ACOG
The American College of Obstetricians and Gynecologists

ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 228 *(Replaces Practice Bulletin Number 96, August 2008)*

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Management of Symptomatic Uterine Leiomyomas

Uterine leiomyomas (fibroids) are the most common solid and symptomatic neoplasm in women. They are the leading indication for hysterectomy (1, 2), which is a definitive and effective surgical treatment for leiomyoma. However, many patients benefit from and seek out management options other than hysterectomy because they desire future childbearing or wish to retain their uterus. The purpose of this Practice Bulletin is to provide updated evidence-based recommendations for the medical, procedural, and surgical management of symptomatic leiomyomas. Discussion of the use of morcellation in the surgical management of leiomyomas is beyond the scope of this document and is addressed in a separate American College of Obstetricians and Gynecologists (ACOG) publication (3).

Background

Definition

Uterine leiomyomas are solid neoplasms composed of smooth muscle cells and fibroblasts. Leiomyomas vary in size and location. A standardized leiomyoma subclassification system was developed by the International Federation of Gynecology and Obstetrics (FIGO) to describe uterine leiomyoma location in relation to the endometrial and serosal surfaces (Fig. 1) (4).

Epidemiology

Uterine leiomyomas are common and estimated to occur in up to 70% of women by menopause (5). However, the true incidence and prevalence remain unknown because most cases are asymptomatic and likely go undiagnosed, with approximately only 25% being clinically significant enough to require intervention (5). The incidence of leiomyomas increases with age until menopause (6). Other factors that are associated with an increased risk of uterine leiomyomas include premenopausal status, family history, increasing interval since last birth, hypertension, and obesity (5, 7, 8). Factors that are associated with a decreased incidence of uterine leiomyomas include increasing parity and use of oral hormonal contraceptives or depot medroxyprogesterone acetate (DMPA) for any duration (5).

The prevalence rate of uterine leiomyomas is 2–3 times higher among Black women compared with White women (9, 10). The prevalence of uterine leiomyomas does not appear to be higher among Latina and Asian women as compared with White women, but data are far more limited for these populations (10).

Marked differences exist in disease presentation, severity, treatment, outcomes, and quality of life for Black women compared with White women with uterine leiomyomas. Black women typically develop uterine leiomyomas at an earlier age, are more likely to be anemic, develop clinically significant disease at an earlier age, and have larger uteri at the time of diagnosis (11–13). These observed differences are likely due in large part to systemic racism, as well as to social determinants of health. For instance, U.S.-born Black women who self-report experiencing racism have an increased risk of uterine leiomyomas (14). Experiences of racism can delay women from seeking care for leiomyoma symptoms until they are severe, and racial bias in medicine at the systemic and individual levels may affect the quality of diagnosis and treatment they receive (14). In

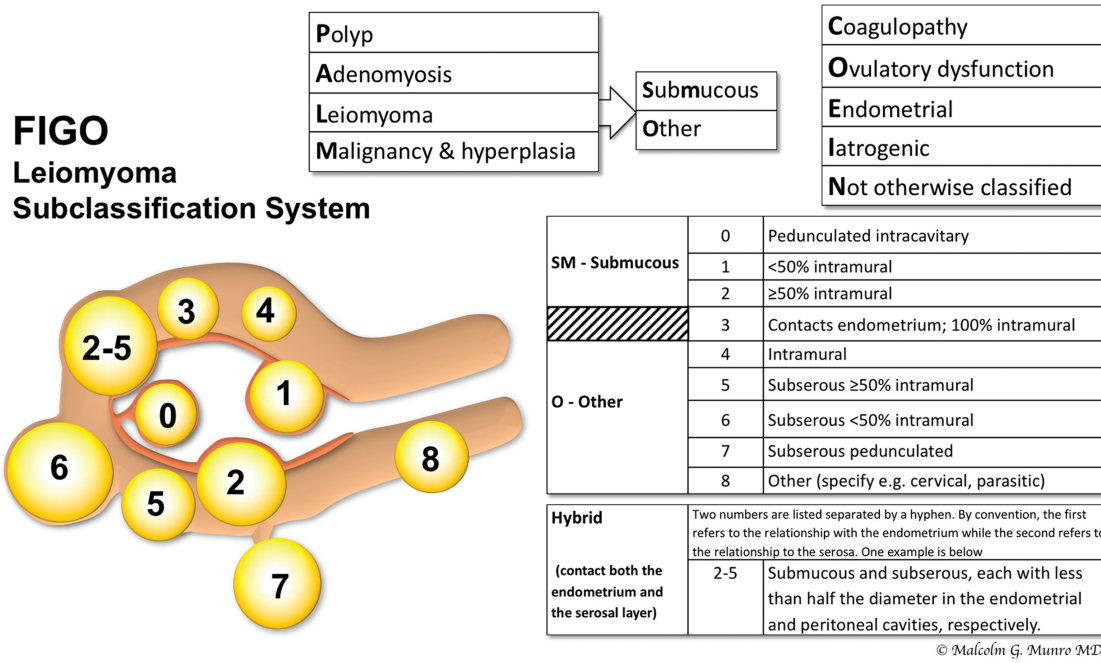

Figure 1. FIGO Abnormal Uterine Bleeding System 2 classification system including the FIGO leiomyoma subclassification system. Abbreviation: FIGO, International Federation of Gynecology and Obstetrics. (Reprinted from Munro MG, Critchley HO, Fraser IS. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. FIGO Menstrual Disorders Committee [published erratum appears in Int J Gynaecol Obstet 2019; 144:237]. Int J Gynaecol Obstet 2018; 143:393–408.)

