Uterine fibroids (leiomyomas): Treatment overview

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INTRODUCTION

Uterine fibroids are very common in reproductive-age females. For some, they are entirely asymptomatic. Moreover, since fibroids can grow, remain stable, and/or potentially regress (during hypoestrogenic states such as menopause) [1,2], patients without symptoms should be educated about the presence of fibroids and potential associated symptoms. However, many patients will present with symptoms including abnormal uterine bleeding, pressure or bulk symptoms, fertility issues, and/or pain that warrant treatment. These patients have a variety of therapeutic options available to address their symptoms.

This topic will present an overview of the treatment options for fibroids, including expectant management. Related topics on the clinical presentation, diagnosis, exclusion of malignancy, and specific procedures for fibroids are presented separately.

- (See "Uterine fibroids (leiomyomas): Epidemiology, clinical features, diagnosis, and natural history".)
- (See "Uterine fibroids (leiomyomas): Differentiating fibroids from uterine sarcomas".)
- (See "Uterine fibroids (leiomyomas): Open abdominal myomectomy procedure".)
- (See "Uterine fibroids (leiomyomas): Laparoscopic myomectomy and other laparoscopic treatments".)
- (See "Uterine fibroids (leiomyomas): Hysteroscopic myomectomy and other transcervical procedures".)

COMMON SYMPTOMS FOR TREATMENT

There are four common symptom categories that are associated with uterine fibroids. Patients can have one or multiple symptoms:

- Heavy or prolonged menstrual bleeding
- Bulk symptoms (abdominal protrusion, bowel or bladder dysfunction, early satiety)
- Reproductive dysfunction (infertility or recurrent pregnancy loss)
- Pain, including painful menses or nonmenstrual pain

Each of these categories is reviewed in detail elsewhere. (See "Uterine fibroids (leiomyomas): Epidemiology, clinical features, diagnosis, and natural history", section on 'Clinical features'.)

Clinicians should be aware that patients may not associate their symptoms with fibroids because the symptoms appear unrelated to the disease or are so insidious in onset that they attribute their symptoms to aging or other common non-fibroid problems [3,4]. For example, a patient with a fibroid uterus, 20 gestational weeks in size, who has urinary frequency, back pain, and early satiety may not be aware that these symptoms can be related to uterine enlargement and a subserosal fibroid near the bladder. Another patient may have heavy menstrual bleeding lasting for 12 days every month, but since fibroids run in families, the patient may have been told by family members that this is normal menses [4]. For this group of patients, education about symptoms, correlation between physical examination or imaging and other anatomic landmarks, and correlation of uterine size with the gestational week of pregnancy can be helpful since most patients have symptoms attributable to increased uterine size with uterus enlargement equivalent to 12 weeks of gestation.

PRETREATMENT ASSESSMENT

Before selecting a course of treatment, both clinical and laboratory investigations are performed to exclude concomitant disease or serious sequelae of disease, such as anemia resulting from heavy menstrual bleeding. Imaging studies may also be warranted, particularly if surgical or interventional treatment requires additional understanding of the anatomy and/or if there is increased suspicion of a uterine sarcoma (eg, peri- or postmenopausal patients or patients with specific genetic syndromes) [5]. Patients at risk for endometrial cancer should undergo endometrial biopsy.

- (See "Uterine fibroids (leiomyomas): Epidemiology, clinical features, diagnosis, and natural history", section on 'Diagnostic evaluation'.)
- (See "Overview of the evaluation of the endometrium for malignant or premalignant disease".)

The patient's desire for immediate or future childbearing is also assessed prior to choosing any fibroid treatment as the therapies have differing impacts on fertility.

PATIENTS NOT DESIRING FERTILITY

For patients who do not desire fertility, treatment is aimed at symptom reduction. We take a stepwise approach through the treatments below until the symptoms are adequately controlled. As there are limited comparative studies demonstrating superiority of one treatment option over another, patient preference and shared decision-making are used to create the optimal management strategy.

Isolated heavy menstrual bleeding — Heavy menstrual bleeding (HMB) is a common presenting symptom in patients with fibroids. (See "Uterine fibroids (leiomyomas): Epidemiology, clinical features, diagnosis, and natural history", section on 'Heavy or prolonged menstrual bleeding'.)

First tier — First-tier treatment of HMB includes hysteroscopic fibroid resection, if the fibroids are in an appropriate anatomic location, or medical treatment aimed at reducing HMB for those with fibroids in locations not amenable to hysteroscopic resection.

Hysteroscopic resection of submucosal fibroids — For patients with HMB, the first step is determining if there is a submucosal fibroid because of the safety and efficacy of hysteroscopic myomectomy as a treatment [6]. Submucosal fibroids amenable to hysteroscopic resection include International Federation of Gynecology and Obstetrics (FIGO) type 0, type 1, or type 2 (figure 1).

Hysteroscopic myomectomy is an outpatient procedure with rapid recovery, a low risk of complications compared with abdominal procedures, rapid improvement in quality of life, and low risk of reintervention for fibroids [7,8]. Moreover, it is safe for future pregnancy, with virtually no risk for uterine rupture in subsequent pregnancy [9]. However, trial data comparing hysteroscopic resection with other treatments are sparse [10], in part because of ethical concerns for randomly assigning a symptomatic patient to observation, placebo, or more invasive surgery than necessary (eg, laparotomy) and requirement of only intracavitary lesions for a purely hysteroscopic approach.

Initial hysteroscopic myomectomy leads to substantial quality-of-life improvement in most patients [5]. Clinicians should be aware, however, that there is a lower risk of complete resection with increasing size of the fibroid, particularly those greater than 5 cm in diameter and >50 percent extension into the myometrium (FIGO type 2) [11]. A variant of hysteroscopic myomectomy is transcervical treatment with radiofrequency ablation. (See "Uterine fibroids (leiomyomas): Laparoscopic myomectomy and other laparoscopic treatments", section on 'Radiofrequency fibroid ablation'.)

Information specific to performing hysteroscopic myomectomy, including patient evaluation, pretreatment, procedure technique, and outcomes, is presented elsewhere.

(See "Uterine fibroids (leiomyomas): Hysteroscopic myomectomy and other transcervical procedures".)

Medical therapy — Patients with all other types of fibroids (ie, not exclusively submucosal) who do not desire pregnancy are offered medical management to reduce their HMB. First-tier agents for HMB do not reduce the fibroid size but improve the bleeding parameters. Patients who also have bulk or pressure symptoms are directed to treatment options that are considered second tier for HMB as these agents reduce fibroid size as well. (See 'Bulk or pain symptoms with or without bleeding' below.)

For patients with fibroid-related HMB, the author offers the following treatments in the order listed below. As direct comparator data are sparse, the treatment order considers the efficacy, safety, tolerability, ease of use, ancillary benefits (eg, contraception), and cost. However, patients and clinicians may reasonably elect to use these agents in a different order based on patient preferences and other factors, such as desire for contraceptive efficacy or local availability.

- **Estrogen-progestin contraceptives** – Combined estrogen-progestin contraceptives (oral contraceptive pills, vaginal ring, or transdermal patch) are the most common medical therapy utilized by patients with HMB and fibroids, especially those who desire contraception [12]. However, there is little high-quality evidence supporting this practice [13]. As estrogen-progestin contraceptives provide a variety of health benefits beyond contraception (including reduction of iron deficiency anemia, uterine cancer, and ovarian cancer; a long clinical history of use; and are inexpensive and widely available), many guidelines still recommend combined estrogen-progestin contraceptives as first-line therapy [5,9,13-15]. The selection of oral pills, vaginal ring, or transdermal patch is driven by patient preferences around dosing and frequency of use. Patients must be appropriate candidates for exogenous estrogen use.

