Hysteroscopic Myomectomy

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KEYWORDS

• Fibroids • Submucosal • Hysteroscopic myomectomy

KEY POINTS

- Uterine fibroids are very common, and some are symptomatic.
- There is a wide spectrum of fibroids in terms of location, number, size, and symptomatology.
- Asymptomatic fibroids can be managed expectantly.
- Submucosal fibroids are implicated in abnormal uterine bleeding and subfertility.
- Hysteroscopic myomectomy is the treatment of choice for symptomatic submucosal myomas.

Video content accompanies this article at http://www.obgyn.theclinics.com.

INTRODUCTION

Hysteroscopy is an essential tool in every gynecologic practice offering minimally invasive evaluation and treatment for intrauterine pathology. Technology used in hysteroscopic procedures has improved steadily throughout the last two decades with improvements in optics, fluid management systems, and instrumentation for removal of intrauterine pathology. Pathology that once might have required an arduous and lengthy hospital procedure under general anesthesia can now be treated in minutes in an office setting. Similarly, leiomyomas that would have required hysterectomy for treatment can now be easily and efficiently resected in the operating room. These advancements have enabled a paradigm shift to the consideration of hysteroscopy for all patients with suspected endometrial pathology. It has also allowed the transition of many hysteroscopic procedures to the office setting. Advances in technology have allowed for faster operating times and more complete treatment of intrauterine pathology. Simultaneously, the efficiency and the safety of uterine cavity evaluation and

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treatment provide patients with faster recovery and return to normal activities. With the hysteroscopic evaluation of the uterine cavity, the role of blind biopsies, dilation and curettage, and polypectomy is becoming increasingly questionable.[1] This article seeks to provide an in-depth and up-to-date exploration of hysteroscopic myomectomy, with a concise review of the pathology, clinical presentation, and the preoperative and postoperative management.

LEIOMYOMAS

Uterine leiomyomas arise from the smooth muscle cells and fibroblasts of the myometrium, although the exact inciting factor for growth is not known. Upregulation of steroid receptors can also increase growth factors and mitogenic factors that recruit surrounding immature cells and growing leiomyoma tissue.[2,3] Aromatase activity has also been found to be 2 to 20 fold higher in leiomyoma tissues than in smooth muscle cells in culture.[4] The propagating cells, therefore, create their own hormone-driven environment.

Estrogen has long been thought to be the primary cause of fibroid growth. Estrogen receptors are more prolific in the tissue of leiomyomata when compared with normal myometrial tissue. Nuclear estrogen receptors are made from 2 similar genes forming either alpha or beta receptors (ER α or ER β). Patients who had a solitary leiomyoma were found to have higher levels of ER α, whereas those with multiple leiomyomas had higher levels of ER β.[5] Other studies have pointed to a higher ratio of ER α to ER β in attempting to describe the growth potential of myomas.[6] Regardless of the role of the specific receptor type, estradiol is certainly known to increase progesterone receptors, which increases tissue response to progesterone.[7] Progesterone is an important factor in the growth and proliferation of fibroids. Progesterone was found necessary for the maintenance of the size of uterine leiomyomas, and with its withdrawal, volume significantly decreased.[8]

In 2008, Peddada and colleagues reported on 72 women with a combined 262 leiomyomas who were followed for 12 months using MRI technology. Their study elucidated the variances not just between patients but between each leiomyoma studied. On average, the growth rate of leiomyomas was 9% over 6 months but each tumor grew at a different rate with some even regressing spontaneously. The growth rate was not affected by tumor size or location; however, patients with solitary leiomyomas were found to have faster growth rates than those who had multiple leiomyomas.[9]

EPIDEMIOLOGY

The symptoms of leiomyomas are linked to a patient's reproductive years as this is the time that hormones are consistent and active. Approximately half of women will have a uterine fibroid at some point in their life. Fibroids are the most common pelvic tumor diagnosed in women. It is difficult to understand the exact prevalence of fibroids as many patients are asymptomatic. One study found leiomyomas on histopathology in 77 of 100 uteri after hysterectomy and numerous fibroids were found in 84% of those specimens underlining the commonality of this diagnosis.[10]

There is an increased incidence of leiomyomas in Black women compared with Caucasian women. Studies of gene expression in leiomyoma tissue found that there were higher levels of aromatase mRNA in the leiomyoma tissue of African American women.[11] The rate of growth and the likelihood of rapid expansion of a fibroid decrease with age in Caucasian women, whereas the same does not occur in African American women.[9]

Patients who are obese, have increased alcohol intake, increased soybean milk consumption, a diet high in red meat, or have vitamin D deficiency are at greater risk.[12,13] Patients with high blood pressure also have a greater predilection to leiomyoma growth.[14] Lastly, there are genetic linkages believed to be associated with leiomyomas. Family history is a risk factor for uterine fibroids.[15] A genome-wide SNP linkage panel was created and analyzed 261 sister pairs finding linkages that reached genome-wide significance.[16] However, much work is needed to better understand and categorize this potential genetic predisposition.

SYMPTOMATOLOGY

Fibroids can frequently be asymptomatic or incidentally diagnosed. Asymptomatic women should be educated about the benign nature of these tumors and reassured about their clinical course. A review of concerning symptoms and reasons to present to a health care setting can help to alleviate patients' anxiety and avoid unnecessary interventions.

For symptomatic women, approximately 70% of uterine fibroids manifest themselves with symptoms of abnormal uterine bleeding (AUB). This is the most common indication for hysteroscopic myomectomy. Submucosal fibroids are associated with AUB in an estimated 5% to 10% of cases,[17] plausibly secondary to distortion of the endometrial cavity leading to greater endometrial surface area and inability of the uterine musculature to adequately contract and tamponade the spiral arteries providing blood to the endometrium.[18] Other conjectures involve dysregulation of angiogenic factors such as vascular endothelial growth factor, platelet-derived growth factor, and so forth.[19] Hysteroscopic resection of leiomyomas has been reported to achieve symptomatic relief rates of 70% to 99%.[20]

Aside from bleeding, reasons for resection of submucosal fibroids range from concerns about infertility to dysmenorrhea and pelvic pain. A thorough review of the literature attributes an estimated 1% to 2.4% of infertility cases to uterine leiomyomas when no other cause of infertility has been diagnosed.[21] Infertility issues caused by submucosal fibroids have not been borne out in the literature and it is not known if fibroids affect natural fertility.[22] Some limited studies have suggested that patients who are aged less than 40 years and have had infertility for fewer than 5 years might benefit more from myomectomy resection for infertility.[23] The American Society for Reproductive Medicine currently states that resection should take place for cavity-distorting myomas to improve pregnancy rates and decrease the risk of early pregnancy loss.[24]

Patients with subserosal or large pedunculated fibroids will often comment on pelvic pressure, constipation, or bladder irritability.

