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# Uterine myomas: management

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**Objective:** To review the currently available literature regarding the current management alternatives available to women with uterine myomas.
**Design:** Literature review of 198 articles pertaining to uterine myomas.
**Result(s):** Many advances have been made in the management of uterine myomas. Watchful waiting; medical therapy; hysteroscopic myomectomy; endometrial ablation; laparoscopic myomectomy; abdominal myomectomy; abdominal, vaginal, and laparoscopic hysterectomy; uterine artery embolization; uterine artery occlusion; and focused ultrasound are now available.
**Conclusion(s):** Many options are now available to women with uterine myomas. The presently available literature regarding the treatment of myomas is summarized. (Fertil Steril® 2007;88:255–71. ©2007 by American Society for Reproductive Medicine.)

**Key Words:** Uterine myomas, myomas, fibroids, myomectomy, laparoscopic myomectomy, hysteroscopic myomectomy, endometrial ablation, hysterectomy, uterine artery embolization, focused ultrasound

Twenty-five years ago, this journal published a classic review of uterine myoma that was authored by Buttram and Reiter (1). At that time, treatment options were essentially limited to observation, hysterectomy, or less common, abdominal myomectomy. Presently, medical therapy, hysteroscopic myomectomy, laparoscopic myomectomy, uterine artery embolization (UAE), and focused ultrasound are also available treatments.

Although myomas are prevalent, myoma research is underfunded compared with other nonmalignant diseases. Treatment innovation has been slow, perhaps because many women with myomas are asymptomatic, myomas are benign, and mortality is very low (2). If offered hysterectomy as a first, and sometimes only, treatment option, some women choose to accommodate to their symptoms and stop seeking treatment. This may lead physicians to underestimate the true impact of the condition. However, women having hysterectomies because of myoma-related symptoms have significantly worse scores on SF-36 quality-of-life questionnaires than do women diagnosed with hypertension, heart disease, chronic lung disease, or arthritis (3).

An analysis of medical literature published between 1975 and 2000 attempted to answer questions fundamental to understanding outcomes of myoma treatment (4). The investigators questioned the risks and benefits of myoma treatments for women of different races, ages, ethnicities, or childbearing concerns; which specific clinical situations might benefit from the range of now-available treatments; the risks and benefits of myomectomy and hysterectomy for treatment of symptomatic and asymptomatic myomas; the outcomes for women with one vs. multiple myomas after myomectomy; which women might require additional treatment after myomectomy; whether, after myomectomy, the potential need for additional therapy increased risks compared with initial treatment with hysterectomy; and finally, the costs incurred for any of the available treatments. After an exhaustive review of the literature, scrutiny of 637 relevant articles, and careful study of 200 articles, those investigators found definitive answers to none of these fundamental questions.

Women and their physicians need information on which to base decisions regarding possible treatments. Prospective, randomized studies are difficult to conduct because of physician training and preferences, patient preferences, and women's understandable reluctance to be randomized to a major surgical procedure. This article will attempt to summarize the presently available literature regarding the management of myomas.

## WATCHFUL WAITING

There is no evidence that failure to treat myomas results in harm, except in women who have severe anemia from myoma-related menorrhagia or who have hydronephrosis caused by obstruction of at least one ureter by an enlarged,

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myomatous uterus. Predicting future myoma growth or onset of new symptoms is not possible (5). Studies of myoma treatments have found no significant change in uterine size or myoma volume over 6–12 months of follow-up in placebo arms (6, 7). A nonrandomized study of women who had uterine size of $\geq$8 weeks and who chose hysterectomy or watchful waiting found that 77% of women choosing observation had no significant changes in the self-reported amount of bleeding, pain, or degree of bothersome symptoms at the end of 1 year (8). Furthermore, mental health, general health, and activity indexes also were unchanged. Of the 106 women who initially chose watchful waiting, 24 (23%) opted for hysterectomy during the course of the year.

Therefore, for some women with myomas who are mildly or moderately symptomatic, watchful waiting may allow surgery to be deferred, perhaps indefinitely. Studies are needed to determine whether this strategy works for a longer period of time. Randomized studies of treatment or no treatment also are needed (4). As women approach menopause, watchful waiting may be considered, because there is limited time to develop new symptoms and, after menopause, bleeding stops and myomas decrease in size (9). Although the degree to which bulk symptoms resolve after menopause also has not been studied, the declining incidence of hysterectomy for myomas after menopause implies that symptoms do decline considerably (Fig. 1).

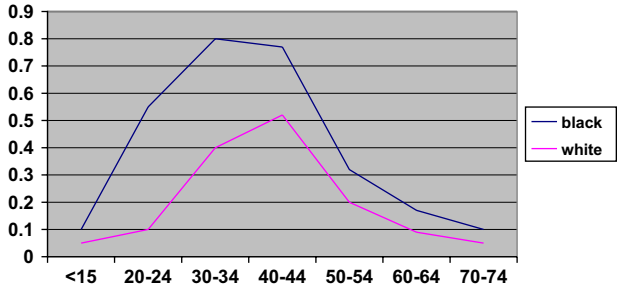
## MEDICAL THERAPY

### Non-Steroidal Anti-Inflammatory Drugs

Nonsteroidal anti-inflammatory drugs have not been shown to be effective in women with myomas. A placebo-controlled, double-blind study of 25 women with menorrhagia, 11 of whom also had myomas, found a 36% decrease in blood loss among women with idiopathic menorrhagia but no decrease in women with myomas. No other studies have examined this treatment (10).