addition, differences in social determinants of health such as limitations on access to quality education, jobs, stable housing, safe neighborhoods, nutritious foods, and health insurance are associated with inequitable leiomyoma treatment among Black women (10, 15). Racial disparities in treatment, such as higher rates of hysterectomy and myomectomy (compared with nonsurgical therapy) and open hysterectomy (compared with minimally invasive approaches) have been reported among Black women compared with White women even after adjusting for clinical factors such as uterine weight (10, 16).

Black women also are significantly underrepresented in uterine leiomyoma research (10). The Comparing Options for Management: Patient-centered Results for Uterine Fibroids (COMPARE-UF) registry aims to provide comparative data on patient-centered treatment outcomes among a racially and ethnically diverse population of premenopausal women with uterine leiomyomas (10, 17). Additional research that is explicitly focused on health disparities in uterine leiomyoma care also is needed to help reduce inequities and improve care.

Symptoms

Prolonged or heavy menstrual bleeding, with or without anemia, and the sequelae of uterine enlargement are the most common presenting symptoms of patients with uterine leiomyomas. Abnormal uterine bleeding associated with leiomyomas is referred to as AUB-L (Fig. 1) (18). Pelvic pressure, urinary frequency, and constipation also can result from the presence of large leiomyomas within the pelvis and are collectively referred to as bulk symptoms (2, 18, 19).

Diagnosis

Clinical evaluation for suspected leiomyomas begins with a complete medical history and an abdominal and pelvic examination. Transvaginal ultrasonography is useful as a screening test to assess for leiomyomas (18). Sonohysterography is useful to identify and distinguish between type 0, type 1, and type 2 leiomyomas, in which the percentage of submucosal component varies (Fig. 1) (18). Hysteroscopy is useful to distinguish between type 2 and type 3 leiomyomas, in which there is contact with the endometrium but there may not be distortion of the endometrial cavity (Fig. 1). Magnetic resonance imaging can be useful in surgical planning, determining vascularity and degeneration, and distinguishing between type 4 and type 5 leiomyomas, in which there is an intramural component, with or without a submucosal component (Fig. 1) (4).

Diagnostic evaluation should exclude other causes of AUB and pelvic masses (18). Clinicians also should consider the possibility that a uterine mass may be a malignant sarcoma. (For more information, see ACOG Committee Opinion No. 822 *Uterine Morcellation for Presumed Leiomyomas*) (3).

Treatment Options

There are a variety of treatment options for leiomyomas, including expectant, medical, interventional, and surgical therapies. Although evidence exists regarding outcomes with specific therapies, comparative effectiveness data are lacking for leiomyoma management options (20). When considering treatment options, patient-specific symptoms and severity should be addressed. If a patient describes symptoms that are neither severe, nor debilitating, expectant management may be appropriate. Medical treatments primarily address bleeding symptoms. Procedural interventions and surgical approaches treat bulk symptoms by decreasing uterine mass. Although there is evidence to suggest that nonsteroidal anti-inflammatory drugs are associated with modest improvement in heavy menstrual bleeding (21), there is no evidence for their use specifically for the treatment of AUB-L (20). Complementary and alternative medicines, including acupuncture and herbal preparations, are used by many patients to treat uterine leiomyomas (22); however, there is a lack of evidence to support their efficacy (23, 24).

Given that the threshold and preference for treatment is individual, a patient-centered, shared decision-making approach should be used when devising a management strategy so that patients can make an informed decision that best meets their short-term and long-term goals (17). Patients should be counseled on all treatment options that are available and accessible, with a discussion of the risks and benefits of the various treatment options to guide patient counseling and shared decision making.

Clinical Considerations and Recommendations

▶ ***What are the benefits and risks of expectant management for uterine leiomyomas?***

Expectant management of uterine leiomyomas can be considered for patients who are asymptomatic or for those who do not desire intervention. Existing data regarding expectant management of leiomyomas primarily come from comparator arms of clinical trials of active therapy. Among patients who opt for expectant management of uterine leiomyomas, bleeding characteristics, hemoglobin levels, and leiomyoma size do not appear to change in a clinically meaningful way at short-term follow-up of 1 year or less (20). If a patient is asymptomatic, or simply does not desire active management, it may be appropriate to consider long-term expectant management. Patients should be counseled to return for follow up if symptoms become bothersome or if active management or pregnancy is desired.