The Fibroid Growth Study published by Davis and colleagues in 2009 discovered that patients, regardless of the number and size of fibroids, equally chose surgical intervention for symptomatic fibroids.[25] Effective medical management options to mitigate the pain and heavy bleeding episodes would likely lead to a decreased need for surgical intervention.

CLASSIFICATIONS OF FIBROIDS

Several classifications have been proposed for uterine leiomyomas. In 2011, the FIGO classification of uterine leiomyomas (**Fig. 1**) has been introduced and has since been widely accepted and used to understand symptomatology as well as for surgical planning. Gynecologists have used FIGO types 1 to 8 to discuss surgical approaches and outcomes for abdominal and hysteroscopic procedures.[26,27] Hysteroscopic

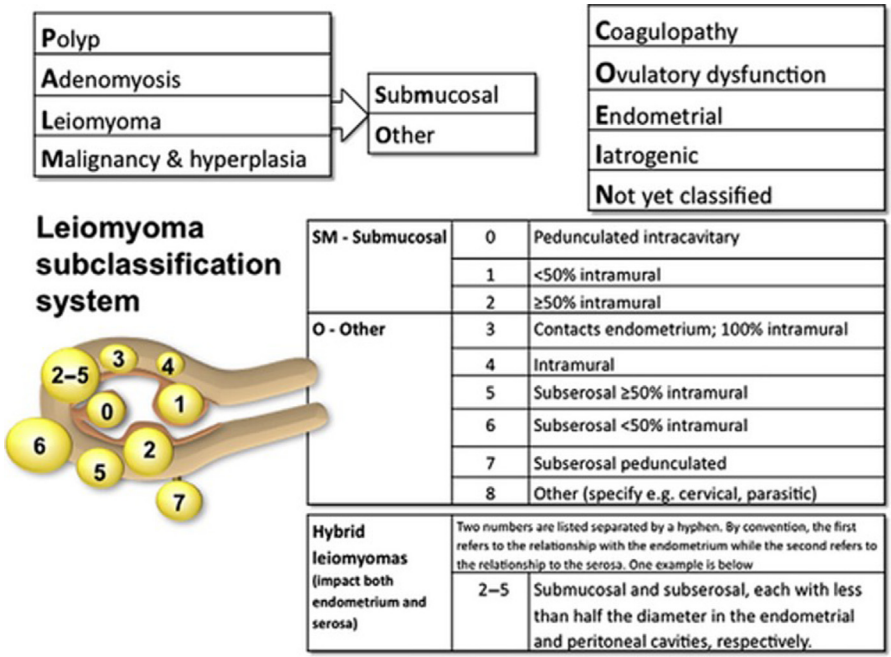

Fig. 1. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. (*From* Munro MG, Critchley HO, Broder MS, Fraser IS; FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. Int J Gynaecol Obstet. 2011;113(1):3-13. https://doi.org/10.1016/j.ijgo.2010.11.011; with permission.)

myomectomy is typically confined to FIGO type 0 through type 2, and occasionally type 3 (**Fig. 2**).

STEP-W Classification

Another classification system, developed in 2005 by Lasmar and colleagues (**Fig. 3**), used 5 parameters to classify submucosal fibroids to estimate the degree of difficulty of the hysteroscopic myomectomy.[28]

These 5 parameters included size, topography, extension of the base in relation to the uterine wall, penetration into the myometrium, and whether the fibroid is arising from the lateral wall (STEP-W). In a study of 62 hysteroscopic myomectomies, Lasmar and colleagues showed that the STEP-W classification had a good correlation with surgical difficulty. A follow-up multicenter study in 2011 with 465 myomectomies again showed a good correlation of the STEP-W classification with complete or incomplete removal of the fibroid at the time of hysteroscopic myomectomy.[29]

IMAGING

Appropriate evaluation of the location and number of uterine fibroids is crucial for the evaluation of patient complaints, counseling, options for treatment, and surgical planning.

Imaging almost universally begins with transvaginal ultrasound. Pelvic ultrasound has excellent sensitivity for diagnosing fibroids with limitations increasing if the

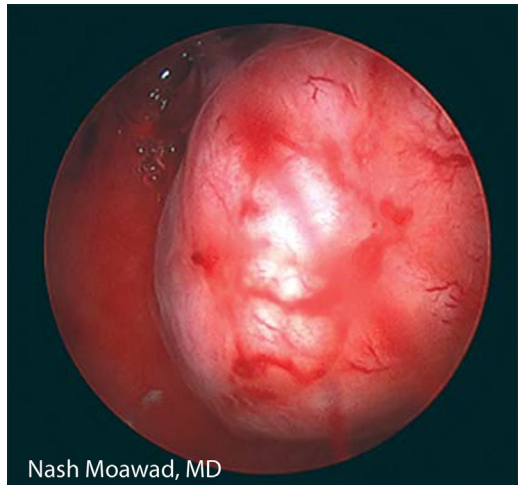

Fig. 2. Type 1 submucosal fibroid.

patient is pregnant, if there are multiple fibroids, or if the patient cannot tolerate transvaginal ultrasound.[30] If diagnostic hysteroscopy is readily available in the office, many physicians will use hysteroscopy to complement ultrasound findings. Some gynecologists argue for evaluation with saline infusion sonography (SIS) for proper evaluation of the fibroid and its relationship to the uterine cavity. When findings from transvaginal ultrasound are inconclusive about the type of fibroid found, the addition of SIS is a good second-line diagnostic procedure.[31] Both procedures are found to be effective in diagnosing intracavitary fibroids with excellent agreement (92%) between modalities in the case of types 0 1 fibroids.[30,32] MRI is also frequently used for preoperative workup and surgical planning, particularly for larger

	Size (cm)	Topography	Extension of the base	Penetration	Lateral Wall	Total
0	>2 to 5	Low	≤1/3	0	+1	
1	>2 to 5	Middle	>1/3 to 2/3	≤50%		
2	>5	Upper	>2/3	>50%		
Score	+	+	+	+	+	

Score	Group	Complexity and therapeutic options
0 to 4	I	Low complexity hysteroscopic myomectomy.
5 to 6	II	High complexity hysteroscopic myomectomy. Consider GnRH use? Consider Two-step hysteroscopic myomectomy.
7 to 9	III	Consider alternatives to the hysteroscopic technique

Fig. 3. LASMAR/STEP-W Classification for submucosal leiomyomas and prediction of surgical difficulty. (*From* Lasmar RB, Lasmar BP, Celeste RK, da Rosa DB, Depes Dde B, Lopes RG. A new system to classify submucous myomas: a Brazilian multicenter study. J Minim Invasive Gynecol. 2012;19(5):575-580. https://doi.org/10.1016/j.jmig.2012.03.026; with permission.)

and multiple fibroids requiring laparoscopic or robot-assisted myomectomy. A randomized control trial (RCT) of 18 women undergoing ultrasound and MRI showed that MRI had superior sensitivity with better correlation to the actual size of pathology over transvaginal ultrasound.[33] However, patient characteristics such as sexual activity, pelvic pain, and anxiety levels should also be considered when ordering imaging for the evaluation of fibroids. Patients were found to have higher levels of fear, anxiety, and mental and physical issues after MRI versus TVUS but greater embarrassment during TVUS.[34]

It is important to also note the role that ultrasound imaging can play for the practitioner in cases of difficult hysteroscopy or concern for transmural leiomyomas requiring resection.[35] Ultrasound-guidance has been used in the operating room with great success and should be considered for patients with distorted anatomy or difficult entry into the uterus.