**FIGURE 1**

Hysterectomies for fibroids (percentages vs. patient age in years).




*Parker. Management of uterine myomas. Fertil Steril 2007.*

### Gonadotropin-Releasing Hormone

Gonadotropin-releasing hormone agonists (GnRH-a) have been shown to decrease uterine volume, myoma volume, and bleeding. However, the benefits of GnRH-a are limited by side effects and by risks associated with long-term use. The effects on uterine and myoma volume appear to be the result of decreased levels of estrogen and progesterone (P) that are induced by GnRH-a, but other mechanisms, including induction of myoma degeneration and hyaline necrosis, a decrease in the size or number of leiomyoma cells, a reduction in extracellular matrix, or a decrease in blood flow to the uterus, may be important.

A study using Doppler sonography to assess uterine blood flow in seven women after 4 months of GnRH-a found a significant reduction in arterial blood flow in both the uterus and myomas (11). Treatment with GnRH-a leads to decreased expression of basic fibroblast growth factor, vascular endothelial growth factor, and platelet-derived growth factor, growth factors that have been implicated in myoma vascular supply and growth, and to decreased numbers of vessels and angiogenic vessels (12).

Daily subcutaneous (SC) injections of GnRH-a were found to decrease uterine size from 13.8 weeks to 9.5 weeks after 8 weeks of treatment (13, 14). Monthly GnRH-a, given for 6 months, reduces myoma volume by 30%, non-myoma volume by 43%, and total uterine volume by 35% (15). Reduction in uterine size occurs mostly within the first 3 months of treatment (6). Other studies confirm these findings (16–18). Menorrhagia responds well to GnRH-a; 37 of 38 women had resolution by 6 months (6). After discontinuation of GnRH-a, menses return in 4–8 weeks, and uterine size returns to pretreatment levels within 4–6 months (19). However, 64% of women remained asymptomatic 8–12 months after treatment.

Side effects occur in 95% of women who are treated with GnRH-a (19). Seventy-eight percent experience hot flushes; 32%, vaginal dryness; and 55%, transient frontal headaches that start 2 weeks after initiation of therapy and last about 2 weeks. However, only 8% of women terminated treatment with GnRH-a because of side effects. Arthralgia, myalgia, insomnia, edema, headaches, emotional lability, depression, and decreased libido are less commonly reported. The hypoestrogenic state induced by GnRH-a causes significant bone loss after 6 months of therapy (20).

In an effort to reduce side effects, inhibit bone loss, and allow longer term use of GnRH-a, low doses of estrogen and progestins may be added while GnRH-a is continued. After 3 months of treatment with GnRH-a and a 36% reduction in uterine volume, women continued the GnRH-a and received daily estropipate (0.625 mg) plus norethindrone (0.7 mg) on days 1–14, without any significant increase in uterine size (21). There was a statistically significant 3% decrease in bone density after 3 months of GnRH-a alone, but no further bone loss occurred after estrogen and progestins were added back. However, a study of long-term use of

GnRH-a over 6 years found a wide range of reduction in bone density among women and no difference in bone loss between groups that were given estrogen and progestin vs. those treated with GnRH-a alone (22). A reduction of bone loss has been reported after 6 months of treatment with GnRH-a and add-back of etidronate (400 mg/d for 2 wk, given every 2 months) (23).

A small randomized, prospective study found that women treated with GnRH plus tibolone, a synthetic hormone related to norethynodrel, had no significant differences in myoma symptoms when compared with women who had been treated with GnRH-a alone (24). However, the GnRH–tibolone group had reduced hot flushes, night sweats, and vaginal dryness and no loss of bone mineral density. Another study found no regrowth of myomas after 3 years of GnRH-a and tibolone therapy (7). Another study compared perimenopausal women treated with GnRH-a and tibolone for 12 months with women after hysterectomy and bilateral salpingo-oophorectomy and with an untreated control group. Twelve months after discontinuation of tibolone and 12 months after surgery, both groups had significantly more bone loss than did women going through natural menopause over the same interval (25). Tibolone presently is available in Europe.

Progestins also have an important influence on myoma growth (26). Women given GnRH-a and a placebo daily were found to have a 73% reduction in total uterine size. Women receiving GnRH-a with medroxyprogesterone acetate (20 mg) that was started at the onset of therapy and continued for 12 weeks had no decrease in total uterine volume. Subsequent crossover of the two groups confirmed these findings.

Interestingly, women with uterine myomas that were treated with GnRH-a and raloxifene, a selective estrogen-receptor modulator, for 18 months had a significant decrease in uterine and myoma volumes but had no change in bone mineral density or bone metabolic markers (27). Hot flushes were common, but no woman dropped out of the study for this reason.

