with heavy bleeding caused by uterine fibroids.

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subsequent hematoma formation.[16] It seems prudent that surgeons should adhere to time-tested techniques for abdominal myomectomy. Even with use of ideal surgical techniques, however, individual wound-healing characteristics may predispose to uterine rupture.

CASE Resolved

After giving proper informed consent, the patient underwent laparoscopic myomectomy and electromechanical morcellation. Her 2 fibroids were removed, with a blood loss of 200 mL, and that afternoon she was discharged from the surgery center with written postoperative instructions and oral pain medication. A telephone call the next day found her comfortable, with no nausea or vomiting, and happy to be fibroid free. Pathologic inspection of the morcellated tissue confirmed that the fibroids were benign. At 2-week follow-up, the patient was no longer taking pain medication and was ready to return to work and normal activity. Her fatigue persisted, though, and she arranged to take time to rest during the day.

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runninghead
OBG MANAGEMENT

Electrosurgical hysteroscopy: Principles and expert techniques for optimizing the resectoscope loop

For gyn surgeons, the hysteroscopic resectoscope loop offers the ability to achieve electrosurgical hemostasis, decrease blood loss, and improve visibility. It continues to be a crucial instrument in operative gynecology.

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Hysteroscopic mechanical morcellators have gained popularity given their ease of use. Consequently, the resectoscope loop is being used less frequently, which has resulted in less familiarity with this device. The resectoscope loop, however, not only is cost effective but also allows for multiple distinct advantages, such as cold loop dissection of myomas and the ability to obtain electrosurgical hemostasis during operative hysteroscopy.

In this article, we review the basics of electrosurgical principles, compare outcomes associated with monopolar and bipolar resectoscopes, and discuss tips and tricks for optimizing surgical techniques when using the resectoscope loop for hysteroscopic myomectomy.

Evolution of hysteroscopy

The term *hysteroscopy* comes from the Greek words *hystera*, for uterus, and *skopeo*, meaning "to see." The idea to investigate the uterus dates back to the year 1000 when physicians used a mirror with light to peer into the vaginal vault.

The first known successful hysteroscopy occurred in 1869 when Pantaleoni used an endoscope with a light source to identify uterine polyps in a 60-year-old woman with abnormal uterine bleeding. In 1898, Simon Duplay and Spiro Clado published the first textbook on hysteroscopy in which they described several models of hysteroscopic instruments and techniques.

In the 1950s, Harold Horace Hopkins and Karl Storz modified the shape and length of lenses within the endoscope by substituting longer cylindrical lenses for the old spherical lenses; this permitted improved image brightness and sharpness as well as a smaller diameter of the hysteroscope. Between the 1970s and 1980s, technological improvements allowed for the creation of practical and usable hysteroscopic instruments such as the resectoscope. The resectoscope, originally used in urology for transurethral resection of the prostate, was modified for hysteroscopy by incorporating the use of electrosurgical currents to aid in procedures.

Over the past few decades, continued refinements in technology have improved visualization and surgical techniques. For example, image clarity has been markedly improved, and narrow hysteroscope diameters, as small as 3 to 5 mm, require minimal to no cervical dilation.

Monopolar and bipolar resectoscopes

Electrosurgery is the application of an alternating electrical current to tissue to achieve the clinical effects of surgical cutting or hemostasis via cell vaporization or coagulation. Current runs from the electrosurgical unit (ESU) to the active electrode of the surgical instrument, then goes from the active electrode through the patient's tissue to the return electrode, and then travels back to the ESU. This flow of current creates an electrical circuit (**FIGURE**, page 23).

All electrosurgical devices have an active and a return electrode. The difference between monopolar and bipolar resectoscope devices lies in how the resectoscope loop is constructed. Bipolar resectoscope loops house the active and return electrodes on the same tip of the surgical device, which limits how much of the

current flows through the patient. Alternatively, monopolar resectoscopes have only the active electrode on the tip of the device and the return electrode is off the surgical field, so the current flows through more of the patient. On monopolar electrosurgical devices, the current runs from the ESU to the active electrode (monopolar loop), which is then applied to tissue to produce the desired tissue effect. The current then travels via a path of least resistance from the surgical field through the patient to the return electrode, which is usually placed on the patient's thigh, and then back to the ESU. The return electrode is often referred to as the grounding pad.

How monopolar energy works

When first developed, all resectoscopes used monopolar energy. As such, throughout the 1990s, the monopolar resectoscope was the gold standard for performing electrosurgical hysteroscopy. Because the current travels a long distance between the active and the return electrode in a monopolar setup, a hypotonic, nonelectrolyte-rich medium (a poor conductor), such as glycine 1.5%, mannitol 5%, or sorbitol 3%, must be used. If an electrolyte-rich medium, such as normal saline, is used with a monopolar device, the current would be dispersed throughout the medium outside the operative field, causing unwanted tissue effects.

Although nonelectrolyte distension media improve visibility when encountering bleeding, they can be associated with hyponatremia, hyperglycemia, and even lifethreatening cerebral edema. Furthermore, glycine use is contraindicated in patients with renal or hepatic failure since oxidative deamination may cause hyperammonemia. Because of these numerous risk factors, the fluid deficit for hypotonic, nonelectrolyte distension media is limited to 1,000 mL, with a suggested maximum fluid deficit of 750 mL for elderly or fragile patients. Additionally, because the return electrode is off the surgical field in monopolar surgery, there is a risk of current diversion to the cervix, vagina, or vulva because the current travels between the active electrode on the surgical field to the return electrode on the patient's thigh. The risk of current diversion is greater if there is damage to electrode insulation, loss of contact between the external sheath and the cervix, or direct coupling between the electrode and the surrounding tissue.

FIGURE Electrosurgical circuit

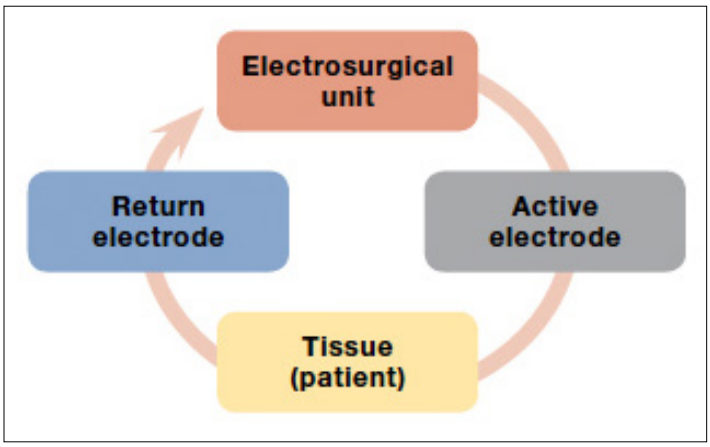

TABLE 1 Benefits of using the resectoscope loop for hysteroscopic myomectomy

Benefits of the resectoscope loop compared with the hysteroscopic morcellator
• The ability to achieve electrosurgical hemostasis is unique to the resectoscope loop and may result in: —Less blood loss —Improved visibility allowing for a more efficient and safer surgery
• Lower intrauterine pressures for uterine distension, resulting in: —Less intravasation of uterine distension media —Better exposure of FIGO 2 submucosal fibroids
• Blunt cold loop dissection to enucleate intramural components of FIGO 1 or FIGO 2 submucosal myomas —More complete excision of FIGO 1 or FIGO 2 submucosal fibroids
Benefits of the bipolar resectoscope loop versus the monopolar device
• Decreased voltage requirement with less electrosurgical injury risk
• Greater volume allowed for fluid deficit, which: —May enable a longer procedure and more complete hysteroscopic resection —Poses less risk of fluid-related complications, such as hyponatremia

Abbreviation: FIGO, International Federation of Gynecology and Obstetrics.