Expectant management may be particularly appropriate in patients who do not have bothersome symptoms or are experiencing perimenopausal symptoms (25). Although the prevalence of clinically significant leiomyomas peaks in the perimenopausal years, it declines after menopause (26) because leiomyomas do not have the necessary levels of estrogen and progesterone to sustain their development and growth (27). Additionally, menopause is a time when abnormal or heavy uterine bleeding caused by benign pathologies may resolve spontaneously with the cessation of menses.

▶ ***What are the benefits and risks of medical management for uterine leiomyomas?***

Medical treatment options for uterine leiomyomas include agents that address only bleeding symptoms (gonadotropin-releasing hormone [GnRH] antagonists, levonorgestrel-releasing intrauterine devices [LNG-IUDs], contraceptive steroids, and tranexamic acid) and medications that reduce both bleeding and leiomyoma size (GnRH agonists and selective progesterone receptor modulators). Some medical therapies for uterine leiomyomas are indicated for long-term use, whereas others are meant to be a bridge to surgical treatments, interventional procedures, or menopause. Because there is insufficient comparative evidence to guide recommendations on first-line medical therapy (20), the following discussion presents medical management options according to symptoms addressed rather than in order of clinical preference. Treatment decisions should be guided by an individual patient's symptoms and treatment goals.

Medical Therapies for Bleeding Symptoms

Gonadotropin-Releasing Hormone Antagonists With Hormonal Add-Back Therapy

An oral GnRH antagonist with hormonal add-back therapy can be considered for the treatment of AUB-L for up to 2 years. Elagolix is an oral gonadotropin-releasing hormone antagonist that results in reversible, dose-dependent, suppression of gonadotropins and ovarian sex hormones. The combination of elagolix (300 mg

twice daily) with add-back therapy (1 mg estradiol and 0.5 mg norethindrone acetate once daily) is U.S. Food and Drug Administration (FDA)-approved for up to 24 months of use to treat heavy menstrual bleeding associated with uterine leiomyomas (ie, AUB-L) (28). The hormonal add-back therapy is indicated to offset the hypoestrogenic effects of elagolix, including hot flushes, increased mean serum lipid levels, and bone mineral density loss (29, 30).

Two randomized controlled trials and corresponding extension studies, conducted in the United States and Canada, demonstrated statistically significant improvements in menstrual blood loss, with 87.9% of study participants achieving a menstrual blood loss volume of less than 80 mL per month at 12 months (29, 30). Statistically significant improvements in menstrual blood loss were observed as early as the first month of treatment (29). Additionally, more than half of participants experienced amenorrhea at 12 months, and significant improvements in quality of life measures were observed (30).

The most frequently reported adverse events in the two randomized controlled trials and extension study were hot flushes and headache (29, 30). The effects of hypoestrogenism on hot flushes and bone mineral density are attenuated with add-back hormone therapy, and the changes in bone mineral density and lipid profiles may be reversible following discontinuation after up to 12 months of therapy (29, 30).

Data on a second oral GnRH antagonist, relugolix, combined with hormonal add-back therapy as a once daily relugolix combination therapy shows similar improvement in heavy menstrual bleeding as elagolix with add-back hormone therapy as well as similar adverse effects (31). The published data for relugolix also demonstrate improvement in pain and bulk symptoms (31). Relugolix was under FDA review for approval at the time of publication of this Practice Bulletin. For the current status, please see the FDA website (32).

Levonorgestrel-Releasing Intrauterine Devices

A 52-mg LNG-IUD can be considered for the treatment of AUB-L. Levonorgestrel-releasing intrauterine devices reduce menstrual bleeding by inducing endometrial decidualization and atrophy and have been found to decrease heavy menstrual bleeding in patients both with and without leiomyomas (33, 34). There is insufficient evidence to support the use of an LNG-IUD for the treatment of uterine leiomyoma symptoms other than bleeding (35).

A prospective, nonrandomized trial of 67 patients with uterine leiomyomas demonstrated a significant reduction in menstrual blood loss within 3 months of insertion (35). By 12 months, 40% of participants had achieved amenorrhea, and 95% of patients who were anemic at the time of insertion experienced resolution. Rates of IUD expulsion are higher in patients with uterine leiomyomas compared with patients without leiomyomas (11% versus 0–3%) (36). The risk of expulsion may be particularly increased in patients with uterine leiomyomas that distort the uterine cavity (37).

Contraceptive Steroid Hormones

Among patients with heavy menstrual bleeding without uterine leiomyomas, combined hormonal contraceptives and progestin-only pills reduce menstrual blood loss and are considered a reasonable option for initial treatment, although a 52-mg LNG-IUD appears to provide greater reduction in menstrual blood loss (38–40). By extrapolation, combined and progestin-only hormonal contraceptives are a reasonable option to consider in the treatment of heavy menstrual bleeding in patients with uterine leiomyomas, although there are limited direct data to support their effectiveness. There is no evidence to support the use of contraceptive steroid hormones to manage bulk symptoms associated with uterine leiomyomas.