  - (See "Combined estrogen-progestin oral contraceptives: Patient selection, counseling, and use".)
  - (See "Contraception: Hormonal contraceptive vaginal rings".)
  - (See "Contraception: Transdermal contraceptive patches".)
  - (See "Combined estrogen-progestin contraception: Side effects and health concerns".)

- **Progestin-releasing intrauterine devices (IUDs)** – For patients who cannot use or do not want estrogen-containing contraceptives, the levonorgestrel (LNG)-releasing IUDs (LNG IUD) are the most effective progestin-only contraceptive for fibroid-related HMB, although supporting data are mainly observational and less strong than for its use with generic HMB [16-18]. Nonetheless, most guidelines support the use of LNG IUDs as a first-line agent for fibroid-related HMB [5,9,13-15]. IUDs also provide highly

effective long-acting contraception. First, identifying patients with significant submucosal fibroids is important since the risk of expulsion of the IUD is greater in patients with fibroids that distort the endometrial cavity. Discussion of various IUDs, candidates, and device selection are presented elsewhere.

- (See "Intrauterine contraception: Background and device types".)
- (See "Intrauterine contraception: Candidates and device selection".)
- (See "Intrauterine contraception: Insertion and removal".)
- (See "Intrauterine contraception: Management of side effects and complications".)

- **Tranexamic acid** – Tranexamic acid is a nonhormonal oral medication that can be taken during menses or during the heavy days of menses. It can be preferred by patients who cannot or do not wish to use hormonal contraceptives or by those who desire a treatment that is used only when symptoms are present. A systematic review reported that it can be more effective than oral progestins [19], and small studies have shown benefit in patients with fibroid-associated HMB [20,21]. Tranexamic acid is available as an oral 1.3 gram dose given three times daily [22]. It is started with the onset of HMB. (See "Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management", section on 'Patients with heavy bleeding' and "Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management", section on 'Tranexamic acid'.)

- **High-dose oral progestins** – High-dose oral progestins do not appear to be as effective for treatment for fibroid-related HMB as the LNG IUD, although high-quality data are limited. In one randomized trial of 60 patients with fibroid-related HMB, those treated with the 52 mg LNG IUD compared with oral norethindrone acetate (NETA, 5 mg twice daily) had a greater decrease in menstrual blood loss from baseline (80 and 56 percent, respectively) at six months, as measured by visual blood scoring (VBS) [23].

  Other progestin therapies (eg, progestin implants, progestin injections) also do not appear to be as effective for fibroid-related HMB as the LNG IUD, although some guidelines advise their use [5,13-16]. (See "Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management", section on 'Progestin-only therapies'.)

Second tier — Effective second-tier medical treatments for fibroid-associated HMB are gonadotropin-releasing hormone (GnRH) agonists and antagonists [13,24]. Uterine artery embolization (UAE) is a minimally invasive treatment option that treats both bleeding and bulk symptoms [25].

Despite evidence supporting use of the progesterone receptor modulators (PRM) ulipristal acetate and mifepristone as daily medical therapy for fibroid-related bleeding, neither is

currently available in most countries for fibroid treatment; in settings where these drugs are available, use is restricted given potential for hepatic toxicity [26-29]. (See 'Treatments not typically recommended' below.)

GnRH analogs — GnRH analogs, including antagonists and agonists, can reduce HMB [24]. Agonists also significantly reduce fibroid volume but have potential adverse effects that limit use.

For patients who do not have an adequate response to first-tier treatment, the author prefers to initiate oral GnRH antagonist combinations (with low dose estrogen and progestin), because they are orally dosed and generally better tolerated compared with agonists, and then moves to a trial of depot GnRH agonists if the antagonist therapy is not adequate to control symptoms. However, patients and clinicians who prefer to initiate GnRH agonists may reasonably do so. In addition, GnRH agonists likely result in a greater reduction in fibroid volume compared with GnRH antagonists.

- **GnRH antagonists** – Oral GnRH antagonists are a relatively new generation of medical therapy. Like GnRH agonists, these agents act centrally and are associated with hypoestrogenic side effects, but they are available as oral formulations rather than injections. GnRH antagonists are often formulated with low-dose steroidal add-back to limit hypoestrogenic side effects, so separate add-back therapy is not required.

  - **Elagolix combination therapy** – Elagolix, in combination with estradiol and norethindrone (ie, elagolix-estradiol-norethindrone), was approved by the US Food and Drug Administration (FDA) in May 2020 for the treatment of fibroid-related HMB for up to 24 months of use [30-32]. This preparation (commercial name Oriahnn) is available as two co-packaged capsules: one contains elagolix 300 mg plus estradiol 1 mg plus norethindrone 0.5 mg to be taken in the morning, and the other contains elagolix 300 mg alone to be taken in the evening.

    In two identical phase III trials comparing six months of elagolix plus hormonal add-back therapy (elagolix 300 mg twice a day with daily estradiol 1 mg and norethindrone acetate 0.5 mg) with placebo for patients with fibroid-related HMB, more patients in the treatment arm met the primary endpoint (menstrual blood loss of less than 80 mL during the final month of treatment **and** at least a 50 percent reduction in menstrual blood loss from baseline to the final month) compared with placebo (range 69 to 77 versus 9 to 10 percent) [33]. When data were analyzed according to specific patient subgroups (eg, age, race, body mass index, fibroid location and size), the proportion of responders was greater for patients in the elagolix add-back arm compared with placebo in every subgroup [34]. Concomitant adenomyosis does not appear to limit the effectiveness for fibroid-related HMB [35]. Sustained reduction of menstrual bleeding was also shown when the treatment was

continued for an additional 6 months (total of 12 months) with 88 percent of patients in the treatment arm meeting the primary endpoint [36].

During treatment with elagolix plus add-back, side effects were modest, including hot flushes (7 percent), night sweats (3 percent), headache (5.5 percent), and nausea (4 percent). Two patients developed liver transaminase levels more than three times the upper limit of normal, resulting in one patient discontinuing treatment. Bone mineral density was also affected; at the end of 12 months of treatment, bone mineral density in the lumbar spine was reduced by 1.5 percent (median Z-score 0.8); however, patients regained some bone density when measured one year following completion of treatment (improvement to reduction of 0.6 percent; median Z-score 1.1). Similar trends were observed in total hip and femoral neck bone density.

The benefit of add-back therapy is that it mitigates many of the hypoestrogenic side effects of elagolix; however, the effect on fibroid volume reduction is also attenuated.

Elagolix alone, without add-back therapy, has been demonstrated to improve fibroid-related HMB and may be considered for patients with a contraindication to add-back therapy; however, this use remains off-label and we do not use elagolix-alone for this indication in our practice. In the randomized trials above, elagolix alone compared with placebo resulted in meeting the primary endpoint in 77 to 84 percent of patients after 6 months and 89 percent of patients after 12 months of therapy [33,36]. Furthermore, fibroid volume was reduced by 40 to 50 percent after 6 months, and an even greater reduction was noted after 12 months of therapy. Common adverse events included night sweats and reductions in bone mineral density (mean reduction of 4.8 percent at the end of 12 months of treatment, with improvement to reduction of 2 percent one year following completion of treatment). Low-dose elagolix (ie, 150 mg once daily) without add-back therapy has also been described [37].

As ovulation suppression with elagolix plus add-back is variable, it should not be considered a contraceptive [38,39].

Use of elagolix for endometriosis-related pain is presented separately. (See "Endometriosis: Medical treatment of pelvic pain", section on 'GnRH antagonists'.)