PREOPERATIVE ASSESSMENT

Patient selection is an important part of all surgical workup. Abnormal bleeding and bulk or pressure symptoms are some of the most common symptoms prompting women to seek care for large uterine fibroids. Patients who are undergoing fertility workup and have a submucosal fibroid are also appropriate candidates for surgical management. Regardless of the surgical approach of myomectomy, patients have improved quality of life scores and decreased symptom severity.[36] This article focuses on surgical management with hysteroscopic myomectomy.

To ensure appropriate shared decision making with patients, all feasible treatment options should be discussed with each patient, including expectant management. Medical management should be the first line when available and appropriate for the patient's symptoms and goals. The patient's comorbid conditions and prior surgical history should be obtained and can help to guide counseling. Lack of desire for future fertility, suspicion of concomitant uterine pathology, or failed prior myomectomy are some examples to consider more definitive surgical management with hysterectomy. Some patients prefer the most conservative approach possible, whereas others may find the potential for regrowth of fibroids and reintervention unacceptable. If future fertility is a consideration, it is important to address the patient's concerns, ensure proper counseling, and engage in consultation with a reproductive endocrinologist as needed before finalizing surgical treatment plans. When patients feel confident in their decision for a particular procedure before surgical intervention, higher patient satisfaction scores result postoperatively.[37] This challenges providers to ensure that they are individualizing patient counseing instead of making broad recommendations based on age or other demographic factors.

A proper physical examination is also necessary and important for many reasons. Providers should ensure that there are no other obvious causes for AUB. Vaginal atrophy should be addressed and gross lesions on the cervix should be properly evaluated. The physical examination should also ensure that there are no prolapsing fibroids or cervical polyps that could cause symptoms of pain or AUB. During the physical examination, the physician should note whether the patient can tolerate speculum examination well and could potentially tolerate an in-office procedure for further workup before surgery or even potentially undergo hysteroscopic management in the office. We also recommend noting whether there is a need to dilate or open the cervix for procedures to be properly prepared with lacrimal duct dilators or scalpel for cruciate incision of the cervix, or for hysteroscopic dilation of the cervix during

vaginoscopy. After the physical examination is performed, proper laboratory assessment and imaging should be subsequently ordered.

Patients with heavy bleeding and concern for anemia should have a complete blood count drawn and proper intervention in the case of severe anemia. If there is concern for mass effect on the bladder or ureters, it is appropriate to order a basic metabolic panel to evaluate kidney function and consider imaging the kidneys and ureters. A pregnancy test should be performed for all reproductive-age women before surgical management. Lastly, those patients who desire future fertility and are undergoing surgery for that sole purpose should be evaluated by a reproductive endocrinologist and determination should be made about their reproductive health and options.

OFFICE HYSTEROSCOPY

Given the advances in technology previously mentioned, office hysteroscopy is more affordable and easier to perform than ever before. Preoperative planning with office hysteroscopy is feasible for surgical planning and appropriate patient counseling. Small, 1 to 2 cm type 0 submucosal myomas can potentially be removed in the office setting using hysteroscopic scissors or tissue removal systems. A prospective study of patient outcomes after hysteroscopic myomectomy found higher successful completion rates when the fibroids were $\leq$3 cm in size.[38] However, this was for all hysteroscopies and even this size may be difficult for patients undergoing an office procedure. Incision of the pseudocapsule during office hysteroscopy may allow the protrusion of the fibroid into the uterine cavity, improving the likelihood of complete resection during subsequent hysteroscopic myomectomy.[39] The advent of the minireseactoscope and the tissue removal devices has improved our ability to remove larger submucosal fibroids in the office setting.

PHARMACOLOGIC INTERVENTION AND PREOPERATIVE PATIENT OPTIMIZATION

Oral and Intravenous Iron Supplementation

Anemia is defined as a hemoglobin level of less than 120 g/L for women. Iron deficiency anemia secondary to chronic blood loss can be treated in numerous ways including blood transfusion, oral iron supplementation, or intravenous (IV) iron infusion. However, blood transfusion is not considered a first-line option, given its risk profile and associated complications and cost. In patients who are undergoing elective surgery without active bleeding and symptomatic anemia, it is preferable to supplement with iron.

Oral iron is a good first-line treatment if patients can tolerate it. There are known gastrointestinal side effects and if the patient has other concomitant issues with malabsorption (Inflammatory Bowel Disease or malignancy), then it can decrease the efficacy of oral treatment. Approximately 70% of patients complain of reflux, constipation, and/or abdominal pain when taking oral supplementation. Various preparations of iron exist, all of which are available over the counter. Recent developments of new ferric compounds and ferrous salts have improved symptomatology and are "not affected by food, milk or medicines which permits its ingestion during or after meals and the tolerability… is much better."[40] It takes approximately 1 to 2 months for the treatment of iron deficiency anemia and another 3 to 6 months to replenish iron stores. If the patient continues to have bleeding throughout that time, this slow method of repletion might be ineffective for the patient.

IV iron is another option for patients with known iron deficiency anemia; IV supplementation works faster with a more substantial increase in hemoglobin levels than its

oral counterpart. When initially introduced in the 1930s, iron preparations caused occasional anaphylactic responses. With the introduction of low-molecular-weight iron and reconfigured complexes, there is no longer a need for test dosing and doses as high as 1 g of iron can be given in a single administration.[41] This is excellent news for many patients who previously might have been at higher risk of blood transfusion without rapid correction of hemoglobin levels.