Advantages of the bipolar resectoscope

Because of the potential risks associated with the monopolar resectoscope, over the past 25 years the bipolar resectoscope emerged as an alternative due to its numerous benefits (**TABLE 1**, page 23).

Unlike monopolar resectoscopes, bipolar resectoscopes require an electrolyte-rich distension medium such as 0.9% normal saline or lactated Ringer's. These isotonic distension media allow a much higher fluid deficit (2,500 mL for healthy patients, 1,500 mL for elderly patients or patients with comorbidities) as the isotonic solution is safer to use. Furthermore, it allows for lower voltage settings and decreased electrical spread compared to the monopolar resectoscope since the current stays between the 2 electrodes. Because isotonic media are miscible with blood, however, a potential drawback is that in cases with bleeding, visibility may be more limited compared to hypotonic distension media.

Evidence on fertility outcomes

Several studies have compared operative and fertility outcomes with the use of monopolar versus bipolar hysteroscopy.

In a randomized controlled trial (RCT) comparing outcomes after hysteroscopy with a monopolar (glycine 1.5%) versus bipolar (0.9% normal saline) 26 French resectoscope loop, Berg and colleagues found that the only significant difference between the 2 groups was that the change in serum sodium pre and postoperatively was greater in the monopolar group despite having a smaller mean fluid deficit (765 mL vs 1,227 mL).[1]

Similarly, in a study of fertility outcomes after monopolar versus bipolar hysteroscopic myomectomy with use of a 26 French resectoscope Collins knife, Roy and colleagues found no significant differences in postoperative pregnancy rates or successful pregnancy outcomes, operative time, fluid deficit, or improvement in menstrual symptoms.[2] However, the monopolar group had a much higher incidence of postoperative hyponatremia (30% vs 0%) that required additional days of hospitalization despite similar fluid deficits of between 600 and 700 mL.[2]

Similar findings were noted in another RCT that compared operative outcomes between monopolar and bipolar resectoscope usage during metroplasty for infertility, with a postoperative hyponatremia incidence of 17.1% in the monopolar group versus 0% in the bipolar group despite similar fluid deficits.[3] Energy type had no effect on reproductive outcomes in either group.[3]

How does the resectoscope compare with mechanical tissue removal systems?

In 2005, the first hysteroscopic mechanical tissue removal system was introduced in the United States, providing an additional treatment method for such intrauterine masses as fibroids and polyps.

Advantages. Rather than using an electrical current, these tissue removal systems use a rotating blade with suction that is introduced through a specially designed rigid hysteroscopic sheath. As the instrument incises the pathology, the tissue is removed from the intrauterine cavity and collected in a specimen bag inside the fluid management system. This immediate removal of tissue allows for insertion of the device only once during initial entry, decreasing both the risk of perforation and operative times. Furthermore, mechanical tissue removal systems can be used with isotonic media, negating the risks associated with hypotonic media. Currently, the 2 mechanical tissue removal systems available in the United States are the **TruClear and the MyoSure hysteroscopic tissue removal systems**. Studies comparing mechanical tissue removal of polyps and myomas with conventional resectoscope resection have found that mechanical tissue removal is associated with reduced operative time, fluid deficit, and number of instrument insertions.[4-8] However, studies have found no significant difference in postoperative patient satisfaction.[7,9]

Additionally, hysteroscopic tissue removal systems have an easier learning curve. Van Dongen and colleagues conducted an RCT to compare resident-in-training comfort levels when learning to use both a mechanical tissue removal system and a traditional resectoscope; they found increased comfort with the hysteroscopic tissue removal system, suggesting greater ease of use.[10]

Drawbacks Despite their many benefits, mechanical tissue removal systems have some disadvantages when compared with the resectoscope. First, mechanical tissue removal systems are associated with higher instrument costs. In addition, they have extremely limited ability to achieve hemostasis when encountering blood vessels during resection, resulting in poor visibility especially when resecting large myomas with feeding vessels.

Hysteroscopic mechanical tissue removal systems typically use higher intrauterine pressures for uterine distension compared with the resectoscope, especially when trying to improve visibility in a bloody surgical field. Increasing the intrauterine pressure with the distension media allows for compression of the blood vessels. As a result, however, submucosal fibroids classified as FIGO 2 (International Federation of Gynecology and Obstetrics) may be less visible since the higher intrauterine pressure can compress both blood vessels and submucosal fibroids

Additionally, mechanical tissue removal systems have limited ability to resect the intramural component of FIGO 1 or FIGO 2 submucosal fibroids since the intramural portion is embedded in the myometrium. Use of the resectoscope loop instead allows for a technique called the cold loop dissection, which uses the resectoscope loop to bluntly dissect and enucleate the intramural component of FIGO 1 and FIGO 2 submucosal myomas from the surrounding myometrium without activating the current. This blunt cold loop dissection technique allows for a deeper and more thorough resection. Often, if the pseudocapsule plane is identified, even the intramural component of FIGO 1 or FIGO 2 submucosal fibroids can be resected, enabling complete removal.

Lastly, mechanical tissue removal systems are not always faster than resectoscopes for all pathology. We prefer using the resectoscope for larger myomas (>3 cm) as the resectoscope

allows for resection and removal of larger myoma chips, helping to decrease operative times. Given the many benefits of the resectoscope, we argue that the resectoscope loop remains a crucial instrument in operative gynecology and that learners should continue to hone their hysteroscopic skills with both the resectoscope and mechanical tissue removal systems.

Tips and tricks for hysteroscopic myomectomy with the resectoscope loop

In the video below, "Bipolar resectoscope: Optimizing safe myomectomy," we review specific surgical techniques for optimizing outcomes and safety with the resectoscope loop. These include:

- bow-and-arrow technique
- identification of the fibroid anatomy (pseudocapsule plane)
- blunt cold loop dissection
- the push-and-tuck method
- efficient electrosurgical hemostasis (**TABLE 2**).

Although we use bipolar energy during this resection, the resection technique using the monopolar loop is the same.