- **Relugolix combination therapy** – A combination tablet containing relugolix-estradiol-norethindrone acetate (commercial name Myfembree) was approved by the US FDA in May 2021 for the treatment of fibroid-related HMB for up to 24 months [40]. Each tablet contains relugolix 40 mg plus estradiol 1 mg plus

norethindrone acetate 0.5 mg in a single daily dose. Potential advantages of relugolix are its once daily dosing and potential for greater reduction of pain and bulk symptoms (compared with twice daily dosing of elagolix combination therapy).

In two identical phase III trials comparing 24 weeks of relugolix combination therapy (40 mg of relugolix, 1 mg of estradiol, and 0.5 mg of norethindrone acetate), delayed relugolix combination therapy (40 mg of relugolix monotherapy, followed by relugolix combination therapy, each for 12 weeks), and placebo, more patients in the relugolix treatment arms achieved the primary endpoint (menstrual blood loss of less than 80 mL during the final month of treatment **and** at least a 50 percent reduction in menstrual blood loss from baseline to the final month) compared with placebo (71 to 80 percent versus 15 to 19 percent) [41]. In addition, combination therapy decreased a number of other secondary endpoints (including anemia, bulk-related symptoms, and uterine volume [reduction of approximately 12 to 15 percent; range -3.2 to -23 percent]) while preserving bone mineral density. In a secondary analysis of these trials, quality-of-life measures (eg, emotional well-being, sexual function) were also improved in the combination therapy group [42].

When data were analyzed according to specific patient subgroups (eg, age, race, ethnicity, uterine volume, baseline menstrual blood loss age), the proportion of responders was greater for patients in the relugolix combination therapy arm compared with placebo in every subgroup [41]. Combination therapy also decreased fibroid-associated pain [41,43]. Of the 277 patients in these trials with moderate to severe pain, more patients treated with combination therapy compared with placebo achieved minimal to no pain (45.2 versus 13.9 percent) [43]. For patients in the combination therapy group, menstrual pain was reduced more than nonmenstrual pain. In extension studies, patients using relugolix combination therapy long term (up to two years) experienced similar improvements in menstrual blood loss; no new safety concerns or changes in bone mineral density were identified [44,45].

Hypersensitivity reactions (eg, anaphylaxis, urticaria, angioedema) have been described [46].

- **Linzagolix** – Linzagolix is an oral GnRH antagonist that is available in Europe for the treatment of moderate to severe fibroid symptoms; it is not available in the United States. Linzagolix is dispensed as a 100 mg or 200 mg once daily tablet and has the option of being administered with or without add-back therapy [47]. The lower dose (100 mg) aims for partial suppression of the hypothalamic-pituitary-ovarian (HPO) axis where the higher dose (200 mg) aims for full suppression.

In two identical phase III trials evaluating the efficacy and safety of linzagolix therapy for the treatment of fibroid-related HMB, more patients treated with linzagolix (with or without 1 mg estradiol and 0.5 mg norethisterone acetate add-back therapy) met the primary endpoint (menstrual blood loss ≤80 mL and ≥50 percent reduction from baseline at 24 weeks) compared with placebo [48]. Specifically, for patients receiving placebo, 100 mg alone, 100 mg plus add-back, 200 mg alone, or 200 mg plus add-back, response rates were 29 to 35 percent, 56 to 57 percent, 66 to 77 percent, 71 to 77 percent, and 76 to 94 percent, respectively. Patients receiving linzagolix alone (either dose) compared with linzagolix plus add-back therapy had greater reductions in fibroid volume. In addition, fewer patients receiving 100 mg (with or without add-back) and 200 mg with add-back experienced hot flushes compared with those treated with 200 mg without add-back therapy. Reductions in bone mineral density were dose dependent and ameliorated with add-back therapy.

- **GnRH agonists** – GnRH agonists are primarily used as either preoperative therapy (typically three to six months in duration) or as transitional therapy for patients in late perimenopause as they move to menopause. For patients with fibroids and anemia who are planning surgery for fibroids but have not responded adequately to iron-only therapy, a short course of preoperative GnRH agonist treatment plus iron is an established option [49].

  Goals of preoperative therapy can include induction of amenorrhea to improve anemia and volume reduction to facilitate a less invasive procedure, such as allowing a vaginal rather than an abdominal hysterectomy. Good quality data exist that GnRH agonists decrease uterine and fibroid volume, increase hemoglobin, and improve perioperative outcomes in patients undergoing hysterectomy and myomectomy [24]. However, side effects must be weighed against benefits [5]. When used alone (ie, without hormonal add-back treatment), the parenteral forms of GnRH agonists (one- and three-month depot formulations given as an intramuscular injection) cause significant hypoestrogenic side effects, including bone loss [50]. There are a variety of steroidal and nonsteroidal add-back therapies that can limit these side effects and permit more long-term use, but these are rarely used unless there are contraindications to surgical or interventional therapies for the fibroids. Discussion of add-back therapy, based on data from patients with endometriosis, is presented separately. (See "Endometriosis: Long-term treatment with gonadotropin-releasing hormone agonists".)

The use of GnRH analogs for the management of fibroid-related bulk or pain symptoms is discussed in detail below. (See 'Bulk or pain symptoms with or without bleeding' below.)

Uterine artery embolization — For premenopausal patients who do not desire future fertility, uterine fibroid embolization (UAE) is a minimally invasive option for management of fibroid-related symptoms. Substantial randomized clinical trial data support its efficacy, making it a second-tier treatment for patients who do not have access to oral GnRH antagonists, and a third-tier treatment where those agents are available [13,51].

Up to 90 percent of patients will report improved or resolved HMB symptoms after treatment. When compared with hysterectomy or myomectomy, patients undergoing UAE have a decreased risk of transfusion, a shortened hospital stay, less pain, and a quicker return to work. However, following UAE, patients have more short-term complications, unscheduled visits, and readmissions, but this may also represent bias since UAE patients were typically discharged from the hospital earlier than those undergoing surgery. Patients undergoing UAE compared with myomectomy (laparoscopic, hysteroscopic, and abdominal) [52-54] and hysterectomy [55] may also experience less favorable quality of life and worse symptom severity. This is discussed in more detail elsewhere. (See "Uterine fibroids (leiomyomas): Treatment with uterine artery embolization", section on 'Outcomes'.)

UAE is not intended for use in patients who desire optimization of future childbearing and is generally avoided in postmenopausal patients (because of the concern of mistakenly treating a uterine sarcoma). In addition, UAE may cause ovarian dysfunction and a loss of ovarian reserve. These issues are presented in detail elsewhere. (See "Uterine fibroids (leiomyomas): Treatment with uterine artery embolization", section on 'Reproductive outcomes'.)

Third tier — Less invasive interventional therapies are available for patients who desire less time away from work and/or uterine preservation. However, these procedures are not intended to be used for patients who desire optimization of future pregnancy. Procedure selection is determined by patient preferences around invasiveness and recovery time as well as treatment availability.

One advantage of third-tier fibroid therapies is that they offer minimally invasive approaches to treatment. Depending on patient characteristics and preferences, patients may also reasonably proceed to traditional surgical therapy. (See 'Traditional surgery' below.)