Misoprostol

Preoperative preparation with misoprostol has been adopted into practice by many physicians to decrease bleeding during surgery. Its use has been established for open and laparoscopic myomectomies.[42] A meta-analysis of misoprostol use before myomectomy showed a statistically significant decrease in blood loss of 0.68 g/dL without significant side effects.[43] However, extrapolating that data to hysteroscopic myomectomy has yet to lead to any definitive conclusions about blood loss. Misoprostol in assisting with cervical dilation can be helpful for patients in whom entry into the uterine cavity might be difficult. However, the softening of the cervix can also lead to overdilation and fluid loss during the procedure. Decisions to use misoprostol should be individualized.[44]

Ulipristal Acetate

Ulipristal acetate (a selective progesterone receptor modulator) has also been studied for potential use before surgical intervention on intrauterine fibroids. Preoperative treatment for 3 to 6 months before intervention increased the percentage of completely resected type 0 to 1 fibroids compared with patients who went immediately to surgery (89%–68.9%).[45] Another study determined that its use before hysteroscopic management did not negatively affect surgical outcomes but more data are needed to determine its clinical utility.[46]

GnRH Agonist

The use of GnRH agonists in preparation for hysteroscopic myomectomy is limited to the treatment of baseline anemia in preparation for surgery, and to potentially decrease the size of submucosal fibroids if it will facilitate the procedure and improve the likelihood of complete removal of the fibroid. In patients in whom heavy menstrual bleeding is causing significant anemia, pretreatment with GnRH agonists can stop bleeding for long enough to improve hemoglobin levels before surgery[47] There is suggestion that the greatest benefit may be in pretreatment with GnRH agonist therapy before hysteroscopic resection. GnRH agonist treatment causes endometrial atrophy, which assists with hysteroscopic visualization, thereby decreasing operative time. Studies have also shown decreased fluid absorption during hysteroscopy in pretreated uteri. Lower fluid absorption levels decrease the risks during prolonged resection for a large submucosal fibroid. One study showed improvement in complete fibroid resection with the use of GnRH agonist treatment before hysteroscopic myomectomy when compared with controls (3% vs 20%),[48] though others have not found the same improvement when performing cold loop resection.[49] A randomized, multicenter study showed decreased operative times and decreased fluid absorption when a GnRH analogue was used before hysteroscopic resection of submucosal fibroids.[50] A small study of 25 patients also evaluated and found benefit in pretreatment for hysteroscopic myomectomy in patients who were considered inoperative because of leiomyoma size.[51] Certainly, more research is needed to understand the utility before hysteroscopic procedures.

HYSTEROSCOPIC MYOMECTOMY—THE PROCEDURE

Optimization

Paracervical blocks

There is conflicting evidence about paracervical blocks and their efficacy in outpatient procedures. It has been studied more thoroughly in the Family Planning literature for use during surgical procedures requiring dilation of the cervix. This form of anesthesia has been proven effective in other procedures including second-trimester laminaria placement and intrauterine device placement.[52] Its use compared to other forms of pain management in operative hysteroscopy has not been shown to be superior in many studies.[53] A Cochrane Database review which included 26 studies on the utility of paracervical block did not conclusively determine whether paracervical injection of local anesthetic made any difference. It was not found to be superior, but 10 studies compared paracervical block with placebo and found a decreased risk of severe pain (RR 0.16) and reduced pain on cervical dilation and during the time of uterine intervention. There was no evidence to infer its superiority to other pain management options.[54] Only 55% of women would recommend this form of analgesia after undergoing a procedure with paracervical block.[55] Given that its efficacy cannot be proven regarding hysteroscopy but has been found to be beneficial with other forms of cervical and uterine manipulation, this form of analgesia should be used as an additional tool at the physician's discretion after proper patient counseling.

Normal dosing of lidocaine is shown in the following table. Dosing varies depending on the type of analgesic used and whether it is mixed with epinephrine. It is important to recall the side effects of toxicity. First, the patient's lips or tongue will become numb, which prompts patients to complain of "tingling lips" or slurred speech. Next, cardiovascular effects, such as hypotension, bradycardia, or arrhythmias, can occur. Muscle twitching or tremors and seizures can then occur and finally respiratory depression and cardiac arrest. Patients should be properly informed of the side effects of lidocaine toxicity and encouraged to report side effects immediately to avoid severe complications.

	Dosage	Maximum Dosage Without Epinephrine	Maximum Dosage With Epinephrine
Lidocaine	1% = 10 mg/mL 2% = 20 mg/mL	5 mg/kg	7 mg/kg

Vasopressin

Vasopressin has long been used in laparoscopy and open cases to decrease blood flow to fibroids during myomectomy, thereby decreasing surgical blood loss and potentially improving visualization, maximizing efficiency, and decreasing the risk of complications. During hysteroscopy, vasopressin can be injected directly into the myoma using a cystoscopic needle through the operative channel under hysteroscopic guidance. A prospective, double-blind RCT of 40 women found that there was a statistically significant improvement in the surgical field, decreased operative blood loss, and decreased fluid intravasation. However, this did not translate to reduced operative time.[56] Another option is to inject vasopressin into the cervical stroma. This has been associated with decreased fluid intravasation, decreased blood loss, and decreased operative time.

Current recommendations call for 10 units of vasopressin in 100 to 200 mL of normal saline, which is injected in small aliquots with care being taken to avoid any

intravascular injection. There is no consensus on the limit of vasopressin that should be used in a procedure but a maximum of 4 to 6 units has been proposed.[57] Repeat dosing can be performed at approximately 45 minutes duration if bleeding increases. The full duration of action of vasopressin is believed to be 2 to 8 hours. Intravascular injection or overinjection has been associated with cardiovascular complications such as severe bradycardia, hypertension, and even death. Judicious use is imperative in patients with prior cardiovascular issues or significant renal disease.

Fluid Management and Distension Media

Contemporary hysteroscopic surgery has evolved to use 1 of 2 fluid distending media; electrolyte-rich or electrolyte-poor depending on the type of energy used for the procedure. Electrolyte-poor solutions such as 5% dextrose, 1.5% glycine, 3% sorbitol, or 5% mannitol must be used with monopolar energy to allow for monopolar current to be effectively focused and prevent it from getting dispersed throughout the uterus. Electrolyte-rich solutions include normal saline and lactated Ringer solutions, which are used in conjunction with bipolar energy.

Recommendations are made to use an intrauterine pressure of 70 to 80 mm Hg, which is approximately equal to the mean arterial pressure for the average patient. The goal is to decrease the risk of intravasation due to higher pressures. If visualization is decreased because of bleeding or large pathology and higher pressures are necessary, the pressure may be increased for a short period to achieve adequate visualization and facilitate completion of the procedure.

There are various ways to instill fluid in a hysteroscopic procedure, including gravity for fluid pressure with each increase in height of 0.3 m increasing the fluid pressure by 25 mm Hg. This can be assisted by a pressure bag that continues flow to the hysteroscopic system even with low levels of fluid. We recommend the use of automated systems for most operative hysteroscopies, given their ease of use and delivery of constant pressure and continuous flow of the distension media.

It is important to monitor the "fluid deficit" for patients during each procedure. There are many automated systems now in use that automatically account for the input and output of fluid. If there is significant bleeding during the procedure, this should also be acknowledged as it can artificially increase the amount of return and underestimate the fluid deficit. There are also reports of incorrectly filled fluid bags that can be as much as 6% higher than the 3L stated on the bags.[58] These limitations make it favorable to use an automated system when available.

