Uterine Fibroid Tumors: Diagnosis and Treatment

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The incidence of uterine fibroid tumors increases as women grow older, and they may occur in more than 30 percent of women 40 to 60 years of age. Risk factors include nulliparity, obesity, family history, black race, and hypertension. Many tumors are asymptomatic and may be diagnosed incidentally. Although a causal relationship has not been established, fibroid tumors are associated with menorrhagia, pelvic pain, pelvic or urinary obstructive symptoms, infertility, and pregnancy loss. Transvaginal ultrasonography, magnetic resonance imaging, sonohysterography, and hysteroscopy are available to evaluate the size and position of tumors. Ultrasonography should be used initially because it is the least invasive and most cost-effective investigation. Treatment options include hysterectomy, myomectomy, uterine artery embolization, myolysis, and medical therapy. Treatment must be individualized based on such considerations as the presence and severity of symptoms, the patient's desire for definitive treatment, the desire to preserve childbearing capacity, the importance of uterine preservation, infertility related to uterine cavity distortions, and previous pregnancy complications related to fibroid tumors. (Am Fam Physician 2007;75:1503-8. Copyright © 2007 American Academy of Family Physicians.)

▶ **See related editorial on page 1452.**

▶ **Patient information:** A handout on uterine artery embolization is available at http://familydoctor.org/601.xml.

Many women develop uterine fibroid tumors (i.e., leiomyomas) as they grow older. In one study, the prevalence of ultrasound-identified tumors ranged from 4 percent in women 20 to 30 years of age to 11 to 18 percent in women 30 to 40 years of age and 33 percent in women 40 to 60 years of age.[1] Studies report that 5.4 to 77 percent of women have uterine fibroid tumors, depending on the population studied and the diagnostic method used.[1,2] Women often consult family physicians because of symptoms related to fibroid tumors or after the lesions have been diagnosed incidentally during physical or radiologic examinations. This article reviews the epidemiology and etiology of uterine fibroid tumors, common clinical presentations, diagnostic strategies, and treatment options.

Epidemiology and Etiology

Leiomyomas are the most common female reproductive tract tumors. They are probably of unicellular origin,[3] and their growth rate is influenced by estrogen, growth hormone, and progesterone. Although studies have not clarified the exact process, uterine fibroid tumors arise during the reproductive years and tend to enlarge during pregnancy and regress after menopause. The use of estrogen agonists is associated with an increased incidence of fibroid tumors,[4] and growth hormone appears to act synergistically with estradiol in affecting the growth of fibroid tumors. Conversely, progesterone appears to inhibit their growth.

Several studies have documented an increased incidence of uterine fibroid tumors in black women.[5] Some evidence also indicates that black women are more likely than white women to have larger and more symptomatic tumors at the time of treatment.[6-10] *Table 1*[5-10] lists factors associated with the development of fibroid tumors. Recent evidence suggests that women with hypertension have a higher risk of fibroid tumors, possibly through smooth muscle injury or cytokine release.[11]

Clinical Features

Because of the high prevalence of uterine fibroid tumors and the fact that many are asymptomatic, attributing symptoms specifically to the tumors is problematic. Although evidence is largely drawn from uncontrolled studies, uterine fibroid tumors are commonly identified in women who have

SORT: KEY RECCOMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Pelvic and transvaginal ultrasonography should be used as the initial study to confirm the diagnosis of uterine fibroid tumors.	C	24
Expectant management is the treatment of choice for women with asymptomatic uterine fibroid tumors.	B	25-27
Hysterectomy may improve symptoms, quality of life, and psychological function in women with symptomatic uterine fibroid tumors.	B	30, 31
There currently is insufficient evidence to determine the best treatment approach for women with uterine fibroid tumors.	C	27, 33

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 1430 or http://www.aafp.org/afpsort.xml.

menorrhagia, pelvic pain, obstructive symptoms, infertility, or pregnancy loss.