A randomized trial of patients with uterine leiomyomas of 5 cm or less in diameter compared use of a combined oral contraceptive (30 mcg ethinyl estradiol and 150 mcg levonorgestrel) with a 52-mg LNG-IUD to decrease menstrual bleeding (41). In this study, menstrual blood loss decreased in oral contraceptive users during 12 months of treatment, but blood loss was significantly less in the 52-mg LNG-IUD group (41). Limited data from an uncontrolled trial of depot medroxyprogesterone acetate among 20 patients with uterine leiomyomas found a decrease in menstrual bleeding, an increase in hemoglobin levels, and a decrease in uterine leiomyoma volume during 6 months of treatment (42).

Tranexamic Acid

Tranexamic acid can be considered for the treatment of AUB-L. Tranexamic acid is an antifibrinolytic medication that prevents fibrin degradation, and it is an effective treatment for heavy menstrual bleeding (43–45). Limited data also show that tranexamic acid is associated with a statistically significant decrease in AUB-L (20).

Medical Therapies for Bleeding Symptoms and Uterine Enlargement

Gonadotropin-Releasing Hormone Agonists

Gonadotropin-releasing hormone (GnRH) agonists, either with or without add-back hormonal therapy, are

recommended for the short-term treatment of AUB-L and uterine enlargement associated with uterine leiomyomas and as a bridge to other treatment strategies. GnRH agonists induce hypogonadism, which causes a reduction in menstrual bleeding that often results in amenorrhea. Use of a GnRH agonist is a short-term management strategy that is meant to bridge treatment to interventional procedures, surgical management, menopause, or other medical therapies.

Treatment with GnRH agonists is associated with reduction in leiomyoma size and overall size of the uterus, decreased AUB-L and dysmenorrhea, and improvement in quality-of-life measures (ie, days of bleeding, pelvic pressure, pelvic pain, urinary frequency, and constipation) (20, 46). Leiomyoma regrowth, often back to pretreatment levels, is observed between 3 and 9 months after cessation of treatment, which explains why it is primarily used as a bridge therapy (20). There is a lack of long-term follow-up data regarding maintenance of treatment effects on menstrual bleeding and pain (20).

GnRH agonists often are used to reduce uterine volume before surgical therapy, which may facilitate the use of a minimally invasive surgical route, allow for a smaller incision, or enable the use of an incision type associated with decreased morbidity (46). The use of a GnRH agonist before surgical management also is associated with an increase in preoperative hemoglobin levels by an average of 0.88 g/dL (46).

Concomitant therapy with low-dose estrogen or progestin, or both, may mitigate the hypoestrogenic adverse effects of GnRH agonists, which include menopausal symptoms, unfavorable changes in lipid profile, and a decrease in bone density (20, 47). The type, dose, and route of delivery for add-back therapy varies depending on patient preference and the severity of symptoms, but a regimen of oral conjugated estrogen 0.625 mg and norethindrone acetate 2.5–5.0 mg daily is commonly used (47–50). Because of the risk of long-term hypoestrogenic adverse effects, treatment with GnRH agonists typically is limited to 6 months without add-back therapy and 12 months with add-back therapy (47).

Selective Progesterone Receptor Modulators

Although selective progesterone receptor modulators such as mifepristone and ulipristal acetate exhibit efficacy in the short-term treatment of AUB and uterine enlargement associated with uterine leiomyomas, currently they are not approved in the United States for the treatment of leiomyomas (20, 51). Ulipristal acetate is approved outside the United States, but postmarketing reports of rare but serious liver injury, including need for liver transplantation, have prompted the European Medicines Agency and other regulatory agencies to significantly limit the use of daily ulipristal acetate for leiomyoma treatment (52).

▶ ***What are the benefits and risks of procedural interventions for uterine leiomyomas?***

Uterine Artery Embolization

Uterine artery embolization (UAE) is recommended as an interventional procedure for the treatment of uterine leiomyomas in patients who desire uterine preservation and are counseled about the limited available data on reproductive outcomes. During UAE, an embolic agent is delivered through catherization of both uterine arteries, typically through a single incision, to cause leiomyoma devascularization and involution. Uterine artery embolization is consistently associated with a significant reduction in leiomyoma and uterine volume that is maintained for up to 5 years based on long-term follow-up data (20, 53). Improvements in bleeding symptoms have been observed, including increased incidence of amenorrhea, improvement in bleeding scores, and a decrease in self-reported heavy menstrual bleeding (20). Patient satisfaction and quality-of-life ratings 2–5 years after treatment are similar among patients undergoing UAE, hysterectomy, or myomectomy (20, 54).