The Technology

Hysteroscopic myomectomy is the conservative minimally invasive procedure used to definitively resect submucosal fibroids. Its low-risk profile and excellent outcomes make it a mainstay of treatment for symptomatic submucosal fibroids.[59] There are numerous technologies that can be used with the goal of removing the fibroid in its entirety whether it is a G0, G1, or G2 type fibroid. There is a plethora of hysteroscopic devices used for resection of leiomyoma, which are reviewed in the following sections.

Wire loop resectoscope

The wire loop resectoscope is a commonly used instrument in a hysteroscopic myomectomy, using an operative hysteroscope (Resectoscope) (**Figs. 4–6**). Ideally, a 12° scope would be used to keep the tip of the wire loop in view throughout the entire procedure. Use of a 0° scope limits visualization. The resectoscope can be used with either monopolar or bipolar current. A study looking at monopolar versus bipolar electrosurgery looked at side effects after hysteroscopy. It was noted that bipolar

Fig. 4. Bipolar loop electrode used for hysteroscopic myomectomy of large type 1 submucosal myoma.

electrosurgery had a better safety profile because of the use of isotonic solution to distend the endometrial cavity. It is critical to use the correct distention medium when using the electrosurgery as discussed previously in this chapter. The monopolar device requires an electrolyte-poor solution, which was found to cause significant electrolyte disturbance in this study. Patients' serum sodium levels dropped by approximately 5 mmol/L (138.7 mmol/L to 133.8 mmol/L).[60] Monopolar devices are also known to cause higher thermal spread because of their low-frequency current, which penetrates further into the tissue and spreads further from the point of contact. This can inadvertently lead to thermal damage of the surrounding endometrium and myometrium during dissection. Bipolar current remains between the electrodes of the device and is found to have a depth of penetration of less than 1 mm as compared with 3 to 5 mm with monopolar systems.[61] The loop electrode is used to resect tissue starting at the cephalad portion of the myoma and moving caudad, shaving off pieces with electrosurgery while maintaining hemostasis. This movement prevents the unnecessary risk of perforation that can occur with a forward caudad to cephalad motion. Bipolar devices have higher coagulation capacities, which prevents the need for repeated coagulation during a procedure due to bleeding. It is important to continue the resection to include the intramural portion of the submucosal fibroid, after separating it within the pseudocapsule plane. Manipulating the intrauterine pressure is

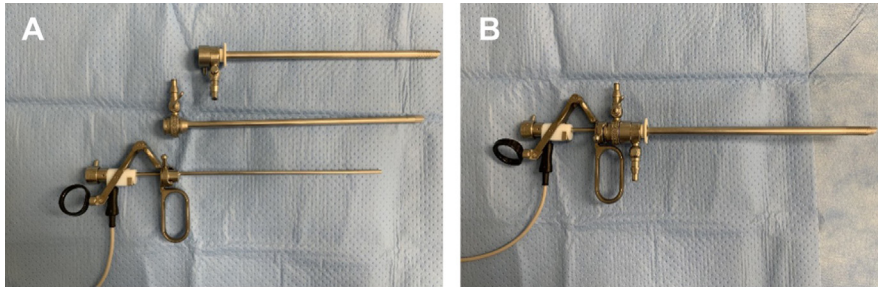

Fig. 5. (*A*) Resectoscope with bipolar cord attached, inflow and outflow channels shown in ascending order. (*B*) Resectoscope with bipolar cord attached, inflow and outflow channels attached.

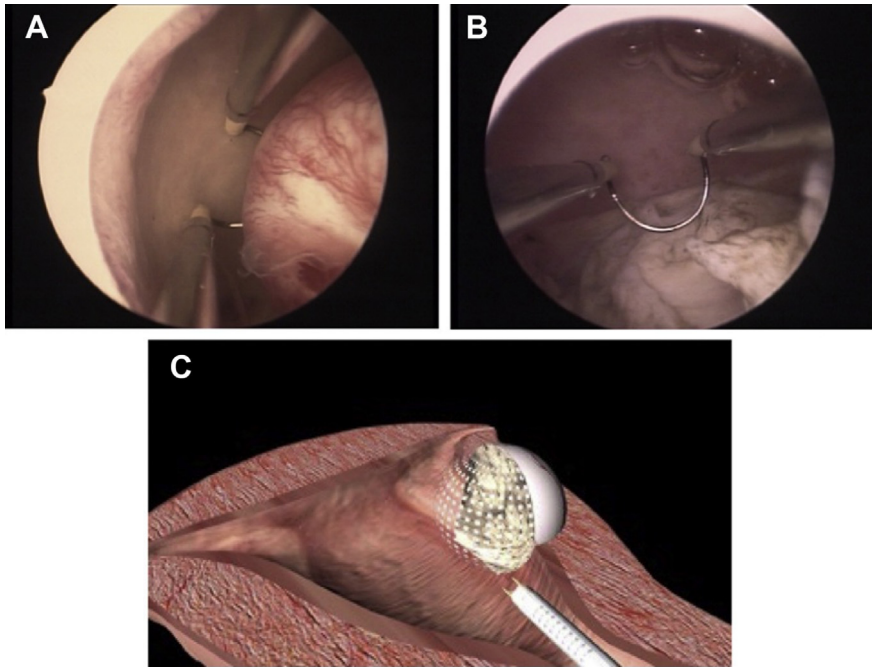

Fig. 6. (*A*,*B*) Slices of the submucosal myoma are progressively resected using the electrosurgical loop. (*C*) The Cold Loop technique is used to bluntly dissect the fibroid from the surrounding myometrium in the pseudocapsule plain. (*From* Mazzon I, Favilli A, Grasso M, Horvath S, Di Renzo GC, Gerli S. Is Cold Loop Hysteroscopic Myomectomy a Safe and Effective Technique for the Treatment of Submucous Myomas With Intramural Development? A Series of 1434 Surgical Procedures. J Minim Invasive Gynecol. 2015;22(5):792-798. https://doi.org/10.1016/j.jmig.2015.03.004; with permission.)

important to allow the fibroid to protrude further into the uterine cavity and facilitate complete resection. The procedure is limited by the maximum allowable fluid deficit. As discussed previously, a higher fluid deficit with isotonic electrolyte solution is permissible compared with an electrolyte-poor solution, which causes greater serum electrolyte disturbances. Once the predetermined deficit is reached, the procedure should be concluded, and a staged procedure can be considered later if needed.