TABLE 2 Tips and tricks for hysteroscopic myomectomy

• Perform an initial survey to identify fibroid anatomy, submucosal fibroid type, and uterine landmarks.
• Dig deep to optimize efficiency and obtain bigger fibroids chips with each pass.
• Take full-length bites using the bow-and-arrow technique to create long strips.
• Do not leave hanging pieces that impair visibility.
• Use the push-and-tuck technique to minimize the number of times the scope needs to be removed.
• Achieve hemostasis by desiccating bleeders to maintain visibility.
• Optimize blunt dissection to preserve the pseudocapsule.

The takeaway

The resectoscope loop is a valuable tool that offers gynecologic surgeons a wider range of techniques for myomectomy. It also offers several surgical and clinical advantages. It is important to train residents in the use of both hysteroscopic mechanical tissue removal systems and resectoscope loops.

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Ob.Gyn. News
MASTER CLASS

Transcervical ablation of symptomatic uterine fibroids under US guidance

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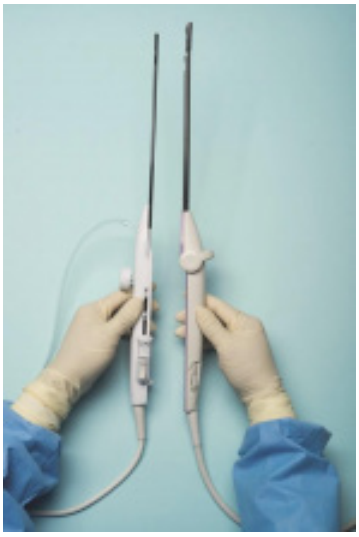
September 30, 2019

On August 29, 2019, the first commercial case utilizing the Sonata system to transcervically ablate symptomatic uterine fibroids under ultrasound guidance was performed at Stamford (Connecticut) Hospital. This truly minimally invasive new treatment expands our options in the surgical management of uterine fibroids.



Uterine fibroids are the most common benign tumors of the reproductive tract. It has been estimated that nearly half of the 70%-80% of women who develop fibroids during their reproductive years are symptomatic. Given that some patients present with fertility concerns, it also has been estimated that at least one in three women with fibroids have symptoms such as heavy bleeding (menorrhagia) and bulk symptoms, pain (dyspareunia, dysmenorrhea, noncyclic pain), and increased urinary frequency.

Fibroids are the most common cause of hysterectomy in the United States, with 240,000 (40% of 600,000) performed annually, yet research shows that many women are interested in minimally invasive options and in uterine conservation. In a 2013 national survey published in the *American Journal of Obstetrics and Gynecology*, 79% of women expressed an interest in minimally invasive approaches for fibroid treatment, and over 50% reported a desire for uterine conservation.[1]

Both myomectomy and uterine artery embolization are uterine-sparing procedures. However, uterine artery embolization should not be performed in a woman interested in pregnancy. Moreover, there are reports of ovarian reserve issues when the procedure is performed in women in their later reproductive years.

Depending on the technique performed, women undergoing hysteroscopic myomectomy are at risk of fluid overload, hyponatremia, gas-related embolism, and postoperative adhesions. The suture requirements of a laparoscopic myomectomy make this approach an often-difficult one to master, even with robotic assistance. It also requires intubation and potentially places the patient at risk for bleeding and infection. Furthermore, long-term risks include adhesions and the need for C-section with pregnancy.

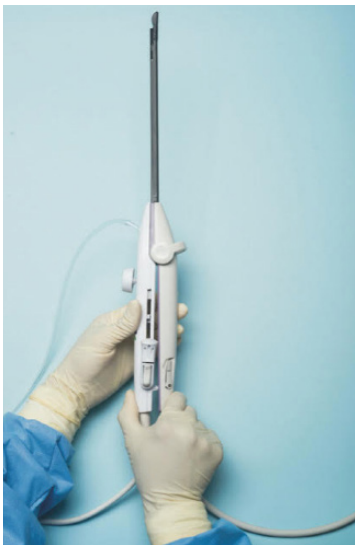
The impact of uterine fibroids on patients' lives and their desire for uterine conservation has spurred growing interest in the use of radiofrequency (RF) energy to ablate uterine fibroids. In a 2018 systematic review of nonresective treatments for uterine fibroids published in the *International Journal of Hyperthermia*, investigators found that the pooled fibroid volume reductions at 6 months after RF ablation and uterine artery embolization were 70% and 54%, respectively.[2]

The first commercially available system utilizing RF frequency to shrink fibrosis – Acessa – involves laparoscopy, and thus requires abdominal incisions. In August 2018, the Sonata system (Gynesonics: Redwood, California) received US Food and Drug

Administration clearance after having received European CE-Mark approval in 2010 (for the original device, the VizAblate) and in 2014 (for the next-generation device, the Sonata).

The technology

For a complete description of transcervical, intrauterine sonography–guided radiofrequency ablation of uterine fibroids, one can refer to the excellent outline by David Toub, MD, in *Current Obstetrics and Gynecology Reports*.[3] Basically, the Sonata system allows for real-time, image-guided treatment through the use of a reusable intrauterine ultrasound (IUUS) probe, a single-use RF ablation (RFA) handpiece, and graphical guidance software for diagnosis and targeting.



Coupling of the Sonata RFA handpiece and IUUS probe

Initially, the IUUS probe enables identification of fibroids from within the uterine cavity, then guides deployment of an introducer and needle electrode into the targeted fibroid(s). The probe image is curvilinear, penetrates more than 9 cm, and provides a 90-degree field of view.

The RFA handpiece contains the introducer and needle electrode array. It snaps together with the IUUS probe to form and integrate into a single treatment device that contains all controls needed to place and size the ablation. Mechanical stops and lockouts within the RFA handpiece further enhance proper localization and sizing of the ablation.

The system's graphical guidance software, also known as the SMART Guide, is a real-time graphical overlay on the ultrasound display, which enables one to visually select deployment length, width, and position of the ablation guides. In so doing, the mechanical stops for the introducer and needle electrodes are determined prior to their insertion into the targeted fibroid(s). This was validated in more than 4,000 ablations in bovine muscle and human-extirpated uteri, as well as in vivo at time of laparotomy.

By displaying the ellipsoidal region where the ablation will take place (ablation zone) along with a surrounding ellipsoid (thermal safety border) where tissue temperature will be elevated, the SMART Guide provides a safer and more accurate understanding of the ablation than if it showed only the ablation zone.

Coupling completed

COURTESY GYNESONICS

As with transabdominal or transvaginal sonography, the serosa will appear hyperechoic at the time of intrauterine ultrasound. By using the SMART Guide, the ablation is sized and positioned to encompass as much of the fibroid as possible while maintaining thermal energy within the uterine serosal margin. Once the desired ablation size has been selected, and safe placement of the needle electrodes is confirmed by rotating the IUUS probe in multiple planes, therapeutic RF energy is delivered to the fibroid; the fixed treatment cycle is dependent on ablation size.