Rates of reintervention (with hysterectomy, repeat embolization, myomectomy, medical management, or endometrial ablation) as high as 19–38% have been reported 2–5 years after UAE (20), although a recent meta-analysis demonstrated a reintervention rate of 14.4% at 60 months (55). The risk of requiring further surgical intervention within 2 years after UAE has been reported to be twofold to fivefold higher compared with hysterectomy or myomectomy (54). The risk of requiring a blood transfusion is significantly lower with UAE compared with surgical interventions (20, 54). A meta-analysis of two trials that included 277 patients total found a low incidence of transfusion among those who received UAE compared with patients who underwent surgery (odds ratio [OR], 0.07; 95% CI, 0.01–0.52) (54). And, no cases of blood transfusion were reported in a review of three studies (186 patients total) of UAE compared with myomectomy or hysterectomy (20). Compared with any type of surgery for uterine leiomyomas, UAE is associated with similar rates of major postprocedural complications (OR, 0.65; 95% CI, 0.33–1.26); however, UAE has a higher rate of minor postprocedural complications (OR, 1.99; 95% CI, 1.41–2.81) (54, 56). Major complications of UAE have been reported in 1–12% of cases and may include unplanned hysterectomy, rehospitalization,

ovarian failure, and pulmonary embolism (20, 57). Minor complications occur in 21–64% of cases and are variably defined among different UAE studies (57). Minor complications may include pain, fever, and nausea associated with postembolization syndrome; vaginal discharge; and pelvic infection. Uterine artery embolization can be performed as an ambulatory procedure and is associated with a shorter procedural time, shorter hospital stay, and faster recovery time compared with surgical interventions (54). However, the rates of unscheduled visits and readmission are higher with UAE than with surgical interventions (OR, 2.74; 95% CI, 1.42–5.26) (54).

Data are limited on the effects of UAE on fertility and future pregnancy (20), and there is conflicting evidence on the effects on ovarian reserve. Rates of ovarian failure after UAE (defined as a follicle stimulating hormone level greater than 40 IU/L at 1 year after treatment) have been reported to be as high as 12% and 18% at 12 and 24 months, respectively, which is comparable to the rates associated with hysterectomy (20). In contrast, a more recent meta-analysis of six studies and 353 participants demonstrated no effect on ovarian reserve, as measured by serum concentrations of antimüllerian hormone and follicle stimulating hormone at 12 months postprocedure, although antral follicle count in two of the studies demonstrated a significant decline at 3 months (58). Compared with expectant management, and matched for age and leiomyoma location, uterine leiomyoma treatment with UAE is associated with an increased risk of pregnancy loss (35.2% versus 16.5%; OR, 2.8; 95% CI, 2.0–3.8), cesarean delivery (66% versus 48.5%; OR, 2.1; 95% CI, 1.4–2.9), and postpartum hemorrhage (13.9% versus 2.5%; OR, 6.4; 95% CI, 3.5–11.7) (59). There is conflicting evidence on reproductive outcomes of UAE compared with myomectomy, and small sample sizes in the available studies make it difficult to draw comparative conclusions (54, 60).

Radiofrequency Ablation

Laparoscopic radiofrequency ablation can be considered as a minimally invasive treatment option for the management of symptomatic leiomyomas in patients who desire uterine preservation and are counseled about the limited available data on reproductive outcomes. Radiofrequency ablation (RFA) can be delivered by a laparoscopic, transvaginal, or transcervical approach, using ultrasound guidance to induce coagulative necrosis in targeted uterine leiomyomas. All of the approaches are similarly effective in reducing uterine leiomyoma volume and in improving quality of life metrics, but the laparoscopic approach has been studied the most rigorously (61). Although RFA is a reasonable option to consider for the treatment of symptomatic uterine leiomyomas, access to this technology is currently limited.

Although laparoscopic RFA with a leiomyoma-specific FDA-approved device has been studied primarily in nonrandomized trials (62), two recent meta-analyses summarize long-term data on the use of RFA to treat a wide variety of leiomyoma types and sizes (61, 63). In these two meta-analyses, which included over 1,800 patients, uterine leiomyoma volume reduction ranged from 32% to 66% at 12 months, and 77% at greater than 12 months follow up (61, 63). The cumulative rate of postoperative surgical reintervention for leiomyoma-related symptoms was 4.2%, 8.2%, and 11.5% at 1, 2, and 3 years, respectively (61). Statistically and clinically significant improvements were observed in health-related quality of life and symptom severity in long-term follow up (up to 36 months) (61). Complication reporting was highly inconsistent, but no serious procedural complications such as death or injury to visceral structures was reported in any of the included studies. Neither meta-analysis reported outcomes on menstrual bleeding.

In a case-series of 30 pregnancies after laparoscopic RFA, there were 26 full-term live births and four pregnancy losses (64). Although in this small case series there were no cases of preterm delivery, uterine rupture, placental abruption, placenta accreta, or intrauterine growth restriction (64), sample size precludes any definitive conclusions about risk or incidence of pregnancy complications.

Focused Ultrasound

Focused ultrasound surgery, guided by diagnostic ultrasound or magnetic resonance, is a noninvasive treatment modality that uses multiple high-intensity ultrasound waves to cause coagulative necrosis of uterine leiomyomas. Currently only magnetic resonance-guided focused ultrasound is FDA approved for the treatment of uterine leiomyomas. Limited, low-quality data suggest that magnetic resonance-guided focused ultrasound and high-intensity focused ultrasound are associated with a reduction in leiomyoma and uterine size (20, 65). However, small randomized comparative trial data suggest that compared with UAE, magnetic resonance-guided focused ultrasound is associated with less improvement in symptoms and quality-of-life measures and a higher risk of reintervention (66). In a recent meta-analysis, the rate of reintervention at 60 months was 53.9% (55). Additional data are needed before recommendations can be made regarding the use of this treatment for uterine leiomyomas.