Focused ultrasound surgery — Focused ultrasound surgery utilizes high intensity ultrasound energy to induce coagulative necrosis of fibroids. The treatment can be guided by ultrasound, most widely used in China and typically called high intensity focused ultrasound (HIFU) [56,57], or by magnetic resonance imaging (MRI), termed MRgFUS in the rest of the world. This noninvasive, thermoablative technique applies

multiple waves of ultrasound energy through the abdominal wall and can be performed as an outpatient procedure with sedation [58-62]. With HIFU, an abdominal probe is placed on the abdomen with the patient supine, while with MRgFUS, the ultrasound source is within the bed of the MRI machine, and the patient is positioned prone over the transducer. Like surgical myomectomy, each fibroid is targeted individually, and, thus, size, vascularity, heterogeneity, calcifications, and abdominal scars through which the ultrasound energy passes can all affect treatment. Ideal treatment candidates have three or fewer fibroids, size less than 10 centimeters in maximal dimension, homogenous and dark on T2-weighted images, and well-vascularized without calcification [63,64]. MRI visualizes the anatomic structures and provides real-time thermal monitoring to optimize tissue destruction with optimization of safety. It appears that MRgFUS results in a reduction in myoma volume of approximately 37 to 40 percent [65].

- **Outcomes** – Symptomatic improvement is observed within the first three months postprocedure, and this improvement has been maintained at least through 24 to 36 months of follow-up, with more complete ablation leading to better outcomes [60,66-68]. Adverse event rates appear to be decreased with increased practitioner experience, despite more extensive treatment [60]. The procedure is time-consuming and costly, but short-term morbidity is low and recovery is rapid. Analyses based on quality-of-life measures have found the procedure to be cost-effective [69,70]. Review by the United Kingdom's National Institute for Health and Care Excellence suggests the data are adequate to support clinical use of MRgFUS [71] and more limited data support use of HIFU [72,73].

- **Comparison with UAE** – MRgFUS was compared with UAE in the Fibroid Interventions: Reducing Symptoms Today and Tomorrow (FIRSTT) study, which included 81 patients with combined analysis of observational and randomized data [74]. Complication rates were low in both groups, but patients undergoing UAE used more opioid pain medications, and patients with significant pain at baseline were more likely to have adverse events with either treatment [75]. Over 24 months, quality of life improved, and general fibroid symptoms and pain scores declined significantly with both treatments, but to a greater extent in the UAE arm in which patients had symptom scores that were consistent with patients without fibroids [76]. MRgFUS compared with UAE resulted in a higher rate of reintervention for symptomatic fibroids (30.0 versus 12.5 percent) within three years [76]. Reintervention was more likely when treatments occurred at younger ages and in patients with higher pretreatment AMH levels. Finally, AMH levels at 24 months were lower in the UAE group [76].

- **Postprocedure pregnancy** – There are reports of pregnancies following MRgFUS for uterine fibroids [77-80] and ultrasound-guided HIFU [81,82]. The case series of

MRgFUS described 54 pregnancies in 51 patients with mean birth weight of 3.3 kg and a 64 percent vaginal delivery rate. There was no specific pattern of complications; 9 percent of patients had placentation problems, but, in this series, all had prior uterine surgery as a risk factor for this complication [80]. The HIFU series described 80 pregnancies in 78 patients who delivered at a mean of 38.1±2.2 weeks, with 89 percent of pregnancies resulting in delivery and 85 percent in term delivery [82].

Endometrial ablation — There is a limited role for endometrial ablation in patients with uterine fibroids and HMB, such as for patients with bleeding disorders [83]. In the author's practice, use of an LNG IUD is generally preferable to endometrial ablation since the IUD does not require surgery, is reversible, provides contraception, and minimizes the risk of an extrauterine pregnancy following endometrial ablation. (See 'Medical therapy' above.)

Traditional surgery — For patients who do not desire future fertility and have persistent fibroid-related symptoms despite the above therapies or who desire surgical treatment, options include hysterectomy and myomectomy. Hysterectomy involves removal of the uterine corpus, including the fibroids, while myomectomy removes only the fibroids and leaves the uterus in situ.

- **Hysterectomy** – Hysterectomy, or complete removal of the fibroid uterus, provides definitive therapy and, thus, has been the mainstay of surgical treatment for a century. In the United States, over 80 percent of hysterectomies are performed for benign disease, and one-third to over one-half are performed for uterine fibroids, which results in a lifetime hysterectomy prevalence of 45 percent [84,85]. Hysterectomy eliminates both the risk of new fibroids forming and all types of abnormal uterine bleeding, and it improves quality of life, even when compared with uterine-sparing options [55,86-88]. However, hysterectomy has also been associated with long-term morbidity.

  - **Outcomes** – While short-term outcomes are good [88,89], there has been an increased focus on the long-term morbidity associated with hysterectomy, both with and without bilateral oophorectomy. Studies of hysterectomy with bilateral oophorectomy, which is seldom required for fibroids, have reported increased risk of fracture [90], multiple morbidity [91], all-cause mortality [92], cardiovascular disease [93], and neurologic dysfunction [94,95]. Hysterectomy with ovarian conservation, the more common procedure for patients with fibroids, has also been associated with increased risk of earlier menopause [96], decreased ovarian reserve [97,98], mood disorders [99], and cardiovascular morbidity [100]. The impact of hysterectomy on subsequent pelvic organ prolapse and pelvic floor dysfunction is a subject of debate. Additionally, there is increasing evidence that factors other than disease extent, including a history of abuse, may be associated with undergoing hysterectomy

[86,101]. Concerns related to hysterectomy, with or without oophorectomy, are presented in detail separately.

- (See "Elective oophorectomy or ovarian conservation at the time of hysterectomy", section on 'Long-term health risks'.)
- (See "Hysterectomy (benign indications): Patient-important issues and surgical complications", section on 'Decreased ovarian function or earlier menopause'.)
- (See "Hysterectomy (benign indications): Patient-important issues and surgical complications", section on 'Cardiovascular and metabolic morbidity'.)

- **Indications** – The author prefers to avoid the procedure, even with ovarian conservation, because of the long-term risks discussed above. In the author's practice, hysterectomy is reserved for patients who previously have had unsuccessful conservative therapy or who have significant concomitant diseases, such as adenomyosis, cervical dysplasia, or uterine prolapse, for which hysterectomy is curative for both conditions. Additionally, when hysterectomy is performed for uterine fibroids, unless there are high-risk mutations for breast or ovarian cancer such as *BRCA1* and *BRCA2* or ovarian pathology, ovarian conservation appears to be indicated.

  - (See "Hysterectomy (benign indications): Selection of surgical route", section on 'Hysterectomy indications and alternatives'.)
  - (See "Elective oophorectomy or ovarian conservation at the time of hysterectomy".)

  For patients who elect hysterectomy, the approach to selecting the route (abdominal or vagina) and surgical type (traditional, vaginal, laparoscopic, robotic) is discussed elsewhere. (See "Hysterectomy (benign indications): Selection of surgical route".)

- **Myomectomy** – Given the success of less invasive alternatives, including UAE and MRgFUS, the author advises myomectomy only in patients who do not have another uterine-sparing option or if there is a suspicion of sarcoma and the patient strongly desires a uterine-sparing technique knowing it may compromise outcome if sarcoma is found.

  - (See "Uterine fibroids (leiomyomas): Laparoscopic myomectomy and other laparoscopic treatments".)
  - (See "Uterine fibroids (leiomyomas): Open abdominal myomectomy procedure".)
  - (See "Uterine fibroids (leiomyomas): Differentiating fibroids from uterine sarcomas".)

Bulk or pain symptoms with or without bleeding — For patients whose main symptoms include bulk or pain, with or without HMB, treatment options include UAE (or MRgFUS for patients who are optimal candidates and decline UAE) and GnRH analogs. Patients and clinicians must balance procedure risk and longer recovery of UAE with the hypoestrogenic symptoms associated with long-term use of GnRH analogs. If not effective, or if patients

desire more definitive surgical therapy, then myomectomy and hysterectomy are discussed. Selection of embolization, medication, or surgery depends upon patient preferences around side effects, invasiveness, recovery time, need for prolonged treatment (more than six months), and risk of the treatment compared with risk of symptom recurrence. Other deciding factors include availability and cost.