**Preoperative use of GnRH-a** A Cochrane review found that women with myomas treated preoperatively with 3–4 months of GnRH-a had significantly reduced uterine volume and uterine size, improved preoperative hemoglobin, and reduced operating times and hospital stays (28). Although operative blood loss was less for both abdominal hysterectomy and abdominal myomectomy patients, there was no significant difference in transfusion rates. Women with myomas and initial mean hemoglobin concentrations of 10.2 g/dL were randomized preoperatively to GnRH-a plus oral iron or to placebo plus oral iron. After 12 weeks, 74% of the women treated with GnRH-a and iron had hemoglobin concentrations of $>$12 g/dL, compared with 46% of the women treated with iron alone (29).

Pretreatment with GnRH-a may avoid a vertical abdominal incision for the performance of myomectomy or hysterectomy (28). Pretreatment with GnRH-a before planned hysterectomy also may allow conversion from planned abdominal hysterectomy to vaginal hysterectomy. Twenty-five women randomized to preoperative GnRH-a treatment for 8 weeks were compared with 25 women without treatment. Women treated with GnRH-a had a significant decrease in uterine size, from 15.7 weeks to 11.2 weeks, and 76% were able to undergo vaginal hysterectomy, compared with 16% in the placebo group (30).

**Gonadotropin-releasing hormone agonists as temporary treatment for perimenopausal women** Women in late perimenopause who are symptomatic from uterine myomas may consider short-term use of GnRH-a. Gonadotropin-releasing hormone agonist was given monthly for 6 months to 34 perimenopausal women with symptomatic myomas, 12 of whom required repeat treatment after 6 months (31). Fifteen women went into natural menopause during the study, and 31 women avoided surgery for myomas. Although not specifically studied, add-back therapy may also be considered in this setting.

**Gonadotropin-releasing hormone antagonist** The GnRH antagonist ganirelix was given (daily by SC injection) to 20 women with uterine myomas (32). The immediate suppression of endogenous GnRH, without an initial flare, resulted in a rapid decrease in myoma and uterine volumes. Evaluation of uterine size by sonography found a maximum myoma volume reduction of 43% (range, 14%–77%) after 19 days. Magnetic resonance imaging at 19 days found a 29% reduction in myoma volume (range, 36%–62%). Treatment was accompanied by hypoestrogenic symptoms. The investigators suggested that when long-acting compounds are available, GnRH antagonists may be the drug of choice if medical treatment is used before surgery.

### Progesterone-Mediated Medical Treatment

The reduction in uterine size after treatment with the P-blocking drug RU-486 is similar to that found with GnRH-a (33). A prospective, randomized, controlled trial using either 5 or 10 mg of RU-486 for 1 year found that both doses induced a 48% decrease in mean uterine volume after 6 months.

Because of the P-blocking action of RU-486, endometrial hyperplasia may result from unopposed exposure of the endometrium to estrogen. A systematic review found endometrial hyperplasia in 10 (28%) of 36 women who were screened with endometrial biopsies (34). Thirty-eight percent of women experienced hot flushes, and 4% had elevated liver transaminases. Another study found that in women treated with 10 mg, 5 (13.9%) of 36 had simple endometrial hyperplasia at 6 months, and 1 (5%) of 21, at 12 months. No samples showed atypical hyperplasia (35).

Asoprisnil, a selective P receptor modulator, binds to P receptors, which are increased in myoma tissue. Doses of 10 and 25 mg are effective in shrinking myomas and suppress both abnormal and normal uterine bleeding, with no effects on circulating estrogen levels, no clinical symptoms of estrogen deprivation, and no breakthrough bleeding (36). The compound has an inhibitory effect on the endometrium as

a result of suppressed endometrial angiogenesis and/or function of spiral arteries, and this effect is the likely explanation for a decrease in abnormal bleeding. This medication is currently undergoing US Food and Drug Administration clinical trials.

### Progesterone-Releasing Intrauterine Device

In women with myomas, uterine size of $\leq$12 weeks, and a normal uterine cavity, levonorgestrel-releasing intrauterine systems have been shown to substantially reduce menstrual bleeding (37). Sixty-seven women who met these criteria were followed with pictorial assessment of menstrual bleeding, and within 3 months, 22 (85%) of 26 women with documented menorrhagia had normal bleeding. By 12 months, 40% of all women were amenorrheic, and all but 1 woman had hemoglobin concentrations of >12 g/dL.

### Alternative Medicine Treatment

A nonrandomized, nonblinded study compared myoma growth in 37 women treated with Chinese medicine, body therapy, and guided imagery with that in 37 controls who were treated with nonsteroidal anti-inflammatory medications, progestins, or oral contraceptive pills. After 6 months, sonographic evaluation demonstrated that myomas stopped growing or shrank in 22 (59%) of 37 treated women, compared with in 3 (8%) of 37 controls. Although symptoms responded equally well in both groups, satisfaction was higher in the treatment group. Participants in the study, however, actively sought alternative therapy, so assessment of satisfaction may reflect selection bias (38).