Endometrial Ablation

Limited data suggest that AUB-L is improved with endometrial ablation and is maintained in the year

following ablation (20). However, there is insufficient evidence to make a clinical recommendation regarding the use of endometrial ablation for the treatment of uterine leiomyomas.

▶ ***What are the benefits and risks of surgical management for uterine leiomyomas?***

Surgical treatment options for uterine leiomyomas include myomectomy and hysterectomy. Goals of treatment should be defined for each patient, including desire for uterine preservation and future fertility, as well as primary symptomatology, including bleeding and bulk symptoms. The most minimally invasive route is recommended whenever feasible. Gonadotropin-releasing hormone agonists are often used to reduce uterine volume before surgical therapy (see *Medical Therapies for Bleeding Symptoms and Uterine Enlargement* earlier in this document). However, if the specimen or uterus is too large to be removed intact, or there is not a surgical orifice for intact specimen removal, such as with laparoscopic myomectomy, morcellation is required. A discussion of the role of morcellation at the time of myomectomy or hysterectomy for presumed leiomyomas is beyond the scope of this document. For more information, please see ACOG's separate publication on this topic (3).

Preoperative Anemia

Preoperative anemia is associated with a higher risk of perioperative blood transfusion and may result in increased operative morbidity and mortality (67, 68). Although there are no randomized trials that assess the efficacy of iron supplementation preoperatively, given the low risks associated with iron supplementation, it should be considered in patients who are anemic and plan to undergo myomectomy (other than hysteroscopic) or hysterectomy for symptomatic uterine leiomyomas.

Myomectomy

Myomectomy is recommended as a surgical management option for symptomatic leiomyomas in patients who desire uterine preservation or future pregnancy and are counseled about the risk of recurrence. Myomectomy is a uterine-sparing treatment option that removes accessible leiomyomas, which allows for future pregnancy. It can be performed with hysteroscopic, laparoscopic, robotic, or abdominal (laparotomy) techniques. Substantial quality-of-life improvement has been demonstrated with all routes of myomectomy (20, 69, 70). There is insufficient evidence, however, to conclude whether myomectomy improves AUB-L (20). Risk of transfusion with myomectomy does not appear to differ between laparoscopic and abdominal surgical routes, and ranges from 0% to 5% (20). Use of dilute vasopressin during myomectomy is associated with decreased operative blood loss (71, 72) and a decreased risk of blood transfusion (72). Pregnancy rates after myomectomy appear to be influenced by leiomyoma type, with submucosal leiomyomas associated with higher pregnancy rates than subserosal and intramural leiomyomas (20). Recurrence of uterine leiomyomas after myomectomy increases over time and approaches 25% at 40 months (20). In a meta-analysis, the combined reintervention rate at 60 months was 12.2% for abdominal, laparoscopic, and robotic-assisted myomectomy (55).

When myomectomy is selected for the surgical management of symptomatic uterine leiomyomas, a minimally invasive approach should be considered when feasible and appropriate. Although minimally invasive myomectomy is preferable to abdominal myomectomy whenever possible, the selection of route of myomectomy is influenced by various factors, including leiomyoma type, size, and number; surgeon training and experience; availability of requisite equipment; and preference of the informed patient. Obstetrician–gynecologists and patients should engage in a shared decision-making discussion about the risks and benefits of all approaches to myomectomy based on the specific clinical situation and in the context of each patient's values and preferences.

Hysteroscopic Myomectomy

Hysteroscopic myomectomy is a surgical treatment option for patients with isolated submucosal leiomyomas (type 0, type 1, and some type 2) who desire uterine preservation. Hysteroscopic myomectomy is an outpatient procedure with rapid return to usual activities (average of 0 days) and work (median of 4 days), and a low risk of complications (1–3%) (70, 73–75). The need for subsequent treatment after initial hysteroscopic myomectomy likely depends on characteristics of the leiomyoma removed, including size and the extent of intracavitary involvement. Smaller submucosal leiomyomas, and those that are less than 50% intramural (type 1) are more likely to be completely resected, with a lower risk of recurrence (76). Major improvements in quality of life measures and symptom severity scores have been observed in the 6–12 weeks after hysteroscopic myomectomy (70), and reintervention rates as low as 7% at 60 months have been reported (55).