Cold loop dissection

Cold loop dissection (**Fig. 7**) is another option for removal of submucosal fibroids that is advocated for because of its low-risk profile and its respect for tissue integrity, by taking advantage of the pseudocapsule and using this plane for blunt dissection. This technique is considered optimal for fibroids with an intramural component because of its safety profile and decreased risk to surrounding tissue. First introduced by Mazzon in 1995,[62] this technique can be combined with the resectoscopic technique to achieve complete removal of the deeper portions of types 1 and 2 submucosal myomas.[63] The same resectoscope that was described earlier is used with a few additional steps. The technique begins with normal dissection of the intramural component of the fibroid with monopolar or bipolar electrocautery. When the level of the endometrium is reached, it is critical to stop dissecting the fibroid tissue with electrocautery. The next step is to find and develop the plane between the myoma

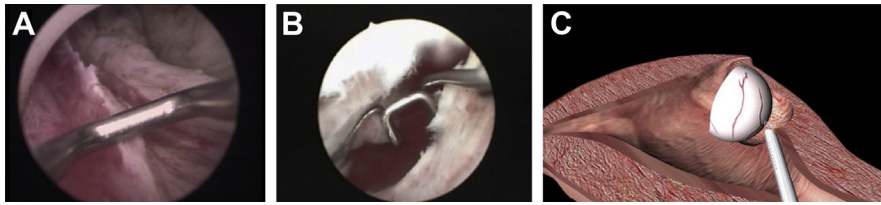

Fig. 7. (*A*) The electric cutting loop is subsequently replaced with a cold loop, which is inserted into the cleavage plane and repeatedly applied along the surface of the myoma. (*B*, *C*) Then the cold loop is used to detach the fibroconnective bridges that anchor the myoma to the pseudocapsule. (*From* Mazzon I, Favilli A, Grasso M, Horvath S, Di Renzo GC, Gerli S. Is Cold Loop Hysteroscopic Myomectomy a Safe and Effective Technique for the Treatment of Submucous Myomas With Intramural Development? A Series of 1434 Surgical Procedures. J Minim Invasive Gynecol. 2015;22(5):792-798. https://doi.org/10.1016/j.jmig.2015.03.004; with permission.)

and the myometrium. There are various cold loop attachments that can then be used to bluntly dissect the connective tissue that anchors the fibroid to the surrounding myometrium. As more of the myoma enters the cavity after separation from the surrounding tissue, it can be removed using electrocautery if desired. A large retrospective review of 1215 patients showed a completion rate of 83.7% with one surgical procedure. And importantly, the complication rate was 0.84% with no perforations in this cohort.[62]

For illustration of a combination of resectoscopic myomectomy and the cold loop technique, please refer to Video 1.

Tissue extraction devices

Tissue extraction devices for hysteroscopic myomectomy work by using fragmentation and suction for simultaneous dissection and removal of tissue from the uterine cavity. There are various brands that have come on the market (eg, Myosure, Truclear, Symphion) and are mainly used for types 0 and 1 intrauterine leiomyomas (**Figs. 8** and **9**). A rotating blade incises the fibroid, and it is suctioned into a straining canister to separate the tissue from distension media for pathologic evaluation after the procedure. This technique alleviates the need for removal of fibroid "chips" from the cavity and it is easier for trainees to learn. A reusable 0° hysteroscope is coupled with a

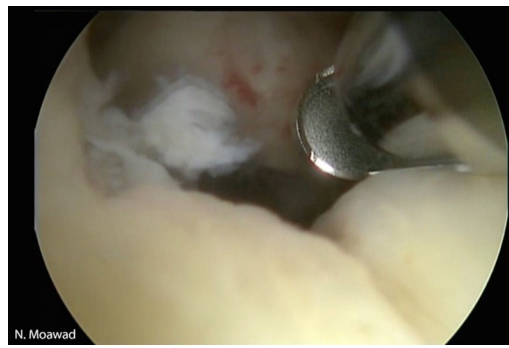

Fig. 8. Hysteroscopic tissue removal systems are the most recent advances in hysteroscopic myomectomy.

Fig. 9. Hysteroscopic tissue removal systems (*Left*: Myosure; *Right*: TruClear). (*From* Meulenbroeks D, Hamerlynck TW, Saglam-Kara S, Van Rijssel NK, Van Vliet HA, Schoot BC. Hysteroscopic Tissue Removal Systems: A Randomized In Vitro Comparison [published correction appears in J Minim Invasive Gynecol. 2017 Nov - Dec;24(7):1245]. J Minim Invasive Gynecol. 2017;24(1):159-164. https://doi.org/10.1016/j.jmig.2016.08.829; with permission).

single-use tissue extraction device that is inserted into an operative channel. These devices are disposable and require specific tubing to be connected to various fluid management systems. There are, however, limitations with these devices. First, the cost of the single-use elements is high and may be prohibitive to certain patients or in certain low-resource environments. It is also difficult to resect fundal fibroids as well as the deeper portions of types 1 and 2 fibroids with these devices. Lastly, some studies have found that dense myomas or those with calcifications can dull the rotating blades and make efficient or complete extraction difficult. One study showed that switching to a resectoscope in these cases allowed for finalization of the procedure.[64] However, another meta-analyses showed statistically significant improvement ($P = .002$) in complete resection of pathology when tissue extraction devices were used.[65] Depending on the size, makeup, and location of the fibroid, the surgeon should decide their preference for the type of device for submucosal fibroid resection.

Comparison of device type. As mentioned previously, the size, number, and type of the myomas encountered can affect the success rate of each procedure. A size greater than 3 cm is positively correlated with increased risk for need for multiple procedures.[38] A systematic review of hysteroscopic removal of submucosal fibroids reiterated that the classification of the fibroid is what is most related to the success rate for complete removal. Types 0 and 1 have a higher likelihood of complete resection than type 2.[66] In another cohort study, the size of myomas resected was also directly correlated with the likelihood of success for completion in a single-step procedure (OR 1.052). The larger the myoma, the more likely it would need to be performed in a multistep procedure.[67] The same study found that a type 0 fibroid had a 100% chance of resection in a single-step procedure, whereas the likelihood of removing a type 2 fibroid in a single-step procedure decreased to 82.55%. A systematic review of hysteroscopic removal of submucosal fibroids reiterated that the classification of the fibroid is what is most related to the success rate for complete removal. Types 0 and 1 have a higher likelihood of complete resection than type 2.[66] There is no doubt that the characteristics of the myoma will determine the probability of successful completion.

Some studies have attempted to discern which types of devices might have a high likelihood of success. A study looking specifically at tissue extraction devices found that it was not the device but the size of the fibroid that determined success. In that study, fibroids greater than 40 mm had a 48% chance of complete resection during an initial surgery and 10% of patients required further surgical intervention.[68] The efficacy of the resectoscope in removing submucosal fibroids shows mixed data. Litta

and colleagues[69] noted a 100% rate of complete resection of types 1 and 2 with the bipolar resectoscope. Similarly, a review by Friedman and colleagues strongly stated that the strength of the resectoscope lies in its ability to tackle type 2 myomas.[70] A recently published study of 53 patients indicated that the newest iteration of the Myosure device completely resects type 2 fibroids in 96% of procedures.[71] The purported benefits of hysteroscopic tissue extraction devices lie in their improved visualization as this leads to shorter operative times.[72,73] However, there are critiques that these studies that look at operative times do not account for the difficulty in removal of type 2 myomas, which is more often undertaken with the resectoscope. Yet another review by each provider must choose their technique based on level of comfort with each device as well as size and type of fibroid encountered. An individualized approach to each patient and procedure is recommended.