An uncontrolled study reported treatment of 110 women with myomas of <10 cm with the Chinese herbal medicine Kuei-chin-fu-ling-wan for $\geq$12 weeks. Clinical and sonographic evaluation found complete resolution of myomas in 19% of women, a decrease in size in 43%, no change in 34%, and an increase in 4%. Menorrhagia improved in 60 (95%) of 63 women, and dysmenorrhea improved in 48 (94%) of 51. However, 15 (14%) of the 110 women chose to have a hysterectomy during the 4 years of the study (39).

### Future Directions for Medical Therapy

Forthcoming medical treatments for myomas will likely include compounds that block the action of growth factors that regulate cellular proliferation and/or collagen production (40). Normal myometrium has little or no aromatase, an enzyme that converts circulating androgen to estrogen. Myoma cells, however, express aromatase in situ, perhaps in amounts sufficient to support their own growth, and large myomas have higher aromatase expression than do small myomas. One hopes that new aromatase inhibitors can be found that avoid systemic hypo-estrogenic symptoms by inhibiting myoma, but not ovarian, estrogen production (41).

Myomas have increased production of collagen. Pirfenidone, an anti-fibrotic compound (Marnac, Inc., Dallas, TX), decreases expression of collagen type I and III messenger RNA in cultured myometrial cells. Results of these studies, however, suggest that pirfenidone may inhibit new myoma growth but not affect myomas already present. Clinical studies of effectiveness are lacking for myomas, but treatment of pulmonary fibrosis shows a high incidence of side effects, with 87% of patients experiencing nausea, fatigue, or a photosensitive rash (42, 43).

## SURGICAL TREATMENT OPTIONS

Surgical treatment options currently include abdominal myomectomy; laparoscopic myomectomy; hysteroscopic myomectomy; endometrial ablation; and abdominal, vaginal, and laparoscopic hysterectomy.

Abdominal myomectomy long has been used as a conservative treatment for uterine myomas, and much of the literature predates the use of randomized controlled trials. Myomectomy has been stated to relieve symptoms in 80% of women (1). But there is scant literature documenting the efficacy of abdominal myomectomy in reducing myoma-related symptoms. Many large series reporting abdominal myomectomy do not report data for relief of symptoms after surgery (44–49).

There are few studies that compare available treatment outcomes and even fewer that compare patient satisfaction or quality of life after treatment.

A prospective, nonrandomized study comparing myomectomy with UAE reported that 75% of women in the myomectomy group had a significant decrease in symptom scores after 6 months (50). Because patient and physician preferences make recruitment difficult, it is challenging to perform randomized surgical trials. Presently, women and their gynecologists must make management decisions on the basis of well-performed case–control studies.

Serious medical conditions, such as severe anemia or ureteral obstruction, often need to be addressed surgically. Surgical intervention may also be indicated in women who have myomas that are associated with menorrhagia, pelvic pain or pressure, or urinary frequency or incontinence that compromises quality of life. Women with large symptomatic myomas who have completed childbearing are most often recommended to have a hysterectomy. A recent study found that uterine myomas were the indication for surgery in 198,000 (33%) of the 598,000 hysterectomies performed in 1999. In contrast, only 30,000 myomectomies were performed during that year (51).

### Abdominal Myomectomy

"The restoration and maintenance of physiologic function is, or should be, the ultimate goal of surgical treatment," said Bonney, an early advocate of abdominal myomectomy, in 1931 (52). However, women may be informed that myomectomy is not appropriate because hysterectomy is safer or is

associated with less blood loss or because sarcoma may be present. Recent reports do not support these concerns (53–55).

Myomectomy even may be considered for women with large uterine myomas who desire to retain their uterus. A study of 91 women with uterine size of >16 weeks (range, 16–36 wk) reported no conversions to hysterectomy. Complications included one bowel injury, one bladder injury, and one reoperation for incarcerated bowel. With use of a cell saver in 70 women, only 7 required homologous blood transfusion (56). A retrospective cohort study compared the morbidity of abdominal hysterectomy in 89 women who had myomas with that of 103 women who had abdominal myomectomy (57). Unfortunately, the study was not adjusted for uterine size (in the hysterectomy group, 15.2 wk vs. in the myomectomy group, 11.5 wk), and selection bias was likely. Nevertheless, there were no visceral injuries in the myomectomy group, but the hysterectomy group developed two ureteral, one bladder, one bowel, and one nerve injury, and in that group, there were two reoperations for bowel obstruction.

Case–controlled studies suggest that there may be less risk of intraoperative injury with myomectomy when compared with hysterectomy. A retrospective review of 197 women who had myomectomies and 197 women who had similar uterine size and underwent hysterectomies (14.4 vs. 15.6 wk) found that operating times were longer in the myomectomy group (200 vs. 175 min), but estimated blood loss was greater in the hysterectomy group (227 vs. 484 mL) (55). The risks of hemorrhage, febrile morbidity, unintended surgical procedure, life-threatening events, and rehospitalization were no different between groups. However, 26 (13%) of the women in the hysterectomy group developed complications, including 1 who incurred a cystotomy, 1 who incurred ureteral injury, 3 who incurred bowel injuries, 8 who developed ileus, and 6 who developed pelvic abscesses. In contrast, complications occurred in 11 (5%) of the myomectomy patients, including 1 who had a cystotomy, 2 who had a reoperation for small bowel obstruction, and 6 who developed ileus. The investigators concluded that after logistic regression analysis, no clinically significant difference in perioperative morbidity was detected, and myomectomy should be considered as a safe alternative to hysterectomy.