Laparoscopic and Robot-Assisted Myomectomy

Laparoscopic and robot-assisted myomectomy are surgical treatment options for patients with symptomatic type

2 through type 8 leiomyomas, who desire uterine preservation, when the requisite equipment and surgical expertise are available. Surgical approach is a major determinant in return to normal activity, with shorter recovery times observed with a laparoscopic approach compared with laparotomy or mini-laparotomy (20). In an analysis of data from the Comparing Options for Management: Patient-centered Results for Uterine Fibroids registry, laparoscopic myomectomy (including robotic-assisted) was associated with a significantly faster return to work (20-day difference) and a slightly earlier return to normal activities (3-day difference) compared with abdominal myomectomy (70). Laparoscopic myomectomy also is associated with less postoperative pain, shorter hospitalization, and a 50% lower risk of postoperative fever compared with abdominal myomectomy (77). However, short-term quality-of-life outcomes are similar for laparoscopic and abdominal myomectomy, with substantial improvement reported for each procedure at 6–12 weeks after surgery (70). Systematic review data indicate that myoma recurrence risk is similar across surgical approaches (20, 77). This finding is supported by the results of a more recent retrospective cohort study, which did not show an increased recurrence rate with laparoscopic myomectomy versus an abdominal approach in patients with 1–3 uterine leiomyomas (31.3% versus 34.2%, $P=.571$) (78). However, in a separate meta-analysis of existing literature, the authors found an increased recurrence rate with laparoscopic myomectomy in patients with more than five leiomyomas (OR, 1.50; 95% CI, 1.14–1.97) (78). Another retrospective cohort study also showed an increased cumulative risk of recurrence with laparoscopic myomectomy (76.2%) compared with an abdominal approach (63.4%) at 8-year follow up (relative risk [RR], 1.67; 95% CI, 1.27–2.21); however, the study groups were not matched for important confounding variables, such as number and size of leiomyomas and use of GnRH agonists, which may have influenced the results (79). No statistically significant differences have been identified in the risk of emergency reoperation or injury to pelvic organs between surgical routes, but studies may be underpowered to address these rare operative outcomes (77, 80).

Robot-assisted laparoscopic myomectomies are associated with longer operative times compared with abdominal approaches; however, blood loss, rates of transfusion, and length of hospital stays are substantially reduced (81, 82). When compared with conventional laparoscopic approaches, the robot-assisted laparoscopic myomectomy does not offer any advantage for operating time, blood loss, or length of hospital stay; however, laparoscopic myomectomy is associated with a 4.5 times increased risk of conversion to an open approach compared with robot-assisted cases (81, 82). Data on long-term outcomes such as pain control, postoperative fertility, and leiomyoma recurrences are needed (82).

Hysterectomy

Hysterectomy is recommended as a definitive surgical management option for the treatment of AUB-L and bulk symptoms associated with uterine leiomyomas in patients who do not desire future childbearing or do not wish to retain their uterus and are counseled about the long-term health risks. A statistically significant improvement in hemoglobin has been observed at 24 months postoperatively (83, 84), and 70–90% of patients report total or substantial improvement in pressure symptoms (20, 83, 84). Significant quality of life improvement also has been demonstrated at 2 years after surgery (85). Reported risk of transfusion ranges from 0% to 20%, with no significant differences in outcomes by surgical approach; however, overall risk across all studies was difficult to determine because confounding variables such as preoperative anemia and bowel and bladder injury were not consistently reported (20).

Risks associated with hysterectomy and concomitant oophorectomy before menopause are well established and include cardiovascular, neurologic, and somatic morbidity (86–88), as well as an increased risk of mortality (86, 89). There is mixed evidence, however, on the possible long-term risks associated with hysterectomy without oophorectomy. Analyses from a cohort of patients who underwent hysterectomy with ovarian conservation have reported an increase in cardiovascular risks, particularly in individuals who underwent surgery at age 35 years or younger (66, 90). Prospective cohort studies with more diverse study populations, however, have not found increased risks of cardiovascular disease associated with hysterectomy and ovarian conservation (91, 92).

When hysterectomy is selected for the surgical management of symptomatic uterine leiomyomas, the most minimally invasive route is recommended whenever possible, and the vaginal approach is preferred among the minimally invasive approaches when it is feasible. Although the most minimally invasive approach to hysterectomy is preferred whenever possible, selection of the route of hysterectomy for benign causes such as uterine leiomyomas can be influenced by the size and shape of the vagina and uterus; accessibility to the uterus; surgeon training and experience; available hospital technology, devices, and support; and preference of the informed patient (93). Obstetrician–gynecologists and patients should engage in a shared decision-making discussion about the risks and benefits

of all approaches to hysterectomy based on the specific clinical situation and in the context of each patient's values and preferences.

In a Cochrane review of surgical approaches to hysterectomy for benign gynecologic disease, vaginal hysterectomy was associated with faster return to normal activities and better quality of life compared with abdominal hysterectomy (93, 94). Compared with laparoscopic hysterectomy, vaginal hysterectomy was associated with shorter operating time and hospital stay (93, 94). Advantages of laparoscopic hysterectomy compared with open abdominal hysterectomy include faster return to normal activity, shorter duration of hospital stay, and fewer wound infections (94). Robotic-assisted surgery provides an alternative surgical tool for minimally invasive gynecologic surgery, and studies suggest that robotic-assisted hysterectomy has comparable perioperative outcomes to laparoscopic hysterectomy (including blood loss, length of stay, type or number of complications, postoperative pain levels, analgesic use, and recovery time) in centers with experienced surgeons (82, 95–97). Data are conflicting on whether robotic-assisted hysterectomy is associated with longer operative times than conventional laparoscopic hysterectomy (95–98).