TECHNICAL TIPS AND TRICKS

It is important for the surgeon to choose the best tool for the pathology encountered. It is important to understand how each device is used and ensure proper setup. The surgeon must understand how to troubleshoot the hysteroscopic and resectoscopic devices, how to properly adjust and manage fluid media and intrauterine pressure, and how to quickly diagnose and treat complications such as fluid overload or embolism. Each procedure should be individualized depending on the intrauterine pathology. A perfect example is the combination of dissecting the pseudocapsule of a fibroid using the cold loop technique, even if using the regular monopolar and bipolar electrodes without energy and using the energy to resect the fibroid with energy as it protrudes into the uterine cavity. Merging these 2 modalities (cold loop and electrosurgical resection) facilitates complete resection of the deeper intramural portions of fibroids while minimizing thermal damage to the surrounding myometrium and decreasing the risk of uterine perforation. A large type 0 fibroid may be faster to approach using the tissue removal device, whereas a deeper type 1 or 2 fibroid, or a fundal fibroid, will lend itself better to resection using a combination of the wire loop resectoscope and the cold loop technique. Tactfully varying the intrauterine pressure periodically to allow the deeper portions of the fibroid, particularly types 2 and 3, to protrude into the uterine cavity, will facilitate the complete resection of these more challenging fibroids. The intrauterine pressure can be increased periodically to tamponade bleeding to avoid excessive use of energy and associated thermal damage. Withdrawal of the hysteroscope to remove fibroid chips and reinsertion of the hysteroscope should be kept to a minimum, to decrease the length of the procedure and the inevitable bleeding that ensues upon removal of the scope. Decreasing the number of times the scope is removed and reinserted increases efficiency and prevents delays caused by reestablishing visualization of the surgical field after removal of the device. Above all, the goal is to decrease severe morbidity including the rare, but catastrophic, air embolism that can be caused by the scope acting as piston forcing air/gas bubbles into the transected blood vessels.

COMPLICATIONS

Fluid Overload

As discussed earlier, fluid selection is an important part of the procedure itself. Fluid deficit limits were proposed as greater than 1000 mL of electrolyte-poor solution in a healthy, reproductive-age woman or 2500 mL deficit of isotonic, electrolyte-containing solution in a healthy, reproductive-age woman.[74 75] Fluid overload, although rare, is a known complication of hysteroscopy that can become quite

serious. It only occurs in up to 0.2% of cases but physicians performing this procedure should be comfortable with the symptoms of fluid overload as well as its prevention and basic management. Fluid overload is due to absorption of a high volume of fluid through intravasation, transtubal loss, and/or uterine perforation.[74] Risk factors for fluid overload are related to numerous patient factors as well as distention media used, intrauterine pressure, or prolonged operative times.

Patient factors include age and comorbid conditions. Young, healthy patients can tolerate a large amount of fluid absorption without issue. However, older patients or those with cardiopulmonary disorders, anemia, or renal dysfunction are at higher risk for complications. Volume overload, electrolyte abnormalities, and neurologic sequelae are the known side effects of excess fluid absorption. A patient's mean arterial pressure should be noted for these procedures. If the fluid distension pressure is higher than the patient's mean arterial pressure, fluid will more readily be absorbed into the vasculature. Most intrauterine surgery is now performed with saline distention media and bipolar energy, hence minimizing the risk of electrolyte imbalance and hyponatremia, but fluid overload is still a concern. Patients without comorbid conditions can tolerate up to 2500 mL of isotonic fluid deficit without sequelae. However, those with cardiac or pulmonary disorders can develop pulmonary edema and subsequent right heart strain due to excess fluid. Dependent on a patient's age, size, and other medical conditions, the limit of fluid deficit changes.

The type of distension medium used is also important to take into consideration when discussing the effects of overload. Electrolyte disturbances such as hyponatremia and hypo-osmolality should be taken into consideration. As discussed previously, with the use of monopolar electrocautery, it is necessary to use an electrolyte poor media such as glycine or sorbitol to prevent excitation of electrolytes with monopolar current. In the case of use of electrolyte poor fluid for distension, absorption can more readily cause electrolyte imbalance leading to neurologic sequelae. A decrease in serum tonicity forces increased flow of water across the blood-brain barrier, which causes the brain edema with symptoms being more pronounced depending on the abruptness of the change in tonicity.[76] Patients may show symptoms of fatigue, dizziness, gait disturbances, nausea and vomiting, muscle cramps and then confusion, and eventually lethargy and even mortality.[77]

The type of procedure performed also plays a role in fluid overload. When parts of the myometrium are resected, as in many operative hysteroscopy procedures, disrupted blood vessels are exposed to fluid under pressure, which increases intravascular absorption. Any procedure that may cause increased myometrial penetration will thereby increase absorption. Myomectomy carries greater risk because of the large blood vessels often found surrounding the leiomyomata. Larger fibroids also increase operative time, further prolonging the patient's exposure to fluid absorption. Lastly, the need to increase fluid pressure for better visualization can also lead to fluid overload as discussed with patient characteristics.

Air Embolism

Air embolism can occur because of the use of gaseous media, gas introduced with fluid media, or creation of gas bubbles with vaporization during hysteroscopic electrosurgical procedures. Gas embolism can cause cardiovascular collapse and pulmonary edema. The classic "mill wheel" murmur is heard with acute changes in heart rate—either bradycardia or tachycardia. Acute management of gas embolism is out of the scope of this article but the anesthesia team caring for the patient should be quick to recognize signs of cardiovascular collapse to inform the surgical team of complications and treat quickly and efficiently.

Prevention of gas embolism is key and there are some important preventive steps that should be taken. The patient should never be placed in Trendelenburg position. During the priming process before initiation of a procedure, all air should be purged from the tubing before insertion into the uterus. This improves visualization and prevents the introduction of air bubbles into the uterine cavity. Pressure of less than 125 mm Hg should be used when possible to prevent forcing of gas into the vasculature. Insertion and removal of the devices used can also force gas into the cervix. Therefore, limiting the insertion and removal of the scope is also ideal as this is associated with increased risk of air or gas emboli.[78] In one study, gas embolism was significantly higher with a fluid deficit of greater than 1000 mL compared with less than 1000 mL.[79] Respecting fluid deficit limits can help to prevent gas embolism and not just fluid overload.