**Cesarean section and concurrent myomectomy** In carefully selected women, myomectomy may be safely accomplished at the time of cesarean section. One series reported 25 women who had removal of 84 myomas, of 2–10 cm, at the time of cesarean section with a mean estimated blood loss (EBL) of 876 mL (range, 400–1,700 mL) (58). Five women required blood transfusion, but none required a cesarean hysterectomy. A retrospective study compared 111 women who had myomectomy at the time of cesarean section with 257 with documented myomas who had cesarean section but not myomectomy (59). Only 1 (0.9%) woman in the myomectomy group required transfusion, and none required hysterectomy or embolization, and there were no differences between the two groups in mean operative times, incidence of fever, or length of hospital stay. Preoperative pain, an obstructed lower uterine segment, or an unusual appearance of the myoma at the time of surgery led to myomectomy in 14% of the women, but in 86% of the women, myomectomy was incidental, and cases were probably carefully selected. However, the investigators concluded that in experienced hands, myomectomy may be safely performed in selected women during cesarean section.

**Treating preoperative anemia** *Recombinant erythropoietin.* Erythropoietin alfa and epoetin, recombinant forms of erythropoietin, commonly are used to increase preoperative hemoglobin concentrations in cardiac, orthopedic, and neurologic surgery. A randomized study showed that use of epoetin (250 IU/kg per wk, approximately 15,000 IU) for 3 weeks before elective surgery was shown to increase the hemoglobin concentration by 1.6 g/dL and significantly reduce transfusion rates when compared with the case of controls (60). No side effects were experienced. A prospective, nonrandomized study of preoperative epoetin found a significant increase in hemoglobin concentrations before, and after, gynecologic surgery (61).

*Gonadotropin-releasing hormone agonist.* Gonadotropin-releasing hormone agonist may be used preoperatively to stop abnormal bleeding, with a resultant increase of hemoglobin concentration. Menorrhagia responds well to GnRH-a, with one study finding that 37 of 38 women had resolution by 6 months (6). Another study evaluated women with myomas and initial mean hemoglobin concentrations of 10.2 g/dL and randomized the women preoperatively to GnRH-a plus oral iron and to placebo plus oral iron. After 12 weeks, 74% of the women treated with GnRH-a and iron had hemoglobin concentrations of >12 g/dL, compared with 46% of the women treated with iron alone.

**Surgical technique for abdominal myomectomy: reducing blood loss** Surgical techniques available for myomectomy allow safe removal of even large myomas (56). Use of tourniquets and vaso-constrictive substances may be used to limit blood loss. Pitressin, a synthetic vasopressin (Monarch Pharmaceuticals, Bristol, UK), decreases blood loss during myomectomy and, in a prospective, randomized study, was as effective as mechanical occlusion of the uterine and ovarian vessels (62, 63). Vasopressin, an antidiuretic hormone, causes constriction of smooth muscle in the walls of capillaries, small arterioles, and venules. The use of vasopressin to decrease blood loss during myomectomy is an off-label use of this drug.

Uterine incisions made transversely, parallel to the arcuate vessels, may reduce bleeding. A midline vertical uterine incision, suggested elsewhere to avoid inadvertent extension of the incision to the cornua or ascending uterine vessels, cuts across multiple arcuate vessels and may be associated with greater blood loss (64). Transverse incisions may avoid many of these vessels (65). Extending the uterine incisions through the myometrium and entire pseudocapsule until the myoma is identified clearly will identify a less vascular

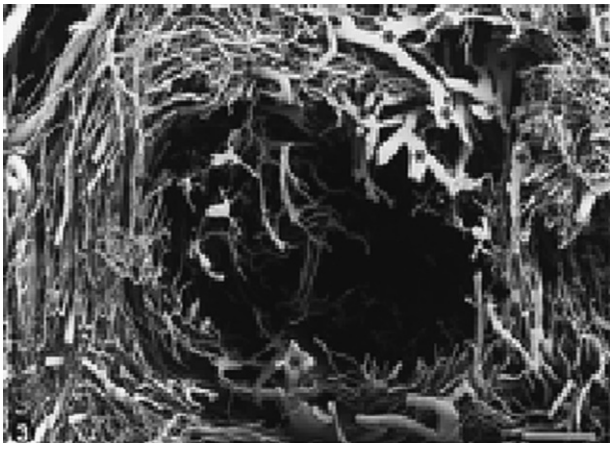
surgical plane. This avascular plane often is deeper than is commonly recognized. It has been noted, on the basis of vascular corrosion casting and examination by electron microscopy, that myomas are completely surrounded by a dense vascular layer that supplies the myoma and that no distinct, so-called vascular pedicle exists at the base of the myoma (66) (Fig. 2).