Hysterectomy Versus Myomectomy

Important factors to consider when deciding between hysterectomy and myomectomy include risk of complications, need for subsequent surgical intervention, and health-related quality of life.

Complications

There does not appear to be a statistically significant difference in the rate of major complications (visceral injury, life-threatening events, urgent return to the operating room, and hospital re-admissions) between abdominal hysterectomy and abdominal myomectomy for uterine size 18 weeks or less of gestation (5% versus 4.6% respectively; RR, 0.94; 95% CI, 0.31–2.89) (99). No statistically significant difference in the rate of blood transfusion among the two surgeries (19% for myomectomy, 22% for abdominal hysterectomy; RR, 0.92; 95% CI, 0.74–1.14) has been demonstrated (99).

Need for Additional Intervention

In a large retrospective review, the 5-year cumulative incidence of a second surgery for leiomyoma after myomectomy was 23%. By 7 years, the cumulative incidence approached 30%. The age-specific cumulative incidence was greatest in patients aged 30–34 years, and lowest in those aged 50 years or older (100). However, in another retrospective analysis, the combined rate of secondary procedures (including hysterectomy and uterine-sparing procedures) was much lower (13.4%) 6 years after myomectomy (101). Age, and likely proximity to menopause, appear to be important determinants for the risk of secondary procedures after myomectomy. In a study of individuals who underwent myomectomy at age 45 years or older, the cumulative recurrence rate after 36 months was 17.1%, with only a 3.3% hysterectomy rate (102).

Quality of Life

Analysis of data from the Comparing Options for Management: Patient-Centered Results for Uterine Fibroids registry indicates that both hysterectomy and myomectomy are associated with substantial improvements in health-related quality-of-life measures and symptom severity at short-term (6–12 weeks) and longer-term (1 year) follow up (69, 103). When stratified by surgical approach, minimally invasive hysterectomy was associated with significantly greater improvement in short-term and long-term symptom severity and in long-term overall health-related quality of life compared with minimally invasive myomectomy (69, 103). However, short-term and long-term quality-of-life outcomes were comparable for abdominal hysterectomy and abdominal myomectomy (69, 103). The authors hypothesize that this finding may reflect that abdominal procedures are associated with a similar likelihood of complete removal of all leiomyomas at 1 year (103).

Summary of Recommendations

Recommendations based on good and consistent scientific evidence (Level A).

- ▶ Gonadotropin-releasing hormone (GnRH) agonists, either with or without add-back hormonal therapy, are recommended for the short-term treatment of AUB-L and uterine enlargement associated with uterine leiomyomas and as a bridge to other treatment strategies.
- ▶ Uterine artery embolization (UAE) is recommended as an interventional procedure for the treatment of uterine leiomyomas in patients who desire uterine preservation and are counseled about the limited available data on reproductive outcomes.
- ▶ When hysterectomy is selected for the surgical management of symptomatic uterine leiomyomas, the most minimally invasive route is recommended whenever possible, and the vaginal approach is preferred among the minimally invasive approaches when it is feasible.

Recommendations based on limited or inconsistent scientific evidence (Level B).

- An oral GnRH antagonist with hormonal add-back therapy can be considered for the treatment of AUB-L for up to 2 years.
- A 52-mg LNG-IUD can be considered for the treatment of AUB-L.
- Tranexamic acid can be considered for the treatment of AUB-L.
- Laparoscopic radiofrequency ablation can be considered as a minimally invasive treatment option for the management of symptomatic leiomyomas in patients who desire uterine preservation and are counseled about the limited available data on reproductive outcomes.
- Myomectomy is recommended as a surgical management option for symptomatic leiomyomas in patients who desire uterine preservation or future pregnancy and are counseled about the risk of recurrence.
- When myomectomy is selected for the surgical management of symptomatic uterine leiomyomas, a minimally invasive approach should be considered when feasible and appropriate.
- Hysterectomy is recommended as a definitive surgical management option for the treatment of AUB-L and bulk symptoms associated with uterine leiomyomas in patients who do not desire future childbearing or do not wish to retain their uterus and are counseled about the long-term health risks.

Recommendations based primarily on consensus and expert opinion (Level C).

- Expectant management of uterine leiomyomas can be considered for patients who are asymptomatic or for those who do not desire intervention.
- Among patients with heavy menstrual bleeding without uterine leiomyomas, combined hormonal contraceptives and progestin-only pills reduce menstrual blood loss and are considered a reasonable option for initial treatment, although a 52-mg LNG-IUD appears to provide greater reduction in menstrual blood loss. By extrapolation, combined and progestin-only hormonal contraceptives are a reasonable option to consider in the treatment of heavy menstrual bleeding in patients with uterine leiomyomas, although there are limited direct data to support their effectiveness.

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The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 2000 and July 2020. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

Published online on May 20, 2021.

American College of Obstetricians and Gynecologists
409 12th Street SW, Washington, DC 20024–2188

Management of symptomatic uterine leiomyomas. ACOG Practice Bulletin No. 228. American College of Obstetricians and Gynecologists. Obstet Gynecol 2021;137:e100–15.

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