Bulk and pain symptoms are more difficult to manage for several reasons. First, slow uterine and fibroid growth can compromise function without abrupt change. Secondly, some bulk symptoms, such as urinary frequency and back pain, can be attributed to habits (frequently drinking water) or common conditions (lower back pain). However, it is increasingly clear that uterine fibroids are associated with both menstrual and nonmenstrual pain without invoking other diseases, such as endometriosis or adenomyosis [102].

Initial treatment options include:

- **UAE** – For patients who do not desire optimization of pregnancy or future fertility, UAE can be used to treat symptoms of pain, pressure, and bulk in addition to HMB. Symptom improvement rates vary by indication, mechanism of assessment, treatment comparator, and duration of follow-up, but they are in the range of 60 to 80 percent. Discussions of UAE procedure details, efficacy, and need for subsequent treatment are presented in detail separately. (See "Uterine fibroids (leiomyomas): Treatment with uterine artery embolization".)

- **GnRH analogs** – GnRH analogs include both agonists (eg, leuprolide acetate depot suspension) and antagonists (elagolix and relugolix). Agonist treatment has been demonstrated to reduce fibroid volume [24], and relugolix has been demonstrated to reduce both fibroid volume and pain (see 'GnRH analogs' above). There are some data suggesting that agonist treatment may reduce bulk symptoms more than relugolix, but data are conflicting [41,103]. Furthermore, it is likely that elagolix combination therapy also decreases pain, but this has not been studied; while pain was a prespecified secondary endpoint in the relugolix trials, there are no comparable data for elagolix combination therapy.

  Both GnRH agonists and antagonists result in hypoestrogenic side effects, which limit their tolerability and long-term use to a maximum of six months without add-back therapy. (See 'GnRH analogs' above.)

For patients with persistent bulk or pain symptoms or those who desire definitive surgical therapy, surgical treatment options include myomectomy and hysterectomy. Myomectomy may be reasonable for patients with a limited number of large lesions in whom discreet fibroid removal is likely to significantly reduce uterine volume or focused pain. However, for patients with diffuse myometrial fibroids or pain that is not specific to one or two lesions,

hysterectomy is preferred as it provides definitive surgical therapy. Both surgical approaches and benefits as related to the treatment of fibroids are reviewed above. (See 'Traditional surgery' above.)

PATIENTS DESIRING FERTILITY

Impact of fibroids on fertility — Fibroids themselves can contribute to a number of reproductive impairments, including infertility and recurrent pregnancy loss, although the available data often come from observational studies and, in some instances, they conflict [104-107]. One of the key confounders is that increasing age is associated with increased risk of infertility, fibroids, and miscarriage [106]. Generally, the literature has concluded that fibroids that distort the cavity (International Federation of Gynecology and Obstetrics [FIGO] types 0 to 3 (figure 1)) have more of an impact on fertility, and surgical treatment can be effective in reversing that impairment [104]. Likewise, the more the fibroids are located near the serosal surface, the less a role they appear to play. There is also likely confounding by age as has been shown in the relationship between fibroids and miscarriage; fibroids are associated with miscarriage in univariate analysis, but, in multivariate analysis, age appears to be the major influence since both fibroids and miscarriage increase with increasing age up to menopause [104,108]. Secondly, infertility and other reproductive dysfunction are often multifactorial, and, thus, a complete infertility evaluation of both partners is indicated before fertility treatment for fibroids [109]. Finally, in populations such as in the United States where much of fertility care is not covered or differentially covered by insurance, there is an incentive to treat fibroids first, which are covered as medical issues, before embarking on out-of-pocket fertility care. (See "Female infertility: Causes", section on 'Uterine fibroids (leiomyomata)'.)

Treatment options — Most medical therapies for uterine fibroids preclude conception, cause adverse effects when employed long-term, and result in rapid symptom rebound when discontinued. Therefore, medical treatment of fibroids in patients attempting to become pregnant is usually unsuccessful. The author takes the following approaches for patients with symptomatic fibroids who desire pregnancy.

Submucosal fibroids only — For patients desiring fertility who present with heavy menstrual bleeding (HMB) and a submucosal fibroid or fibroids (FIGO type 0, type 1, or some type 2 (figure 1)), we recommend hysteroscopic myomectomy both for its minimally invasive relief of symptoms and optimization of fertility. Hysteroscopic myomectomy is appropriate for patients who do, and do not, desire future fertility. Outcomes data for hysteroscopic myomectomy with regard to treating HMB are reviewed above. (See 'Hysteroscopic resection of submucosal fibroids' above.)

For patients desiring pregnancy, wishing to maximize fertility, and presenting with submucosal fibroid or fibroids (FIGO type 0 or type 1) in the absence of other symptoms, we suggest hysteroscopic myomectomy. Although some guidelines [9] suggest removal of submucosal fibroids in asymptomatic patients not actively pursuing pregnancy, we suggest removal of FIGO types 0 and 1 fibroids but not type 2 (figure 1) due to the greater complexity of that surgery and higher risk of a two-stage procedure. Support for this approach mainly stems from the minimally invasive nature of the procedure and the anticipated benefit from removal of fibroids that impact the uterine cavity. However, available evidence is limited, includes surrogate patient groups (eg, patients with endometrial polyps rather than submucosal fibroids), and often lacks data on live birth rates, which is the key endpoint [105,106]. A trial comparing hysteroscopic myomectomy for major cavity abnormalities with expectant management in 181 patients affected by fibroids who had been trying to conceive for a year without success reported improved overall pregnancy rates following myomectomy, but the differences were not statistically significant [110]. A different trial that evaluated the removal of endometrial polyps prior to intrauterine insemination reported improved clinical pregnancy rates after polyp removal (odds ratio 4.41, 95% CI 2.45-7.96, 204 patients), but data on live birth rates were not available [105,111]. A meta-analysis including 442 patients with uterine fibroids and infertility reported nonsignificant trends toward higher clinical pregnancy rates following fibroid removal compared with no intervention; again, live birth rates were not reported [106].

All fibroids other than submucosal — For patients who desire pregnancy and present with bulk symptoms (with or without bleeding) or whose fibroids are not amenable to hysteroscopic resection, we suggest myomectomy via either laparoscopy (with or without robotic assistance) or an open abdominal incision.

Selection of laparoscopic or open technique is determined by the number, size, and location of the fibroids and does not appear to impact live birth rate, although supporting data are limited [106]. As the rate of new fibroid formation is high following uterine-sparing interventions such as myomectomy, fibroids are ideally treated as close to the time of actively pursuing pregnancy as possible. Additionally, since having a term delivery is associated with decreased fibroid risk, timing treatment close to the pursuit of pregnancy appears beneficial [112].

Myomectomy is typically the first option because while less invasive treatments (eg, uterine artery embolization [UAE], focused ultrasound surgery) reduce bulk and shrink fibroids, they do not remove them. However, for patients who have a high risk of intraoperative conversion to hysterectomy, who have had prior myomectomy with recurrent fibroids, and/or who are considering a future pregnancy but will accept the possibility of impaired fertility in exchange for an expedited recovery phase, these less

invasive treatments may be considered appropriate alternatives. (See 'Uterine artery embolization' above and 'Focused ultrasound surgery' above.)