Limiting the number of uterine incisions has been suggested to reduce the possibility of adhesions to the uterine serosa (64). But to extract distant myomas, tunnels must be created within the myometrium, making hemostasis within these defects difficult. Alternatively, an incision can be made directly over a myoma, and only easily accessed myomas can be removed (56). The defect can be closed promptly with layers of running sutures, and hemostasis can be secured immediately. Multiple uterine incisions may be needed, but adhesion barriers may help limit adhesion formation (67).

Cell savers have been used extensively in orthopedic, cardiac, and neurological surgery and should be considered for use during myomectomy (or hysterectomy). These devices suction blood from the operative field, mix it with heparinized saline, and store the blood in a canister. If the patient requires blood reinfusion, the stored blood is washed with saline, filtered, processed by centrifuge to a hematocrit of approximately 50%, and given back to the patient by IV. Therefore, the need for preoperative autologous blood donation or heterologous blood transfusion often can be avoided (68). In a study of 91 women who had myomectomy for uterine size of >16 weeks, the cell saver was used for 70 women who had a mean volume of reinfused, packed red blood cells of 355 mL (56). Use of the cell saver avoids the risks of infection and transfusion reaction. The cost of using a cell saver, compared with donation of autologous blood, has not been studied for abdominal myomectomy. Most hospitals charge a minimal fee for having the cell saver available and charge additionally if it is used. Assuming that most women who donate autologous blood before myomectomy do not require blood transfusion, availability of the cell saver would spare many women the time and expense of donating, storing, and processing autologous blood. The cost of the cell saver for a cohort of women should, therefore, be significantly lower than the cost of autologous blood.

**FIGURE 2**

Vascular corrosion casting of myoma blood supply examined by electron microscopy. Reprinted from Walocha JA, Litwin JA, Miodoński AJ, Vascular system of intramural leiomyomata revealed by corrosion casting and scanning electron microscopy, Hum Reproduction 2003, Vol. 18, No 5, pp. 1088–93. © European Society of Human Reproduction and Embryology. Reproduced by permission of Oxford University Press/Human Reprodution.



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## Laparoscopic Myomectomy

Currently available instruments make laparoscopic myomectomy feasible, although the wide application of this approach is limited by the size and number of myomas reasonably removed, and the technical difficulty of the procedure and of laparoscopic suturing (69). However, prospective, randomized studies comparing abdominal and laparoscopic myomectomy in selected patients show that the laparoscopic procedure is associated with less postoperative pain, shorter hospital stay, and shorter recovery than is abdominal surgery (70).

In 40 women with subserosal and intramural myomas of <6 cm who were randomized to abdominal and laparoscopic myomectomy, estimated blood loss and surgical times were similar, and there were no major complications in either group. A study of 131 women randomized to abdominal and laparoscopic myomectomy for non-pedunculated myomas of >5 cm (mean, 7 cm) found significantly higher postoperative hemoglobin concentrations, lower incidence of postoperative fever, and shorter hospital stays with laparoscopic myomectomy (71).

Case series without controls show the feasibility of laparoscopic surgery in women with large myomas. In a series of 144 women in whom the largest myoma was ≤18 cm (mean, 7.8 cm), only 2 (1.4%) required conversion to laparotomy (72). Of 332 consecutive women undergoing laparoscopic myomectomy for symptomatic myomas of <15 cm, only 3 (0.9%) women required conversion to laparotomy (73).

Port placement should be based on the position and size of the myomas to be removed. Laparoscopic suturing may be more ergonomic if there are two ports on either the patient's right side, for right-handed surgeons, or left side, for left-handed surgeons: a 12-mm port, about 2 cm medial to the iliac crest, for suture access and another 5-mm lateral port, at the level of the umbilicus (74). A left upper quadrant approach may be used for initial access when uterine size is near or above the umbilicus (75).

Pitressin is injected into the myoma. A transverse incision is made directly over the myoma and carried deeply until

definite myoma tissue, and the avascular plane, is noted. The myoma is grasped with a tenaculum for traction, and the plane between the myometrium and myoma is dissected until the myoma is free. Bleeding vessels in the myometrial defect are desiccated with bipolar electrosurgical paddles. Delayed absorbable sutures are placed in one, two, or three layers, as needed, adhering to surgical technique at laparotomy. Morcellation of the myoma, which now is easier with electromechanical devices, is accomplished under direct vision. The pelvis and abdomen are irrigated, the fluid suctioned, and Interceed (Gynecare, Somerville, NJ) is placed as an adhesion barrier.

### Myolysis and Cryomyolysis

A number of energy sources including bipolar electrosurgery, neodymium-doped yttrium-aluminium-garnet laser, and cryogenic probes have been used under laparoscopic direction to reduce myoma size by means of myoma destruction and interference with local vascular supply (76, 77). Although uterine and myoma volumes decreased by approximately 50%, dense adhesions to the uterine serosa were found in 6 (53%) of 15 women undergoing subsequent laparoscopic evaluations for other reasons (78). Most investigators do not recommend myolysis for women who desire future fertility.