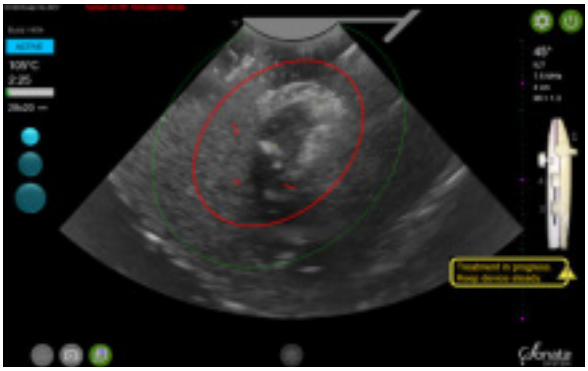
The system will modulate power (up to 150W) to keep temperature at the tips of the needle electrode at 105° C. Moreover, the time of energy delivery at the temperature of 105° – 2-7 minutes – is automatically set based on ablation size, which is a continuum up to 4 cm wide and up to 5 cm long. Multiple ablations may be utilized in a particularly large fibroid.

Unlike hysteroscopic myomectomy, only a small amount of hypotonic solution is instilled within the uterine cavity to enhance acoustic coupling. Furthermore, the treatment device (RFA handpiece and IUUS probe) is only 8.3 mm in diameter. This requires Hegar dilatation of the cervix to 9.

The procedure

After administering anesthesia (regional or sedation), dispersive electrode pads are placed on the anterior thighs. After the cervix is dilated to Hegar dilatation of 9, the treatment device is inserted transcervically into the uterine cavity and the fibroid(s) are identified with the ultrasound probe. The physician plans and optimizes the ablation by sizing and aligning the graphical overlay

targeting guide (the SMART Guide) over the live image. Once the size and location of the ablation are set, the trocar-tipped introducer is advanced into the fibroid. After ensuring the guide is within the serosal boundary, the needle electrodes are deployed.



COURTESY GYNESONICS

The SMART Guide delineates the ablation zone (red ellipsoid) and thermal safety border (green ellipsoid). Everything within the ablation zone will be thermally ablated and undergo coagulative necrosis.

A second visual safety check is completed, and the delivery of RF energy is initiated using a footswitch control. The time of energy delivery is determined based on the size of the desired ablation, up to 7 minutes for the largest ablation size (5 cm x 4 cm). The targeting and treatment steps are repeated as required to treat additional fibroids. Once the treatment is completed, the needle electrodes and introducer are retracted, and the treatment device removed.

Study results and the future

The 12-month safety and effectiveness data for ultrasound-guided transcervical ablation of uterine fibroids were reported in January 2019 in Obstetrics & Gynecology.[4] Women enrolled in the prospective, multicenter, single-arm, interventional trial had 1-10 fibroids—the International Federation of Gynecology and Obstetrics (FIGO) types 1, 2, 3, 4, and 2-5 (pedunculated fibroids excluded)—with diameters of 1-5 centimeters. Patients also were required to have at least one fibroid indenting or impinging on the endometrial cavity (FIGO type 1, 2, 3, or 2-5).

Upon study entry, the pictorial assessment blood loss was required to be 150-500 cc. The study included 147 patients. Both coprimary endpoints were satisfied at 12 months; that is, 65% of patients experienced a 50% or greater reduction in menstrual bleeding, and 99% were free from surgical intervention at 1 year.

The mean pictorial blood loss decreased by 39%, 48%, and 51% at 3, 6, and 12 months respectively. Moreover, 95% of the study population experienced some reduction in menstrual bleeding at 12 months. There also were mean improvements in symptom severity and health-related quality-of-life parameters. Mean maximal fibroid volume reduction per patient was 62%.

More than half of the patients returned to normal activity within 1 day, 96% of patients reported symptom improvement at 12 months, and 97% expressed satisfaction with the procedure and results at 12 months. There were no device-related adverse events.

I am the lead author for the 2-year follow-up study utilizing transcervical RFA of symptomatic uterine fibroids, which currently is in press. Suffice it to say, the quality-of-life data, symptom improvement, and lower rate of surgical reintervention all are significant and compelling. Ultimately, I believe Sonata will not only be a treatment of choice in the appropriate patient presenting with heavy menstrual flow or bulk symptoms secondary to uterine fibroids, but will prove to be beneficial in women with impinging or deep submucosal fibroids and implantation failure.

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Dr. Miller disclosed that he is a consultant for Gynesonics and holds a stock option agreement with the company.

OBG MANAGEMENT

Fibroids: Patient considerations in medical and surgical management

Uterine fibroids can cause abnormal bleeding, pain, and infertility. ObGyns should be prepared to develop a treatment plan based on patient symptoms and goals. A panel offers guidance based on experience and expertise.

Expert Panel:

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Uterine fibroids (myomas or leiomyomas) are common and can cause considerable morbidity, including infertility, in reproductive-aged women. In this roundtable discussion, moderated by OBG Management Editorial Board member Joseph S. Sanfilippo, MD, MBA, 2 experts discuss imaging technologies and classification systems for assessing fibroids, various medical and surgical treatment options, and patient reproductive goals to consider when counseling women with fibroids.

Perspectives on a pervasive problem

Joseph S. Sanfilippo, MD, MBA: First let's discuss the scope of the problem. How prevalent are uterine fibroids, and what are their effects on quality of life?

Linda D. Bradley, MD: Fibroids are extremely prevalent. Depending on age and race, between 60% and 80% of women have them.1 About 50% of women with fibroids have no symptoms[2]; in symptomatic women, the symptoms may vary based on age. Fibroids are more common in women from the African diaspora, who have earlier onset of symptoms, very large or more numerous fibroids, and more symptomatic fibroids, according to some clinical studies.3 While it is a very common disease state, about half of women with fibroids may not have significant symptoms that warrant anything more than watchful waiting or some minimally invasive options.

Ted L. Anderson, MD, PhD: We probably underestimate the scope because we see people coming in with fibroids only when they have a specific problem. There probably are a lot of asymptomatic women out there that we do not know about.

CASE 1: Abnormal uterine bleeding in a young woman desiring pregnancy in the near future

Dr. Sanfilippo: Abnormal uterine bleeding is a common dilemma in my practice. Consider the following case example.

A 24-year-old woman (G1P1) presents with heavy, irregular menses over 6 months' duration. She is interested in pregnancy, not

immediately but in several months. She passes clots, soaks a pad in an hour, and has dysmenorrhea and fatigue. She uses no birth control. She is very distraught, as this bleeding truly has changed her lifestyle.

What is your approach to counseling this patient?

Dr. Bradley: You described a woman whose quality of life is very poor—frequent pad changes, clotting, pain. And she wants to have a child. A patient coming to me with those symptoms does not need to wait 4 to 6 months. I would immediately do some early evaluation.

