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.)
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. Fibroid tumors may produce a dysregulation of local growth factors, causing vascular abnormalities that contribute to menorrhagia and are unrelated to their location in the uterus. One study attributed 11 percent of cases of symptomatic menorrhagia to uterine fibroid tumors. 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.

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. During pregnancy, the combination of large fibroid tumors and uterine enlargement can result in symptoms of urinary tract obstruction, abdominal pain (attributed to the degeneration of fibroid tumors), and, possibly, an increased risk of placental abruption if the tumor is located retroplacentally.

The role of fibroid tumors in infertility is controversial. Many of the studies examining the relationship between these tumors and infertility are retrospective and non-randomized. Current evidence suggests that submucosal and intramural fibroid tumors that distort the uterine cavity can impair in vitro fertilization attempts. 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.

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

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

Diagnosis

The bimanual examination is often the first indication that a patient may have uterine fibroid tumors. Several
studies, including transvaginal ultrasonography, sono-
hysterography, 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 expen-
sive modality for evaluating fibroid tumors.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 embo-
lization, ablative techniques, and medical management
(Table 2). Clinical guidelines have been created to assist
patients and physicians in choosing appropriate manage-
ment options25 (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 increas-
ingly recognized as a reasonable course for women with
asymptomatic small and large fibroid tumors. Even rap-
idly 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 leio-
myosarcomas; rapid growth alone is not an adequate

<p>| Table 2. Comparison of Treatment Options for Women with Uterine Fibroid Tumors |
|----------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|</p>
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Description</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Fertility preserved?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonadotropin-releasing</td>
<td>Preoperative treatment to decrease size of</td>
<td>Decreases blood loss and operative and recovery</td>
<td>Long-term treatment associated with high cost,</td>
<td>Dependent on subsequent procedure</td>
</tr>
<tr>
<td>hormone agonists</td>
<td>tumors before hysterectomy, myomectomy, or</td>
<td>time</td>
<td>menopausal symptoms, and bone loss; increased</td>
<td></td>
</tr>
<tr>
<td></td>
<td>myolysis</td>
<td></td>
<td>recurrence risk with myomectomy</td>
<td></td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>Surgical removal of the uterus</td>
<td>Definitive treatment for women who do not</td>
<td>Surgical risks</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>(transabdominal, transvaginal, or laparoscopic)</td>
<td>wish to preserve fertility</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vaginal procedure associated with less blood</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>loss, pain, and fever and greater patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>satisfaction compared with abdominal</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myolysis</td>
<td>In situ destruction of tumors by heat, laser,</td>
<td>Ease and rapidity of procedure; minimal blood</td>
<td>Delay in reduction of uterine size; unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td></td>
<td>or cryotherapy</td>
<td>loss; rapid recovery time</td>
<td>risk of recurrence; prolonged vaginal bleeding</td>
<td></td>
</tr>
<tr>
<td>Myomectomy</td>
<td>Surgical or endoscopic excision of tumors</td>
<td>Resolution of symptoms with preservation of</td>
<td>Fibroid recurrence rate of 15 to 30 percent at 5</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>fertility, perioperative morbidity similar to</td>
<td>years; success of procedure determined by</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>that with hysterectomy</td>
<td>number and extent of tumors</td>
<td></td>
</tr>
<tr>
<td>Uterine artery</td>
<td>Interventional radiologic procedure to occlude</td>
<td>Minimally invasive; avoids surgery; short</td>
<td>Symptom recurrence of more than 17 percent at</td>
<td>No (limited experience)</td>
</tr>
<tr>
<td>embolization</td>
<td>uterine arteries</td>
<td>hospital stay (24 to 36 hours)</td>
<td>30 months; risk of extended hospitalization</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>for postprocedure pain</td>
<td></td>
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</tbody>
</table>
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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.26 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 Study30 and the Maine Women’s Health Study31 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. 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 |

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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—progesterone 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.32 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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REFERENCES

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