### Adhesions After Myomectomy

Adhesion formation has been well documented after myomectomy (79). A Cochrane review found that Interceed reduced the incidence of adhesion formation, both de novo and reformation, at laparoscopy and laparotomy, but there were insufficient data to support its use to improve pregnancy rates. Gore-Tex (Gore and Associates, Newark, DE) may be superior to Interceed in preventing adhesion formation, but its usefulness is limited by the need to affix it to the uterus and by the need for later removal. The authors found limited evidence of the effectiveness of Seprafilm (Genzyme, Cambridge, MA) in preventing adhesion formation (80).

A well-conducted prospective study randomized 127 women undergoing abdominal myomectomy to treatment or no treatment with Seprafilm at the end of surgery, and the women were evaluated with second-look laparoscopy. Women treated with Seprafilm had significantly fewer adhesions and lower adhesion severity scores, with lower extent and area than untreated women. At least one adnexa was adhesion free in 48% of the treated group, vs. in 31% in the untreated group, a statistically significant difference (67). This study and others found an increased incidence of adhesions with posterior uterine incisions, compared with anterior incisions (81).

In a randomized study, Interceed was placed at the completion of laparoscopic myomectomy in 25 women, and at second-look laparoscopy, 60% of the women had no adhesions found. In the group of 25 women who did not have Interceed placed, only 12% were adhesion free (82). Sixty-three women having an abdominal myomectomy were randomized to intraoperative use of Seprafilm, Dextran, factor 13 with fibrinogen, or a control group. At second-look laparoscopy 7 days later, uterine adhesions were found in 14% of women treated with Seprafilm, in 70% of women treated with Dextran, in 75% of women treated with factor 13 with fibrinogen, and in 69% of women in the control group. Peritoneal adhesions were found in 14%, 29%, 42%, and 69%, respectively (83).

Adhesion formation after laparoscopic and abdominal myomectomy was compared in a case–control study (84). The number and extent of adhesions was lower in the laparoscopy group, although the number of patients was small ($n = 28$).

### Hysteroscopic Myomectomy

Submucous myomas, sometimes associated with increased menstrual bleeding or infertility, may often be removed hysteroscopically. Other etiologies for bleeding or infertility should be considered before treatment is initiated (5). Classification of submucous myomas is based on the degree of the myoma within the cavity: Type 0 myomas are entirely intracavitary, type I myomas have >50% of the myoma within the cavity, and Type II myomas have <50% of the myoma within the cavity (Fig. 3) (85).

**Indication: fertility** The association of submucous myomas with infertility is supported by the fertility literature. A meta-analysis of infertile women with submucous myomas distorting the endometrial cavity found significantly lower pregnancy and delivery rates, compared with infertile controls without myomas (respectively: risk ratio, 0.32; 95% confidence interval, 0.13–0.70 and risk ratio, 0.28; 95% confidence interval, 0.10–0.72). It is important to note that resection of submucous myomas led to a significant increase in the pregnancy rate compared with the case in infertile controls without myomas (risk ratio, 1.72; 95% confidence interval, 1.13–2.58) (86).

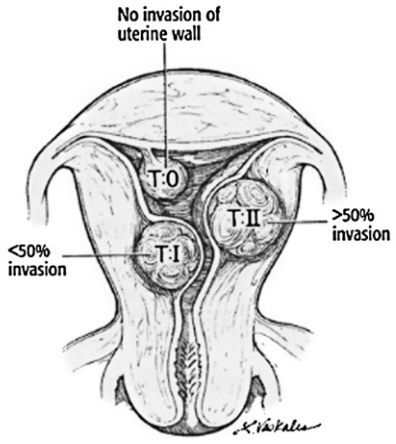
Although the mechanism for the association between submucous myomas and infertility is not well understood, theories include changes in local vascular supply that deprive the implanted embryo of oxygen and nutrients; mechanical obstruction of the tube; or induction of inflammation or local biological factors that interfere with transport, implantation, or embryo development.

**Indication: abnormal bleeding associated with submucous myomas** No meta-analysis of the association of submucous myomas and abnormal uterine bleeding has been performed; however, most studies show a reduction in bleeding after resection. One hundred ninety-six consecutive women with menorrhagia and the presence of one or more submucous myomas were followed for a mean of 73 months (range, 50–104 mo) after hysteroscopic myomectomy (87). Sixty-eight percent of women reported "satisfaction and ability to lead a normal life." Twenty-six (13%) required repeat hysteroscopic procedures, 25 women required hysterectomy, and 10 had recurrent bleeding without further treatment, for

**FIGURE 3**

Classification of submucous myomas based on percentage of myoma within uterine cavity. Reprinted from Fertility and Sterility, Vol. 73, Cohen LS, Valle RF, Role of vaginal sonography and hysterosonography in the endoscopic treatment of uterine myomas, pp 197–204, © 2000, with permission from American Society for Reproductive Medicine.

| Type | Intramural Extension |
|---|---|
| 0 | None |
| I | <50% |
| II | >50% |




*Parker. Management of uterine myomas. Fertil Steril 2007.*

a total failure rate of 31%. Long-term follow-up of 285 consecutive women with menorrhagia or metrorrhagia who had hysteroscopic resection of one or more submucous myomas found that additional surgery was required for 9.5% at 2 years, for 10.8% at 5 years, and for 26.7% at 8 years (88).