Dr. Anderson: Sometimes a patient comes to us and already has had an ultrasonography exam. That is helpful, but I am driven by the fact that this patient is interested in pregnancy. I want to look at the uterine cavity and will probably do an office hysteroscopy to see if she has fibroids that distort the uterine cavity. Are there fibroids inside the cavity? To what degree does that possibly play a role? The presence of fibroids does not necessarily mean there is distortion of the cavity, and some evidence suggests that you do not need to do anything about those fibroids.4 Fibroids actually may not be the source of bleeding. We need to keep an open mind when we do the evaluation.

Imaging technologies and classification aids

Dr. Sanfilippo: Apropos to your comment, is there a role for a sonohysterography in this population?

Dr. Anderson: That is a great technique. Some clinicians prefer to use sonohysterography while others prefer hysteroscopy. I tend to use hysteroscopy, and I have the equipment in the office. Both are great techniques and they answer the same question with respect to cavity evaluation.

Dr. Bradley: We once studied about 150 patients who, on the same day, with 2 separate examiners (one being me), would first undergo saline infusion sonohysterography (SIS) and then hysteroscopy, or vice versa. The sensitivity of identifying an intracavitary lesion is quite good with both. The additional benefit with SIS is that you can look at the adnexa.

In terms of the classification by the International Federation of Gynaecology and Obstetrics (FIGO), sometimes when we do a hysteroscopy, we are not sure how deep a fibroid is—whether it is a type 1 or type 2 or how close it is to the serosa (see illustration, page 26). Are we seeing just the tip of the iceberg? There is a role for imaging, and it is not always an "either/or" situation. There are times, for example, that hysteroscopy will show a type 0. Other times it may not show that, and you look for other things in terms of whether a fibroid abuts the endometrium. The take-home message is that physicians should abandon endometrial biopsy alone and, in this case, not offer a D&C.

In evaluating the endometrium, as gynecologists we should be facile in both technologies. In our workplaces we need to advocate to get trained, to be certified, and to be able to offer both technologies, because sometimes you need both to obtain the right answer.

Dr. Sanfilippo: Let's talk about the FIGO classification, because it is important to have a communication method not only between physicians but with the patient. If we determine that a fibroid is a type 0, and therefore totally intracavitary, management is different than if the fibroid is a type 1 (less than 50% into the myometrium) or type 2 (more than 50%). What is the role for a classification system such as the FIGO?

Dr. Anderson: I like the FIGO classification system. We can show the patient fibroid classification diagrammatically and she will be able to understand exactly what we are talking about. It's helpful for patient education and for surgical planning. The approach to a type 0 fibroid is a no-brainer, but with type 1 and more specifically with type 2, where the bulk of the fibroid is intramural and only a portion of that is intracavitary, fibroid size begins to matter a lot in terms of treatment approach.

Sometimes although a fibroid is intracavitary, a laparoscopic rather than hysteroscopic approach is preferred, as long as you can dissect the fibroid away from the endometrium. FIGO classification is very helpful, but I agree with Dr. Bradley that first you need to do a thorough evaluation to make your operative plan.

Dr. Sanfilippo: I encourage residents to go through an orderly sequence of assessment for evaluating abnormal uterine bleeding, including anatomic and endocrinologic factors. The PALM-COEIN classification system is a great mnemonic for use in evaluating abnormal uterine bleeding (**TABLE**).[5] Is there a role for an aid such as PALM-COEIN in your practice?

Dr. Bradley: I totally agree. In 2011, Malcolm Munro and colleagues in the FIGO Working Group on Menstrual Disorders helped us to have a reporting on outcomes by knowing the size, number, and location of fibroids.[5] This helps us to look for structural causes and then, to get to the answer, we often use imaging such as ultrasonography or saline infusion, sometimes magnetic resonance

TABLE Potential causes of abnormal uterine bleeding according to the PALM-COEIN classification[5]

Polyp **A**denomyosis **L**eiomyoma **M**alignancy & hyperplasia	Structural pathology measurable through imaging or histopathology
Coagulopathy **O**vulatory disorders **E**ndometrial dysfunction **I**atrogenic	Bleeding unrelated to structural abnormalities
Not otherwise classified	

imaging (MRI), because other conditions can coexist—endometrial polyps, adenomyosis, and so on.

The PALM-COEIN system helps us to look at 2 things. One is that in addition to structural causes, there can be hematologic causes. While it is rare in a 24-year-old, we all have had the anecdotal patient who came in 6 months ago, had a fibroid, but had a platelet count of 6,000. Second, we have to look at the patient as a whole. My residents, myself, and our fellows look at any bleeding. Does she have a bleeding diathesis, bruising, nose bleeds; has she been anemic, does she have pica? Has she had a blood transfusion, is she on certain medications? We do not want to create a "silo" and think that the patient can have only a fibroid, because then we may miss an opportunity to treat other disease states. She can have a fibroid coexisting with polycystic ovary syndrome (PCOS), for instance. I like to look at everything so we can offer appropriate treatment modalities.

Dr. Sanfilippo: You bring up a very important point. Coagulopathies are more common statistically at the earlier part of a woman's reproductive age group, soon after menarche, but they also occur toward menopause. We have to be cognizant that a woman can develop a coagulopathy throughout the reproductive years.

Dr. Anderson: You have to look at other medical causes. That is where the PALM-COEIN system can help. It helps you take the blinders off. If you focus on the fibroid and treat the fibroid and the patient still has bleeding, you missed something. You have to consider the whole patient and think of all the nonclassical or nonanatomical things, for example, thyroid disease. The PALM-COEIN helps us to evaluate the patient in a methodical way—every patient every time—so you do not miss something.

The value of MRI

Dr. Sanfilippo: What is the role for MRI, and when do you use it? Is it for only when you do a procedure—laparoscopically, robotically, open—so you have a detailed map of the fibroids?

Dr. Anderson: I love MRI, especially for hysteroscopy. I will print out the MRI image and trace the fibroid because there are things I want to know: exactly how much of the fibroid is inside or outside, where this fibroid is in the uterus, and how much of a normal buffer there is between the edge of that fibroid and the serosa. How aggressive can I be, or how cautious do I need to be, during the resection? Maybe this will be a planned 2-stage resection. MRIs are wonderful for fibroid disease, not only for diagnosis but also for surgical planning and patient counseling.

Dr. Bradley: SIS is also very useful. If the patient has an intracavitary fibroid that is larger than 4.5 to 5 cm and we insert the catheter, however, sometimes you cannot distend the cavity very well. Sometimes large intramural fibroids can compress the cavity, making the procedure difficult in an office setting. You cannot see the limits to help you as a surgical option. Although SIS generally is associated with little pain, some patients may have pain, and some patients cannot tolerate the test.

I would order an MRI for surgical planning when a hysteroscopy is equivocal and if I cannot do an SIS. Also, if a patient who had a hysteroscopic resection with incomplete removal comes to me and is still symptomatic, I want to know the depth of penetration.