Choosing the approach — Laparoscopic myomectomy offers several advantages compared with open abdominal myomectomy, including decreased morbidity and a shorter recovery. However, laparoscopic myomectomy may be limited by characteristics of myomas and surgical expertise (eg, laparoscopic suturing) [113]. Laparoscopic myomectomy may also have higher rates of unplanned hysterectomy compared with an open or hysteroscopic approach. (See "Uterine fibroids (leiomyomas): Laparoscopic myomectomy and other laparoscopic treatments", section on 'Unplanned hysterectomy'.)

- **Laparoscopic myomectomy** – In general, laparoscopic myomectomy, with or without robotic assistance, is an option for patients with the following:
  - Uterine size <17 weeks.
  - Subserosal or intramural fibroids. Pedunculated subserosal fibroids (ie, International Federation of Gynecology and Obstetrics [FIGO] type 7) are the easiest to remove, but myomas in other locations (FIGO type 2 to 6) can also be excised laparoscopically (figure 1). Intracavitary myomas (ie, FIGO type 0 and 1) are difficult to remove during laparoscopic myomectomy and hysteroscopic myomectomy is the procedure of choice for such myomas. Patients with both submucosal and intramural/subserosal myomas may be candidates for concomitant laparoscopic and hysteroscopic myomectomy. (See "Uterine fibroids (leiomyomas): Hysteroscopic myomectomy and other transcervical procedures", section on 'Patient selection'.)
  - A small number (typically less than five) of fibroids [114]. Performing laparoscopic myomectomy in patients with large or numerous myomas is likely to be time consuming, particularly since morcellation is usually required. In addition, removal of such fibroids may lead to increased blood loss, which is better prevented and controlled during open myomectomy. (See "Techniques to reduce blood loss during abdominal or laparoscopic myomectomy", section on 'Intraoperative measures'.)
  - Fibroids that are anterior or fundal in location. Many surgeons find anterior or fundal myomas easier to remove laparoscopically than those that are posterior or proximate to other important structures (eg, uterine vessels, fallopian tubes).

Future childbearing is possible; however, the integrity of the uterine incision during pregnancy has not been evaluated adequately and may be inferior to open abdominal myomectomy. Due to reports of uterine rupture in pregnancy following some laparoscopic myomectomies, surgeons should discuss the risks and benefits of each

option with patients, including possible risk of uterine rupture, as well as provide information regarding their experience with laparoscopic suturing. While robotic assistance may alleviate these problems, supporting data are minimal. (See "Uterine fibroids (leiomyomas): Laparoscopic myomectomy and other laparoscopic treatments", section on 'Counseling about future pregnancy'.)

- **Open abdominal myomectomy** – For patients with more numerous and/or larger fibroids, a laparotomy may be required. Open abdominal myomectomy can be safely performed even with very large uteri in expert hands; absolute size parameters vary among surgeons [115-118]. (See "Uterine fibroids (leiomyomas): Open abdominal myomectomy procedure".)

In a systematic review of six randomized trials including 576 subjects undergoing myomectomy, laparoscopic compared with open abdominal myomectomy had an increase in operative duration (13 minutes longer), but a decrease in blood loss (34 mL less) [119]. However, these differences are small and unlikely to be clinically significant. In addition, while the overall risk of complication was lower for laparoscopic myomectomy (odds ratio [OR] 0.47, 95% CI 0.26-0.85), the risk of major complications (eg, hemorrhage requiring transfusion, visceral injury, thromboembolism) was similar between groups, but the analysis lacked sufficient statistical power to detect this difference. The rate of recurrent myomas was also similar between groups (18 to 20 percent; follow-up period of 6 to 52 months), although this too lacked statistical power.

Interestingly, other data suggest that a laparoscopic approach may result in less severe adhesive disease (particularly fewer adnexal adhesions) which may impact fertility [120], and that surgical complication rates (for both open and laparoscopic procedures) may be higher in Black, Hispanic, and Asian patients compared with White patients [121]. (See "Uterine fibroids (leiomyomas): Laparoscopic myomectomy and other laparoscopic treatments", section on 'Complications' and "Uterine fibroids (leiomyomas): Open abdominal myomectomy procedure", section on 'Complications' and "Uterine fibroids (leiomyomas): Laparoscopic myomectomy and other laparoscopic treatments", section on 'Adhesive disease'.)

Surgical approach does **not** appear to affect ovarian reserve, as measured by anti-müllerian hormone (AMH) levels [122]. While a transient decline in AMH levels may be seen after open myomectomy (and associated with tourniquet use), the effect is transient, and levels appear to return to baseline by three months. (See "Techniques to reduce blood loss during abdominal or laparoscopic myomectomy", section on 'Tourniquets'.)

Further randomized trials are needed to compare these two procedures.

Both submucosal and other fibroids — Patients with symptomatic submucosal and other fibroids may require both hysteroscopic and abdominal/laparoscopic myomectomy.

Role of preventive treatment to improve fertility — There are no data to support empiric removal of asymptomatic or minimally symptomatic fibroids in patients before attempting pregnancy. Because the risk for new fibroid formation is high, this approach can leave patients with recurrent fibroids that require additional intervention as they are pursuing pregnancy [123]. However, for patients with a uterus 16 weeks in size or larger, shortening the interval for trying for pregnancy before embarking on a full fertility evaluation seems prudent (after six months for patients <35 years old and after three months for patients ≥35 years old). (See "Advancing maternal age: Infertility evaluation and management".)

ROLE OF EXPECTANT MANAGEMENT

There are few data on expectant management for patients with uterine fibroids, and they primarily come from the comparator arm of active treatment trials [13]. Moreover, expectant management has typically only been studied for a duration of up to six months. With those constraints, however, there is little evidence of documented harm over 6 to 12 months of observation, and expectant management can be employed [13].

- **Candidates** – While there are no data-informed guidelines, candidates for expectant management may include patients who are:
  - Asymptomatic
  - Attempting pregnancy
  - With lesions that are stable in size as demonstrated by serial imaging studies for one year
  - Peri- or postmenopausal
  - With uteri less than 12 weeks in size (not palpable abdominally)
- **Components of expectant management** – Expectant management involves periodic evaluation of the patient for new symptoms that could be related to fibroids and for evidence of fibroid growth. Such evaluation may be limited to history and physical examination or may require imaging or laboratory studies, typically with pelvic ultrasound and assessment for anemia. The optimal time interval for such evaluation or repeat imaging is not known. In patients with no other symptoms or concerns, yearly evaluation is reasonable. Patients are encouraged to contact their clinicians if new pelvic symptoms develop. Expectant management is not appropriate if anemia worsens despite iron and vitamin supplementation, if transfusion is required for treatment of anemia, if the patient requires emergency evaluation for either anemia or heavy uterine bleeding, or if imaging raises suspicion for uterine sarcoma.

While many providers rely on periodic ultrasound or magnetic resonance imaging to follow patients expectantly, there is no evidence of the usefulness of this process. Nonetheless, since certain therapies depend on the number and/or size of the fibroids present, periodic imaging can be used at annual intervals, especially in patients who have had prior fibroid treatment, to allow the least invasive option for future treatment.

SPECIAL POPULATIONS

Pregnancy and postpartum — Fibroids can undergo degeneration or torsion in pregnancy and the postpartum period, both of which can be associated with significant pain. Degeneration is managed with supportive therapy, while management of torsion varies with the size and location of the fibroid. (See "Uterine fibroids (leiomyomas): Issues in pregnancy", section on 'Degeneration and torsion'.)