Menstrual abnormalities, including menorrhagia, are the most common symptoms associated with uterine fibroid tumors. Submucosal tumors are often cited as a cause of menorrhagia, but there is no evidence that the endometrium over submucosal tumors differs from that overlying other areas of the uterus.[12] Fibroid tumors may produce a dysregulation of local growth factors, causing vascular abnormalities that contribute to menorrhagia[13] and are unrelated to their location in the uterus. One study attributed 11 percent of cases of symptomatic menorrhagia to uterine fibroid tumors.[14] Conversely, a population-based study did not find any evidence relating general abnormalities in menstrual cycle length or heaviness to the presence of fibroid tumors.[15]

Table 1. Factors That Affect the Risk of Uterine Fibroid Tumors

Decreased risk
More than five pregnancies
Postmenopausal status
Prolonged use of oral contraceptives
Smoking
Use of depot medroxyprogesterone acetate (Depo-Provera)
Increased risk
40 years or older
Black race
Family history of uterine fibroid tumors
Nulliparity
Obesity

Information from references 5 through 10.

Pelvic pain and pressure are less commonly attributed to uterine fibroid tumors. Individual case reports have described very large tumors that result in pelvic discomfort, respiratory failure, urinary symptoms, and constipation.[16-18] During pregnancy, the combination of large fibroid tumors and uterine enlargement can result in symptoms of urinary tract obstruction,[19] abdominal pain (attributed to the degeneration of fibroid tumors), and, possibly, an increased risk of placental abruption if the tumor is located retroplacentally.[20]

The role of fibroid tumors in infertility is controversial. Many of the studies examining the relationship between these tumors and infertility are retrospective and nonrandomized. Current evidence suggests that submucosal and intramural fibroid tumors that distort the uterine cavity can impair in vitro fertilization attempts.[21] The impact of intramural and subserosal fibroid tumors that do not distort the intrauterine cavity is unclear. Despite the lack of clear evidence of their role in conception problems, submucosal fibroid tumors, intramural fibroid tumors that distort the uterine cavity, fibroid tumors larger than 5 cm, and multiple fibroid tumors are often treated in patients with otherwise unexplained infertility.[22] The possible role of fibroid tumors in early miscarriage is also controversial. Given the conflicting data and potential observational bias and methodologic problems in studies examining this association, a causal relationship should not be assumed.[23]

Diagnosis

The bimanual examination is often the first indication that a patient may have uterine fibroid tumors. Several

Table 2. Comparison of Treatment Options for Women with Uterine Fibroid Tumors

Treatment	*Description*	*Advantages*	*Disadvantages*	*Fertility preserved?*
Gonadotropin-releasing hormone agonists	Preoperative treatment to decrease size of tumors before hysterectomy, myomectomy, or myolysis	Decreases blood loss and operative and recovery time	Long-term treatment associated with high cost, menopausal symptoms, and bone loss; increased recurrence risk with myomectomy	Dependent on subsequent procedure
Hysterectomy	Surgical removal of the uterus (transabdominal, transvaginal, or laparoscopic)	Definitive treatment for women who do not wish to preserve fertility Vaginal procedure associated with less blood loss, pain, and fever and greater patient satisfaction compared with abdominal procedure	Surgical risks	No
Myolysis	In situ destruction of tumors by heat, laser, or cryotherapy	Ease and rapidity of procedure; minimal blood loss; rapid recovery time	Delay in reduction of uterine size; unknown risk of recurrence; prolonged vaginal bleeding	Unknown
Myomectomy	Surgical or endoscopic excision of tumors	Resolution of symptoms with preservation of fertility; perioperative morbidity similar to that with hysterectomy	Fibroid recurrence rate of 15 to 30 percent at five years; success of procedure determined by number and extent of tumors	Yes
Uterine artery embolization	Interventional radiologic procedure to occlude uterine arteries	Minimally invasive; avoids surgery; short hospital stay (24 to 36 hours)	Symptom recurrence of more than 17 percent at 30 months; risk of extended hospitalization for postprocedure pain	No (limited experience)

studies, including transvaginal ultrasonography, sonohysterography, hysteroscopy, and magnetic resonance imaging (MRI), may be helpful in evaluating these tumors. Transvaginal ultrasonography has the lowest sensitivity and specificity, but it is the best initial test based on its noninvasive nature and cost-efficiency. MRI is preferred when precise myoma mapping is required (usually for surgical purposes), but it is the most expensive modality for evaluating fibroid tumors. Sonohysterography and hysteroscopy can be used to evaluate the extent of submucosal fibroid tumors, but these tests are relatively invasive.[24]