Obtaining an MRI may sometimes be difficult at a particular institution, and some clinicians have to go through the hurdles of getting an ultrasound to get certified and approved. We have to be our patient's advocate and do the peer phone calls; any other specialty would require presurgical planning, and we are no different from other surgeons in that regard.

Dr. Sanfilippo: Yes, that can be a stumbling block. In the operating room, I like to have the images right in front of me, ideally an MRI or an ultrasound scan, as I know how to proceed. Having that visual helps me understand how close the fibroid is to the lining of the uterus.

Tapping into radiologists' expertise

Dr. Bradley: Every quarter we meet with our radiologists, who are very interested in our MRI and SIS reports. They will describe the count and say how many fibroids—that is very helpful instead of just saying she has a bunch of fibroids—but they also will tell us when there is a type 0, a type 2, a type 7 fibroid. The team looks for adenomyosis and for endometriosis that can coexist.

Dr. Anderson: One caution about reading radiology reports is that often someone will come in with a report from an outside hospital or from a small community hospital that may say, "There is a 2-cm submucosal fibroid." Some people might be tempted to take this person right to the OR, but you need to look at the images yourself, because in a radiologist's mind "submucosal" truly means under the mucosa, which in our liturgy would be "intramural." So we need to make sure that we are talking the same language. You should look at the images yourself.

Dr. Sanfilippo: I totally agree. It is also not unreasonable to speak with the radiologists and educate them about the FIGO classification.

Dr. Bradley: I prefer the word "intracavitary" for fibroids. When I see a typed report without the picture, "submucosal" can mean in the cavity or abutting the endometrium.

CASE 2: Woman with heavy bleeding and fibroids seeks nonsurgical treatment

Dr. Sanfilippo: A 39-year-old (G3P3) woman is referred for evaluation for heavy vaginal bleeding, soaking a pad in an hour, which has been going on for months. Her primary ObGyn obtained a pelvic sonogram and noted multiple intramural and subserosal fibroids. A sonohysterogram reveals a submucosal myoma.

The patient is not interested in a hysterectomy. She was treated with birth control pills, with no improvement. She is interested in nonsurgical options. Dr. Bradley, what medical treatments might you offer this patient?

Medical treatment options

Dr. Bradley: If oral contraceptives have not worked, a good option would be tranexamic acid. Years ago our hospital was involved with enrolling patients in the multicenter clinical trial of this drug. The classic patient enrolled had regular, predictable, heavy menstrual cycles with alkaline hematin assay of greater than 80. If the case patient described has regular and predictable heavy bleeding every month at the same time, for the same duration, I would consider the use of tranexamic acid. There are several contraindications for the drug, so those exclusion issues would need to be reviewed. Contraindications include subarachnoid hemorrhage. Cerebral edema and cerebral infarction may be caused by tranexamic acid in such patients. Other contraindications include active intravascular clotting and hypersensitivity.

Another option is to see if a progestin-releasing intrauterine system (IUS) like the levonorgestrel (LNG) IUS would fit into this patient's uterine cavity. Like Ted, I want to look into that cavity. I am not sure what "submucosal fibroid" means. If it has not distorted the cavity, or is totally within the uterine cavity, or abuts the endometrial cavity. The LNG-IUS cannot be placed into a uterine cavity that has intracavitary fibroids or sounds to greater than 12 cm. We are not going to put an LNG-IUS in somebody, at least in general, with a globally enlarged uterine cavity. I could ask, do you do that? You do a bimanual exam, and it is 18-weeks in size. I am not sure that I would put it in, but does it meet those criteria? The package insert for the LNG-IUS specifies upper and lower limits of uterine size for placement. I would start with those 2 options (tranexamic acid and LNG-IUS), and also get some more imaging.

Dr. Anderson: I agree with Linda. The submucosal fibroid could be contributing to this patient's bleeding, but it is not the total contribution. The other fibroids may be completely irrelevant as far as her bleeding is concerned. We may need to deal with that one surgically, which we can do without a hysterectomy, most of the time.

I am a big fan of the LNG-IUS, it has been great in my experience. There are some other treatments available as well, such as gonadotropin–releasing hormone (GnRH) agonists. I tell patients that, while GnRH does work, it is not designed to be long-term therapy. If I have, for example, a 49-year-old patient, I just need to get her to menopause. Longer-term GnRH agonists might be a good option in this case. Otherwise, we could use short-term a GnRH agonist to stop the bleeding for a while so that we can reset the clock and get her started on something like levonorgestrel, tranexamic acid, or one of the other medical therapies. That may be a 2-step combination therapy.

Dr. Sanfilippo: There is a whole category of agents available—selective progesterone receptor modulators (SPRMs), pure progesterone receptor antagonists, ulipristal comes to mind. Clinicians need to know that options are available beyond birth control pills.

Dr. Anderson: As I tell patients, there are also "bridge" options. These are interventional procedures that are not hysterectomy, such as uterine fibroid embolization or endometrial ablation if bleeding is really the problem. We might consider a variety of different approaches. Obviously, we do not typically use fibroid embolization for submucosal fibroids, but it depends on how much of the fibroid is intracavitary and how big it is. Other options are a little more aggressive than medical therapy but they do not involve a hysterectomy.

Pros and cons of uterine artery embolization

Dr. Sanfilippo: If a woman desires future childbearing, is there a role for uterine artery embolization? How would you counsel her about the pros and cons?

Dr. Bradley: At the Cleveland Clinic, we generally do not offer uterine artery embolization if the patient wants a child. While it is an excellent method for treating heavy bleeding and bulk symptoms, the endometrium can be impacted. Patients can develop fistula, adhesions, or concentric narrowing, and changes in anti-Müllerian hormone levels, and there is potential for an Asherman-like syndrome and poor perfusion. I have many hysteroscopic images where the anterior wall of the uterus is nice and pink and the posterior wall is totally pale. The embolic microsphere particles can reach the endometrium—I have seen particles in the endometrium when doing a fibroid resection.

A good early study looked at 555 women for almost a year.[6] If women became pregnant, they had a higher rate of postpartum hemorrhage; placenta accreta, increta, and percreta; and emergent hysterectomy. It was recommended that these women deliver at a tertiary care center due to higher rates of preterm labor and malposition.

If a patient wants a baby, she should find a gynecologic surgeon who does minimally invasive laparoscopic, robotic, or open surgery, because she is more likely to have a take-home baby with a surgical approach than with embolization. In my experience, there is always going to be a patient who wants to keep her uterus at age 49 and who has every comorbidity. I might offer her the embolization just knowing what the odds of pregnancy are.

Dr. Anderson: I agree with Linda but I take a more liberal approach. Sometimes we do a myomectomy because we are trying to enhance fertility, while other times we do a myomectomy to address fibroid-related symptoms. These patients are having specific symptoms, and we want to leave the embolization option open.