Peri- and postmenopause — Since symptoms tend to stabilize or regress once a patient reaches menopause, perimenopausal patients can typically be managed expectantly. Postmenopausal patients with fibroids should be evaluated periodically to ensure that the fibroid or fibroids have not increased in size. There is no consensus as to the frequency of evaluation, but every one to two years seems reasonable in the absence of new symptoms. Postmenopausal patients with new symptoms, particularly uterine bleeding or enlargement, should be evaluated immediately, and malignancy, including leiomyosarcoma, should be excluded. (See "Uterine sarcoma: Classification, epidemiology, clinical manifestations, and diagnosis".)

TREATMENTS NOT TYPICALLY RECOMMENDED

Numerous medical therapies have been tried for fibroid symptoms but are not effective and/or carry unacceptable risks.

- **Progesterone receptor modulators (PRMs)** – Despite evidence supporting use of the PRMs ulipristal acetate (UPA) and mifepristone as daily medical therapy for fibroid-related bleeding [26,124], neither is currently approved in the United States for fibroid treatment. Both UPA and mifepristone remain on the market for one-time use as emergency contraceptives. (See "Emergency contraception".)

  - **UPA** – UPA is not typically used for treatment of uterine fibroids as cases of serious liver toxicity, liver transplantation, and fatalities have been reported [27,125,126]. As such, UPA is not available in the United States for treatment of fibroid-related bleeding by the US Food and Drug Administration [28,29]. In the European Union and Canada, UPA is approved in selected premenopausal patients with uterine fibroids who are not

candidates for, or have previously failed, surgical procedures (including uterine fibroid embolization) for up to four treatment cycles [127].

In randomized trials, UPA compared with placebo resulted in improved fibroid symptom severity and health-related quality of life, and efficacy appeared similar to that of gonadotropin-releasing hormone (GnRH) agonists but with the advantage of oral dosing and lack of hypoestrogenic side effects [26,128]. The original trials for UPA were conducted in European populations where most participants were thin with relatively small uteri [129-131]. When trials were subsequently conducted in more diverse United States populations utilizing both 5 and 10 mg daily doses, the 10 mg dose generally showed greater efficacy [128,132,133].

Repeated cycles of UPA appear to further reduce fibroid-related symptoms. In one randomized trial of patients with fibroid-related heavy menstrual bleeding (HMB), more patients receiving UPA (10 mg) for four cycles compared with one cycle had amenorrhea (89 versus 79.5 percent) and a greater change in total fibroid volume (-72.1 versus -49.9 percent) [134].

UPA as a single dose remains widely available for emergency contraception. Because of differences in dosing, off label use in the US would require a compounding pharmacy. (See "Emergency contraception", section on 'Oral medication emergency contraception methods'.)

- **Mifepristone** – Mifepristone at doses of 5 to 50 mg for three to six months has been reported to decrease heavy menstrual bleeding and, in some studies, fibroid volume [135-138]. However, some studies reported abnormal endometrial histology at the conclusion of therapy [135]. As a compounded formulation of mifepristone is required for these doses, the drug is rarely used for this off-label indication [26,135].

- **Androgenic compounds** – Use of the androgens danazol and gestrinone have been studied in small series from single centers, but there are no comparative data [139,140]. Thus, we do not advise using these agents for fibroid-related symptoms.

- **Aromatase inhibitors** – While one small trial of the aromatase inhibitor letrozole reported decreased fibroid volume following treatment, the trial did not assess fibroid-related symptoms, and the volume reduction was similar to that achieved with GnRH agonist therapy [141]. Two small studies reported that pretreatment with letrozole may improve surgical outcomes [142,143], but these studies have not been repeated.

- **Selective estrogen reuptake modulators (SERMs)** – Studies of the SERM raloxifene have reported mixed outcomes for fibroid treatment [144]. Use of raloxifene as hormonal add-back with GnRH analog treatment for fibroids appeared to reduce bone loss but did not improve quality of life or other fibroid-related symptoms [145].

- **Complementary medicine**

  - **Herbal supplements** – Limited data do not support use of herbal supplements, including black cohosh and Chinese herbal medicine, for fibroid-related symptoms [146-148].

  - **Acupuncture** – Trials assessing acupuncture for the treatment of fibroid-related symptoms are lacking, but small observational studies have suggested improved outcomes with acupuncture [149,150]. Until trial data supporting efficacy are available, we do not advise these interventions as primary treatment of fibroid-related symptoms. However, as risks associated with acupuncture are low, patients who desire a trial of acupuncture as adjunctive therapy may reasonably do so.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Uterine fibroids (leiomyomas)" and "Society guideline links: Abnormal uterine bleeding" and "Society guideline links: Hysteroscopy".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Uterine fibroids (The Basics)" and "Patient education: Uterine artery embolization (The Basics)")

- Beyond the Basics topic (see "Patient education: Uterine fibroids (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **General considerations**
  - Treatment of fibroids is aimed at resolving or reducing the symptoms associated with the lesions. Common symptoms include prolonged or heavy menstrual bleeding (HMB), bulk symptoms, pain, and impaired fertility. Symptoms can be present in isolation or combination. (See 'Common symptoms for treatment' above.)
  - Pretreatment assessment includes clinical and laboratory evaluation, with imaging and endometrial sampling as indicated by either planned procedure or patient risk factors. Peri- and postmenopausal patients are evaluated for sarcoma risk, and all patients with HMB should be evaluated for iron deficiency anemia and the possibility of coexisting endometrial hyperplasia. (See 'Pretreatment assessment' above.)
  - While there are limited data on expectant management for patients with uterine fibroids, there is little evidence of documented harm over 6 to 12 months of observation, and expectant management can be employed. (See 'Role of expectant management' above.)
- **Patients with HMB who do not desire future fertility** – For patients who do not desire future fertility, treatment is aimed at the presenting symptoms and performed in a stepwise approach until the symptoms are adequately controlled. As there are limited comparative studies demonstrating superiority of one treatment option over another, patient preference and shared decision-making are used to create the optimal management strategy.
  - **First tier**
    - For patients with HMB likely from submucosal fibroids, we recommend hysteroscopic myomectomy (**Grade 1B**). Submucosal fibroids include International Federation of Gynecology and Obstetrics (FIGO) type 0, type 1, or some type 2 (figure 1). Hysteroscopic myomectomy is an outpatient procedure with rapid recovery, a low risk of complications compared with abdominal procedures, rapid improvement in quality of life, and low risk of reintervention for fibroids. (See 'Hysteroscopic resection of submucosal fibroids' above.)
    - For patients with all other types of fibroids (ie, not exclusively submucosal) who do not desire pregnancy, we suggest initial treatment with a combined estrogen-progestin contraceptive (oral pills, transdermal patch, or vaginal ring) (**Grade 2C**). Although supporting data are of low quality, these products typically work quickly and are widely available, are low in cost, and are generally well-tolerated. Alternatives that are also

considered include levonorgestrel-releasing intrauterine devices, tranexamic acid, and progestin-only pills. As direct comparator data are sparse, treatment selection is patient-driven and considers variables such as efficacy, safety, tolerability, ease of use, and cost. (See 'Medical therapy' above.)

- **Second tier** – For patients whose symptoms persist despite trial of one or more first-tier therapies, second-tier medical treatments for fibroid-associated HMB include gonadotropin-releasing hormone (GnRH) agonists and antagonists. Uterine artery embolization (UAE) is a minimally invasive treatment option that treats both bleeding and bulk symptoms. Treatment choice is based on patient preferences around side effects, invasiveness, and recovery. Other deciding factors include availability and cost. (See 'Second tier' above.)

- **Third tier** – For patients with persistent symptoms, third-tier treatments include focused ultrasound surgery and, in rare cases, endometrial ablation. These provide less invasive therapies for patients who desire less time away from work and/or uterine preservation. Procedure selection is determined by patient preferences around invasiveness and recovery time as well as treatment availability. (See 'Third tier' above.)