Management

Knowing the full range of treatment options enables family physicians to counsel patients about the optimal management of symptomatic uterine fibroid tumors. The number of treatment options is increasing and includes expectant management, surgery, uterine artery embolization, ablative techniques, and medical management *(Table 2)*. Clinical guidelines have been created to assist patients and physicians in choosing appropriate management options[25] *(Table 3)*. However, a systematic review by the Agency for Healthcare Research and Quality emphasized the paucity of evidence to support specific procedures and treatments based on individual patient characteristics.[26,27]

EXPECTANT MANAGEMENT

Expectant management with observation is increasingly recognized as a reasonable course for women with asymptomatic small and large fibroid tumors. Even rapidly growing tumors should not be removed routinely because the risk of a malignant leiomyosarcoma is small (0.23 percent in one study).[28,29]

SURGICAL TREATMENTS

Selected patients may benefit from surgery. One of the biggest challenges is identifying malignant leiomyosarcomas; rapid growth alone is not an adequate

marker. There is evidence that combining dynamic MRI (i.e., MRI enhanced by gadopentetate dimeglumine) and measurement of serum lactate dehydrogenase levels is useful in distinguishing leiomyosarcoma from benign fibroid tumors.[29] This approach may be useful in evaluating selected patients, such as postmenopausal women with enlarging tumors. Other patients who may benefit from surgery include those with persistent abnormal uterine bleeding or symptoms resulting from uterine bulk that do not respond to conservative measures.[26]

Hysterectomy. The presence of uterine fibroid tumors is the most common indication cited for hysterectomy, accounting for more than 30 percent of these procedures.[26] Although most hysterectomies in women with fibroid tumors are performed for symptomatic relief, the procedure is sometimes recommended to asymptomatic women whose uterine size is estimated to be greater than that at 12 weeks' gestation. Common justifications for this recommendation include the risk that tumors of this size could potentially mask other adnexal pathology, increase operative morbidity rates, and become malignant. Current evidence does not support the treatment of fibroid tumors in asymptomatic women.[25-27]

The Maryland Women's Health Study[30] and the Maine Women's Health Study[31] were large, prospective studies designed to measure the outcomes and effectiveness of hysterectomy for benign conditions. The most common indication for surgery in both studies was uterine fibroid tumors (48.1 and 35 percent, respectively). These studies demonstrated that hysterectomy substantially improves symptoms and quality of life in women with multiple and severe symptoms associated with gynecologic disorders. The Maine study enrolled a comparison group of women who received nonsurgical medical treatment.[31] Medical therapy for abnormal bleeding and chronic pelvic pain produced significant improvements, but one quarter of the nonsurgical group subsequently underwent hysterectomy. Women with uterine fibroid tumors who continued with nonsurgical treatment reported no significant changes in symptoms or quality of life over the one year follow-up. Not all women who are treated surgically report improvement. In the Maryland study, almost 8 percent of women had more or the same number of symptoms 24 months after hysterectomy.[30] Baseline depression, therapy for emotional problems, annual income of less than $35,000, and bilateral oophorectomy were significantly associated with poorer outcomes. Some women in the Maine study reported new symptoms after hysterectomy (e.g., hot flashes, weight gain, depression).[31] Most studies evaluating the effect of hysterectomy on sexuality are poorly designed, but the available evidence suggests that hysterectomy does not adversely affect sexuality.[32]

Myomectomy. Myomectomy (i.e., surgical removal of fibroid tumors while preserving the uterus) traditionally has been performed by laparotomy. Endoscopic myomectomy is now a treatment option for many women, and hysteroscopic myomectomy may be considered in women with symptomatic submucosal fibroid tumors. Ultimately, however, the choice of surgical approach is largely dependent on the expertise of the physician. Although elective cesarean delivery traditionally has been recommended for women who become pregnant after myomectomy (especially when the uterine cavity has been entered), data to support this recommendation are limited.[33]