Bleeding Complications

Significant life-threatening bleeding is rare with hysteroscopic myomectomy, but if encountered, balloon tamponade is recommended as a fast, safe, and cost-effective management tool.[80] As mentioned previously, the use of bipolar or monopolar electrosurgery can facilitate coagulation of encountered vasculature. Care must be taken to ensure appropriate depth of electrosurgery and to avoid excessive thermal spread.

Perforation

Every patient should be counseled about the risks of possible perforation during hysteroscopy. Perforation is a rare complication of hysteroscopic myomectomy and is most commonly encountered at the time of cervical dilation. Cervical stenosis is a risk factor, such as in nulliparous or postmenopausal patients or patients with a history of cervical excisional procedure or cryotherapy. Perforation during the myomectomy is more common in cases of deep myomas involving the myometrium such as types 2 and 3 fibroids and is more common with fundal or cornual fibroids. If perforation using the activated resectoscope loop is encountered, laparoscopy should be performed because of the high risk of thermal damage to the bowel or bladder and the risk of bleeding.[80]

CLINICAL OUTCOMES OF HYSTEROSCOPIC MYOMECTOMY

Staged Procedures

Hysteroscopic procedures have improved in many ways as outlined in this article; however, there are some fibroids that still evade even the most advanced technology. As discussed earlier in detail, the classification of the fibroid plays a large role in determining the likelihood of complete resection with type 2 fibroids being the most difficult to remove. There are 2 classification systems that seek to preoperatively stratify myomas based on suspected level of surgical difficulty: STEP-W score (Lasmar's classification) and the ESGE classification (also with a Wamsteker modification).[81 29] The STEP-W classification was previously mentioned and outlined in this article. New guidelines from the International Society for Gynecologic Endoscopy (ISGE) recommend using the STEP-W classification preoperatively to best counsel patients on the potential need for repeat surgical procedures and to assist surgeons in understanding suspected degree of difficulty.[82] This system uses several imaging characteristics to assess the degree of difficulty of hysteroscopic myomectomy and makes recommendations for treatment options. The goal with the utilization of these systems is to appropriately plan for procedures including the possibility of the need for 2-step

procedures or even counseling against hysteroscopic myomectomy as a primary treatment choice.

When hysteroscopic myomectomy is complicated by fluid overload, patient intolerance, or concerns for other dangerous sequelae, they should immediately be terminated. However, if these concerns do not arise, then there are some techniques that can be attempted to prevent the need for repeat procedures due to incomplete resection. One such technique is called the multiple slicing sessions technique, where portions of the fibroid that are intrauterine are dissected to the level of the endometrium as usual. Next, a combination of "hydromassage," a technique that induces rapid changes in intrauterine pressure, and bimanual massage are used to stimulate uterine contractions forcing more of the fibroid into the uterine cavity for further resection.[83] In situations in which providers are concerned about the difficulty of the procedure, ultrasound guidance should be requested to facilitate safe removal.[84 85]

Abnormal Uterine Bleeding

Multiple studies have reported a high success rate of 70% to 99% with hysteroscopic myomectomy. The rate depends on several variables, including the size, number and location of the fibroids, as well as the surgeon's expertise and whether resection was complete or incomplete. The rate of recurrent abnormal bleeding naturally increases with time, because of regrowth or recurrence of fibroids, incomplete removal, and the development of other etiologies for AUB.[80]

Fertility outcomes

Submucosal leiomyomas are often implicated in the workup of patients with infertility. Hysteroscopic myomectomy is often discussed with patients as part of a grander treatment plan when infertility is diagnosed. However, literature is currently inconsistent in its recommendations for patients with myomas who are seeking fertility treatment. The Practice Committee of the American Society for Reproductive Medicine (ASRM) created a guideline paper that thoroughly discusses the research centered around fertility and leiomyomas.[24] The authors are verbose in their censure of the literature and the difficulty in drawing clear conclusions about true links between subfertility and uterine leiomyomas. Criticisms include variations in types of fibroids studied, ages of patients seeking pregnancy, and inconsistency in whether the patients are undergoing assisted reproductive technology (ART) or attempting spontaneous pregnancy. Also, some studies include submucosal fibroids and others do not. Some articles look only at patients with intramural or subserosal fibroids. Without consistency in the type of fibroids studied, it is difficult to understand what role the type of fibroid plays in infertility. Cassini and colleagues reported fertility improvement from 27% to 43% after hysteroscopic resection of type 0 fibroids.[86 87] Size is another confounder in appropriately studying fibroids; patients can have one large, solitary fibroid or multiple, small fibroids both of which can distort reproductive anatomy in their own way. In a study of 168 women with at least one fibroid greater than 5 cm in size, without distortion of the endometrial cavity, removal still offered positive impacts on ART.[88] In an RCT of patients with at least one intramural fibroid $\leq$4 cm in size, removal did not improve fertility outcomes.[86] Fortunately with all this debate, there are studies that show the removal of subserosal and intramural fibroids does not have a negative impact on fertility.[89] A recent study echoed this finding but with submucosal leiomyomas stating that patients who have undergone surgical correction have similar pregnancy outcomes overall to those patients who have not undergone surgery.[90] Practitioners should be aware of the lack of data to support a correlation between fibroids and subfertility. We seek to better understand the type, size, and

symptoms that indicate the need for myomectomy in the patient undergoing workup for subfertility.

SUMMARY

Submucosal fibroids have been implicated in AUB and can be associated with subfertility. Accurate characterization of the fibroids with imaging studies and hysteroscopy is essential to guide the management strategies. Hysteroscopic myomectomy is a safe and effective minimally invasive option for submucosal myomas, with excellent results. Several technological advances have recently been introduced to improve the safety and efficiency of the procedure, even as an office hysteroscopic procedure in the proper setting and with adequate training.

CLINICS CARE POINTS

- Hysteroscopic myomectomy should be used for removal of all intrauterine fibroids including types 2 and 3 fibroids
- Appropriate workup for patients includes history, physical examination, imaging, and shared decision-making concerning patient's desire for future fertility or uterine-sparing surgery
- Practitioners should be familiar with the available technology for hysteroscopic myomectomy and their various indications (ie, cold loop dissection, resectoscopic surgery, and tissue removal systems)
- Optimizing safety and visualization during a procedure is critical, it is important to prepare especially for cases of large submucosal leiomyomas
- Clinicians performing hysteroscopic myomectomy should be able to quickly diagnose and correct common, sometimes morbid, complications of this procedure
- If safety is compromised or if no further intervention can be performed, a multistep procedure is appropriate
- There is a lack of consensus about fibroids and infertility; hysteroscopic myomectomy does appear to improve pregnancy outcomes but does not have the same positive impact on reducing miscarriage rates

DISCLOSURE

N.S. Moawad: Consultant, Cooper Surgical, Inc, and Myovant Sciences; H. Palin: Nothing to disclose.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found online at https://doi.org/10.1016/j.ogc.2022.02.012.

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