- **Last line** – For patients who do not desire future fertility and have persistent fibroid-related symptoms despite the above treatments or who desire surgical therapy, options include hysterectomy and myomectomy. While hysterectomy is the definitive procedure for relief of symptoms and prevention of recurrent fibroid-related problems (eg, hydronephrosis), it is also associated with long-term morbidity. Given the success of less invasive alternative treatments, including UAE and focused ultrasound surgery, myomectomy is performed only in patients who do not have another uterine-sparing option or if there is a suspicion of sarcoma and the patient strongly desires a uterine-sparing technique knowing it may compromise outcome if sarcoma is found. (See 'Traditional surgery' above.)

- **Patients with bulk or pain symptoms who do not desire future fertility** – For patients whose main symptoms include bulk or pain, with or without HMB, treatment options include GnRH analogs and UAE. Patients and clinicians must balance the hypoestrogenic symptoms associated with long-term use of GnRH analogs with the procedure risk and longer recovery of UAE. If not effective, or if patients desire more definitive surgical therapy, then myomectomy and hysterectomy are options. Selection of medication, embolization, or surgery depends on patient preferences around side effects, invasiveness, recovery time, need for prolonged treatment, and risk of the treatment compared with risk of symptom recurrence. (See 'Bulk or pain symptoms with or without bleeding' above.)

- **Patients who desire fertility** – For patients who desire pregnancy and present with symptoms that are reasonably attributed to fibroids (bleeding, bulk, and, possibly, infertility), myomectomy is typically the first option. Most medical therapies are not used in patients desiring pregnancy because they preclude conception, cause adverse effects when employed long-term, and result in rapid symptom rebound when discontinued. (See 'Treatment options' above.)

  - For patients desiring pregnancy who have symptoms likely caused by fibroids FIGO type 0, type 1, or some type 2 (figure 1), we recommend hysteroscopic myomectomy (**Grade 1B**). Symptoms typically include abnormal or heavy uterine bleeding. Hysteroscopic myomectomy is minimally invasive, provides relief of symptoms, and typically preserves the integrity of the myometrium for future pregnancy. (See 'Submucosal fibroids only' above.)

  - For patients desiring pregnancy, wishing to maximize fertility, and presenting with submucosal fibroid or fibroids (FIGO type 0 or type 1) in the **absence** of other symptoms, we suggest hysteroscopic myomectomy (**Grade 2C**). We offer removal of FIGO types 0 and 1 fibroids but not type 2 (figure 1) due to the greater complexity of that surgery and higher risk of a two-stage procedure. Support for this approach mainly stems from the minimally invasive nature of the procedure and anticipated benefit from removal of fibroids that impact the uterine cavity. However, available evidence is limited, includes surrogate patient groups (eg, patients with endometrial polyps rather than endometrial fibroids), and often lacks data on live birth rates, which is the patient-important endpoint. (See 'Submucosal fibroids only' above.)

  - For patients desiring pregnancy who have bulk symptoms (with or without bleeding) or fibroids that are not amenable to hysteroscopic resection, **and** in whom there are no major contraindications to a surgical approach, we offer open abdominal or laparoscopic myomectomy. Myomectomy is preferred over UAE and focused ultrasound surgery given the lack of information about the safety of pregnancy with these approaches.

    - For patients undergoing myomectomy in whom laparoscopic removal is technically feasible (eg, uterine size <17 weeks, subserosal/submucosal, few in number, anterior or fundal location) **and** who have access to a surgeon with advanced laparoscopic skills, we suggest a laparoscopic rather than open approach (**Grade 2C**). However, the integrity of the uterine incision during pregnancy after laparoscopic myomectomy has not been evaluated adequately and may be inferior to open abdominal myomectomy. (See 'Treatment options' above.)

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Topic 5478 Version 66.0

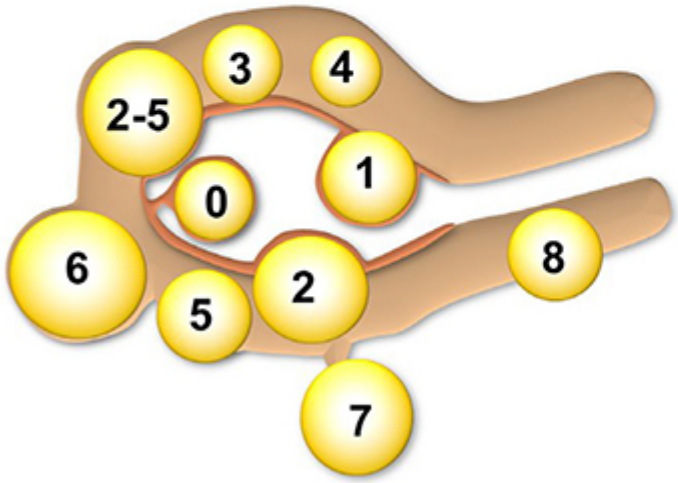
GRAPHICS

PALM-COEIN subclassification system for leiomyomas

Polyp	Submucous
Adenomyosis	Other
Leiomyoma	
Malignancy and hyperplasia	

Coagulopathy
Ovulatory dys
Endometrial
Iatrogenic
Not otherwise

FIGO leiomyoma subclassification system



SM – submucous	0	Pedunculated intracavitary
	1	<50% intramural
	2	≥50% intramural
	3	Contacts endometrium; 100% i
O – Other	4	Intramural
	5	Subserous ≥50% intramural
	6	Subserous <50% intramural
	7	Subserous pedunculated
	8	Other (specify eg, cervical, para

Hybrid (contact both the endometrium and the serosal layer)	Two numbers are listed separated by a By convention, the first refers to the relationship with the endometrium whil second refers to the relationship to the One example is below.	
	2-5	Submucous and subserous, eac than half the diameter in the en and peritoneal cavities, respecti

FIGO leiomyoma subclassification system. System 2 classification system including the FIGO leiomyoma subclassification system. The system that includes the tertiary classification of leiomyomas categorizes the submucous group according to the original Wamsteker et al system[1] and adds categorizations for intramural, subserosal, and transmural lesions. Intracavitary lesions are attached to the endometrium by a narrow stalk (≤10% or the mean of three diameters of the leiomyoma) and are classified as Type 0, whereas Types 1 and 2 require a portion of the lesion to be intramural: with Type 1 being less than 50% of the mean diameter and Type 2 at least 50%. Type 3 lesions are totally intramural but also about the endometrium. Type 3 are formally distinguished from Type 2 with hysteroscopy using the lowest possible intrauterine pressure necessary to allow visualization. Type 4 lesions are intramural leiomyomas that are entirely within the myometrium, with no extension to the endometrial surface or to the serosa. Subserous (Types 5, 6, and 7) leiomyomas represent the mirror image of the submucous leiomyomas: with Type 5 being at least 50% intramural, Type 6 being less than 50% intramural, and Type 7 being attached to the serosa by a stalk that is also ≤10% or the mean of three diameters of the leiomyoma. Classification of lesions that are transmural are categorized by their relationship to both the endometrial and the serosal surfaces. The endometrial relationship is noted first, with the serosal relationship second (eg, Type 2-5). An additional category, Type 8, is reserved for leiomyomas that do not relate to the myometrium at all, and would include cervical lesions (demonstrated), those that exist in the round or broad ligaments without direct attachment to the uterus, and other so-called "parasitic" lesions.

FIGO: International Federation of Gynecology and Obstetrics.

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Graphic 91085 Version 4.0

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