Uterine Artery Embolization. Uterine artery embolization is performed under intravenous sedation. Using a femoral approach, a microcatheter is introduced into the uterine artery. Polyvinyl alcohol foam particles or other occluding agents are then injected. Complete occlusion of both uterine arteries initially was the goal of this treatment, but recent data suggest that incomplete embolization may produce effective infarction of myomas with less severe pain.[34] The Fibroid Registry for Outcomes Data was formed in 1999 to collect prospective data on more than 3,000 women undergoing embolization for fibroid tumors. Short-term outcomes in women included in

Table 3. Recommended Treatment Options for Women with Uterine Fibroid Tumors

Patient characteristics	*Treatment options*
Asymptomatic women	Observation
Symptomatic women who desire fertility preservation	Nonsurgical treatment or myomectomy
Symptomatic women who do not desire future fertility but wish to preserve the uterus	Nonsurgical treatment or myomectomy, myolysis, or uterine artery embolization
Women who desire fertility preservation and have had a pregnancy complicated by uterine fibroid tumors	Myomectomy
Infertile women with distortion of uterine cavity	Myomectomy
Women with severe symptoms who desire definitive treatment	Hysterectomy

this database have been encouraging. In the first 30 days after treatment, the incidence of adverse effects was low, and major complications in the hospital and 30 days postdischarge were uncommon (0.66 and 4.8 percent, respectively).[35] Future data will address long-term outcomes of uterine artery embolization.

Myolysis. Myolysis (i.e., delivering energy to tumors to desiccate them directly or disrupt their blood supply) is most often performed with the neodymium-doped yttrium aluminum garnet (Nd:YAG) laser or bipolar needles. Combination treatment with myolysis and endometrial ablation may reduce the need for subsequent procedures in patients with persistent bleeding.[36]

MEDICAL TREATMENTS

Medical therapy is available for women with symptomatic fibroid tumors who prefer conservative management.

Gonadotropin-Releasing Hormone Agonists. Gonadotropin-releasing hormone (GnRH) agonists are the most well-established therapy for medical management, causing amenorrhea and a rapid reduction in the size of the tumor. However, the benefits of GnRH agonists are tempered by significant side effects resulting from hypoestrogenism (e.g., hot flashes, vaginal dryness, bone demineralization). Because GnRH agonists are not appropriate for long-term use, this therapy is best suited for women in the perimenopausal or preoperative periods.[37]

Hormone Therapy. Hormone therapy with cyclic or noncyclic estrogen–progestin combinations appears to be ineffective in alleviating the symptoms of fibroid tumors and limiting tumor growth.[26] Studies have found no evidence that low-dose contraceptives cause the growth of uterine fibroid tumors; thus, these tumors are not a contraindication to the use of these contraceptives. A small study found significant improvement in bleeding after treatment with depot medroxyprogesterone acetate (Depo-Provera) in 20 African women with menorrhagia attributed to uterine fibroid tumors.[38] A review of six clinical trials with a total of 166 women demonstrated that treatment with mifepristone (Mifeprex) resulted in reduced tumor size and improvement in symptoms.[39] However, none of the studies were placebo controlled or blinded, and a notable adverse effect was the development of endometrial hyperplasia. Better-quality clinical trials are needed before recommendations can be made.

Other Therapies. The selective estrogen receptor modulator raloxifene (Evista) has been shown in one small study to decrease tumor size in postmenopausal women; however, there was no effect on uterine bleeding.[40] Small trials have provided insufficient evidence to assess the effectiveness of nonsteroidal anti-inflammatory drugs in the management of uterine fibroid tumors.[41] A noninvasive treatment using a combination of MRI and ultrasonography (ExAblate 2000) has been approved by the U.S. Food and Drug Administration.[42] This treatment focuses high-intensity sound waves on the tumor, inducing coagulation necrosis. The main advantage is that it is an outpatient procedure with a short recovery time. Long-term follow-up and additional studies are needed to identify women who will benefit most from this treatment.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Navy Medical Department or the U.S. Navy at large.

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