If I have a patient who is 39 and becoming pregnant is not necessarily her goal, but she does not want to have a hysterectomy and if she got pregnant it would be okay, I am going to treat her a little different with respect to fibroid embolization than I would treat someone who is actively trying to have a baby. This goes back to what you were saying, let's treat the patient, not just the fibroid.

Dr. Bradley: That is so important and sentinel. If she really does not want a hysterectomy but does not want a baby, I will ask, "Would you go through in vitro fertilization? Would you take clomiphene?"

If she answers no, then I feel more comfortable, like you, with referring the patient for uterine fibroid embolization. The point is to get the patient with the right team to get the best outcomes.

Surgical approaches, intraoperative agents, and suture technique

Dr. Sanfilippo: Dr. Anderson, tell us about your surgical approaches to fibroids.

Dr. Anderson: At my institution we do have a fellowship in minimally invasive surgery, but I still do a lot of open myomectomies. I have a few guidelines to determine whether I am going to proceed laparoscopically, do a little minilaparotomy incision, or if a gigantic uterus is going to require a big incision. My mantra to my fellows has always been, "minimally invasive is the impact on the patient, not the size of the incision."

Sometimes, prolonged anesthesia and Trendelenburg create more morbidity than a minilaparotomy. If a patient has 4 or 5 fibroids and most of them are intramural and I cannot see them but I want to be able to feel them, and to get a really good closure of the myometrium, I might choose to do a minilaparotomy. But if it is a case of a solitary fibroid, I would be more inclined to operate laparoscopically.

Dr. Bradley: Our protocol is similar. We use MRI liberally. If patients have 4 or more fibroids and they are larger than 8 cm, most will have open surgery. I do not do robotic or laparoscopic procedures, so my referral source is for the larger myomas. We do not put retractors in; we can make incisions. Even if we do a huge Maylard incision, it is cosmetically wonderful. We use a loading dose of IV tranexamic acid with tranexamic acid throughout the surgery, and misoprostol intravaginally prior to surgery, to control uterine bleeding.

Dr. Sanfilippo: Dr. Anderson, is there a role for agents such as vasopressin, and what about routes of administration?

Dr. Anderson: When I do a laparoscopic or open procedure, I inject vasopressin (dilute 20 U in 100 mL of saline) into the pseudocapsule around the fibroid. I also administer rectal misoprostol (400 µg) just before the patient prep is done, which is amazing in reducing blood loss. There is also a role for a GnRH agonist, not necessarily to reduce the size of the uterus but to reduce blood flow in the pelvis and blood loss. Many different techniques are available. I do not use tourniquets, however. If bleeding does occur, I want to see it so I can fix it—not after I have sewn up the uterus and taken off a tourniquet.

Dr. Bradley: Do you use Floseal hemostatic matrix or any other agent to control bleeding?

Dr. Anderson: I do, for local hemostasis.

Dr. Bradley: Some surgeons will use barbed suture.

Dr. Anderson: I do like barbed sutures. In teaching residents to do myomectomy, it is very beneficial. But I am still a big fan of the good old figure-of-8 stitch because it is compressive and you get a good apposition of the tissue, good hemostasis, and strong closure.

Dr. Sanfilippo: We hope that this conversation will change your management of uterine fibroids. I thank Dr. Bradley and Dr. Anderson for a lively and very informative discussion.

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OBG MANAGEMENT

Myomectomy of a large cervical fibroid in a patient desiring future fertility

A technique for myomectomy with uterine preservation in a 33-year-old woman with a 20-cm cervical fibroid, as well as a strategy for preoperative planning (meant to reduce this surgery's high risk for blood loss, urologic injury, and hysterectomy)

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Uterine fibroids are the most common tumors of the uterus. Clinically significant fibroids that arise from the cervix are less common.[1] Removing large cervical fibroids when a patient desires future fertility is a surgical challenge because of the risks of significant blood loss, bladder and ureteral injury, and unplanned hysterectomy. For women who desire future fertility, myomectomy can improve the chances of pregnancy by restoring normal anatomy[2] In this article, we describe a technique for myomectomy with uterine preservation in a patient with a 20-cm cervical fibroid.

CASE Woman with increasing girth and urinary symptoms is unable to conceive

A 33-year-old White woman with a history of 1 prior vaginal delivery presents with symptoms of increasing abdominal girth, intermittent urinary retention and urgency, and inability to become pregnant. She reports normal monthly menstrual periods. On pelvic examination, the ObGyn notes a large fibroid partially protruding through a dilated cervix. Abdominal examination reveals a fundal height at the level of the umbilicus.

Transvaginal ultrasonography shows a uterus that measures 4.5 x 6.1 x 13.6 cm. Arising from the posterior aspect of the uterine fundus, body, and lower uterine segment is a fibroid that measures 9.7 x 15.5 x 18.9 cm. Magnetic resonance imaging is performed and confirms a fibroid measuring 10 x 16 x 20 cm. The inferior-most aspect of the fibroid appears to be within the endometrial cavity and cervical canal. Most of the fibroid, however, is posterior to the uterus, pressing on and anteriorly displacing the endometrial cavity (FIGURE 1, PAGE 35).

What is your surgical approach?

Comprehensive preoperative planning

In this case, the patient should receive extensive preoperative counseling about the significantly increased risk for hysterectomy with an attempted myomectomy. Prior to being scheduled for surgery, she also should have a consultation with a gynecologic oncologist. To optimize visualization during the procedure, we recommend to plan for a midline vertical skin incision. Because of the potential bleeding risks, blood products should be made available in the operating room at the time of surgery.

Techniques for surgery

Intraoperatively, a vertical midline incision exteriorizes the uterus from the peritoneal cavity. Opening of the retroperitoneal spaces allows for identification of the ureters. Perform dissection in the midline away from the ureters. Inject vasopressin (5 U) into the uterine fundus. Incise the uterine serosa over the myoma posteriorly in the midline.

Perform a myomectomy, with gentle "shelling out" of the

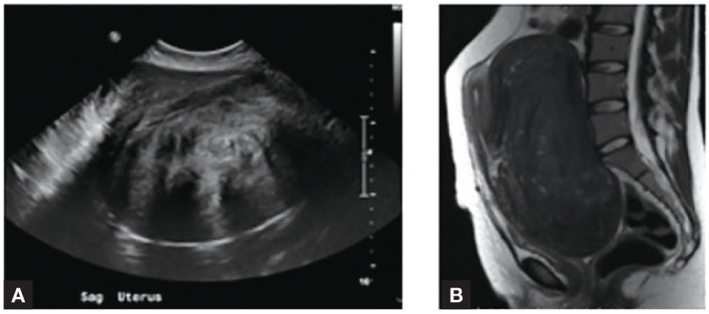
myoma; in this way the specimen can be removed intact. Reapproximate the fibroid cavity in 3 layers with 0-Vicryl (polyglactin 910) suture in a running fashion (**FIGURE 2**).

CASE Resolved

The estimated blood loss during surgery was 50 mL. Final pathology reported a 1,660-g intact myoma. The patient's postoperative course was uncomplicated and she was discharged home on postoperative day 1.

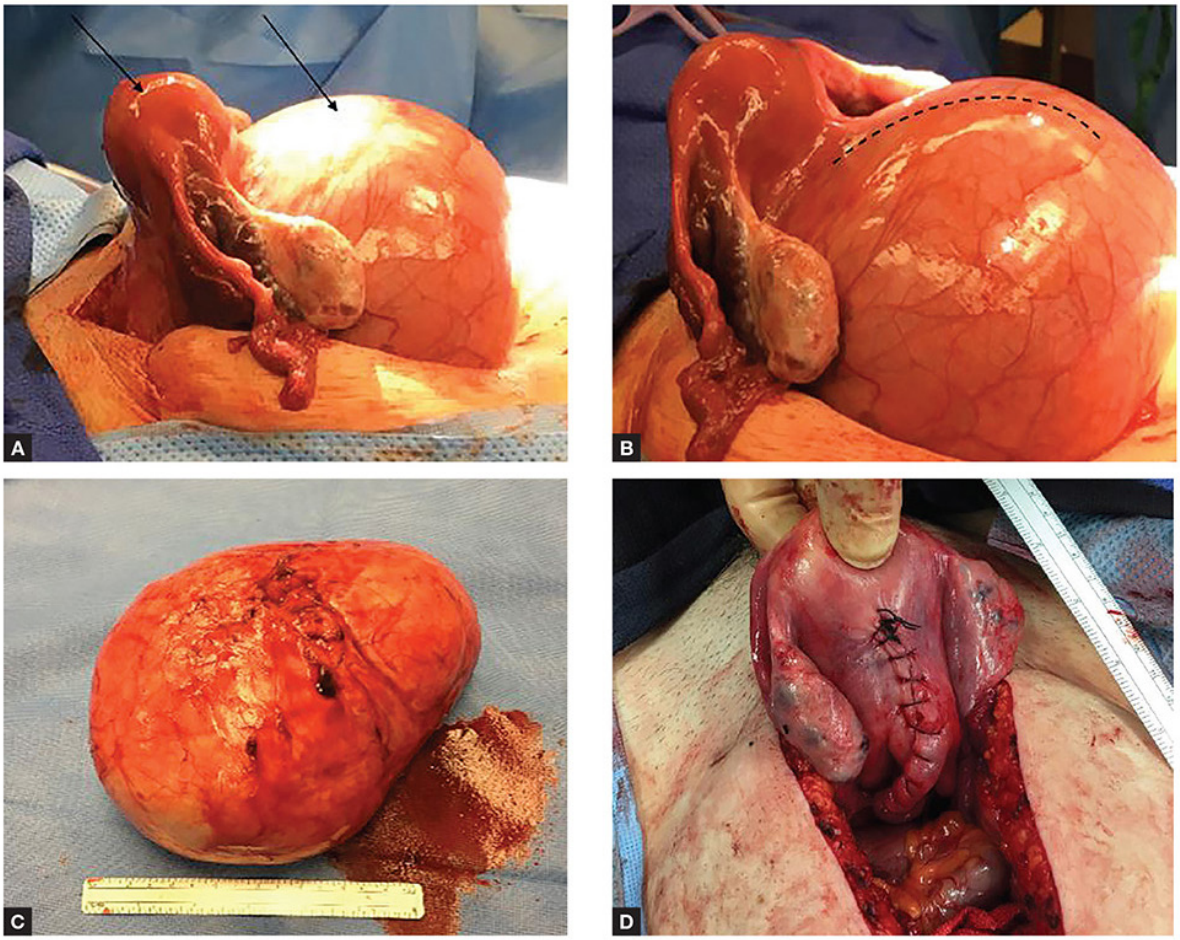
Her postoperative evaluation was 1 month later. Her abdominal incision was well healed. Her fibroid-related symptoms had resolved, and she planned to attempt pregnancy. Cesarean delivery for future pregnancies was recommended.

FIGURE 1 Imaging pinpoints the location of a large uterine fibroid



Transabdominal ultrasonography scan (**A**) and MRI scan (**B**) show a 20-cm fibroid that arises from the posterior uterus and extends inferiorly into the lower uterine segment and cervix.
Abbreviation: MRI, magnetic resonance imaging.

FIGURE 2 Our procedures for removing a 20-cm cervical fibroid



(**A**) Vasopressin injection into the uterus and posterior aspect (arrows) of the fibroid. (**B**) A 10-cm incision (dotted line) made through the posterior lower uterine segment and fibroid serosa. (**C**) Intact removal of the capsule after "shelling out" the fibroid. (**D**) Closure of the fibroid capsule overlying the lower uterine segment and cervix, using 3 layers with 0-Vicryl (polyglactin 910) suture in a running, locking fashion.

Increase the chances of a good outcome

Advanced planning for attempted myomectomy of a large cervical fibroid can increase the probability of a successful outcome. We suggest the following:

Counsel the patient on risks. Our preoperative strategy includes extensive counseling on the significantly increased surgical risks and the possibility of unavoidable hysterectomy. Given the anatomic distortion with respect to the ureters, bladder, and major blood vessels, involving gynecologic oncology is beneficial to the surgery planning process.

Prepare for possible transfusion. Ensure blood products are made available in the operating room in case transfusion is needed.

Control bleeding. Randomized studies have shown that intrauterine injection of vasopressin, through its action as a vasoconstrictor, decreases surgical bleeding.[3,4] While little data are available on vasopressin's most effective dosage and dilution, 5 U at a very dilute concentration (0.1–0.2 U/mL) has been recommended.[5] A midline cervical incision away from lateral structures and gentle shelling out of the cervical fibroid help to avoid intraoperative damage to the bladder, ureters, and vascular supply.

Close in multiple layers. This approach can prevent a potential space for hematoma accumulation.[6] Further, a multiple-layer closure of a myometrial incision may decrease the risk for uterine rupture in subsequent pregnancies.[7]

Advise abstinence postsurgery. There are no consistent data to guide patient counseling regarding recommendations for the timing of conception following myomectomy. We counseled our patient to abstain from vaginal intercourse for 4 weeks, after which time she soon should attempt to conceive. Although there are no published data regarding when it is best to resume sexual relations following such a surgery, we advise a 1-month period primarily to allow healing of the skin incision. Any further delay in attempting to become pregnant may allow for the growth of additional fibroids.

Plan for future deliveries. When the myomais extensively involved, such as in this case, we recommend cesarean delivery for future pregnancies to avoid the known risk of uterine rupture.[8] In general, we recommend cesarean delivery in future pregnancies if an incision larger than 50% of the myometrial thickness is made in the contractile portion of the uterus.

Final takeaway. Despite increased surgical risks, myomectomy of a large cervical fibroid is possible and can alleviate symptoms and improve future fertility.

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