When pictorial assessment was used to estimate menstrual blood loss before and for 41 months after hysteroscopic resection of submucous myomas, a significant decrease in bleeding was reported in 42 (82%) of 51 women with submucous pedunculated, 24 (86%) of 28 women with sessile, and 15 (68%) of 22 women with submucous/intramural myomas (89). After 5 years, 10% of women with normal uterine size and not more than two submucous myomas required reoperation (repeat resection or hysterectomy) (88). In that study, 100% of type 0, 98% of type I, and 91% of type II myomas were completely resected. Half of the women with incomplete resection required reoperation within 2 years.

In selected women who do not desire future childbearing, endometrial ablation with or without hysteroscopic myomectomy may be efficacious. One study that used an objective measure of pad counts after ablation with or without myoma resection found that 48 (94%) of 51 women had resolution of abnormal bleeding after a mean follow-up of 2 years (range, 1–5 y) (90). A study of 62 women followed for an average of 29 months (range, 12–60 mo) found that 74% of the women had hypomenorrhea or amenorrhea, and only 12% required a hysterectomy (91).

One study of 33 women followed for a mean of 8 months after neodymium-doped yttrium-aluminium-garnet laser ablation of the endometrium in the presence of known uterine myomas with total uterine volume of <16 weeks' size reported amenorrhea in 16 women (49%) and eumenorrhea or hypomenorrhea in the other 17 (92). Hydrothermal ablation was used to treat 22 women with known submucous myomas of ≤4 cm, with 91% reporting amenorrhea, hypomenorrhea, or eumenorrhea after a minimum of 12 months' follow-up (93).

### Hysterectomy

Women who present with symptomatic uterine myomas often are offered hysterectomy as treatment (54, 94). In a recent review of hysterectomy in the United States, myomas were the indication for surgery in 40% of abdominal, 17% of vaginal, and 29% of laparoscopic hysterectomies (51).

Women with intractable symptoms that affect their lives and who have not been helped by other therapies may benefit from hysterectomy. The Maine Women's Health Study found that after hysterectomy (35% were performed for myomas) for moderate or severe non–life-threatening symptoms, 72% of women felt "much better," another 16% felt a "little better", and 3% of the women felt worse than they did before surgery (8). Only 3% of the patients reported negative feelings about themselves as women as a result of having had a hysterectomy. However, at the time of the study, alternative modes of surgical therapy such as endometrial ablation, hysteroscopic, laparoscopic or abdominal myomectomy, UAE, or focused ultrasound were not used or not available. As these and other new developments become widely available, it is likely that the need for hysterectomy as treatment for myomas will decrease.

Hysterectomy is not without the possibility of complications. A study of 446 women having hysterectomy for myoma-related symptoms reported that women subjected to hysterectomy found an increased risk of complications as uterine weights increased (54). The risk of blood loss of >500 mL and the need for transfusion was higher when the uterus weighed >500 g, compared with uterine weights of <500 g.

Women who undergo hysterectomy for very large uterine myomas have been shown to have an increased risk of blood loss with increasing uterine size (95). Blood loss of >500 mL occurred in 53 (26%) of 208 women with uterine weight of <500 g, 26 (41%) of 63 women with uterine weight of 500–999 g, and 26 (53%) of 47 women with uterine weight of >1,000 g. However, four cystotomies, one enterotomy,

two pelvic abscesses, and one bowel obstruction occurred in the women with uterine weight of <500 g, and none of these complications occurred in women with larger uteri. Pretreatment with GnRH-a has been found to decrease operative blood loss and also to decrease the need for a vertical abdominal incision for the performance of hysterectomy (28).

Enlarging uterine size has, in the past, been considered an indication for hysterectomy. However, studies in the last decade show that this indication is unfounded. One of 1,332 women subjected to surgery for myomas was found to have leiomyosarcoma, and only 1 of the 371 women with a "rapidly growing uterus" was found to have sarcoma (53).

**Laparoscopic hysterectomy** Laparoscopic hysterectomy, either total or supracervical, may be feasible for women with uterine myomas, with the benefits of less postoperative pain, shorter hospital stay, and faster recovery.

*Laparoscopic hysterectomy compared with vaginal hysterectomy.* If a vaginal hysterectomy is technically feasible for a patient, there is no benefit in performing a laparoscopic hysterectomy. The ability to perform a vaginal hysterectomy on an outpatient basis with good patient acceptance has been established (96). A prospective, randomized study compared laparoscopy-assisted vaginal hysterectomy with standard vaginal hysterectomy in an outpatient setting (97). All patients had a mobile uterus of <16 weeks' size and were believed to be candidates for outpatient surgery. An average of 55 minutes' additional operating time was required for the patients operated on by laparoscopy-assisted vaginal hysterectomy. Added anesthesia time, in addition to the cost of disposable instruments, increased the cost of laparoscopic surgery by $3,000 when compared with standard vaginal hysterectomy. The outcomes of the two groups were otherwise comparable. Other studies have confirmed these findings (98, 99).

*Laparoscopic hysterectomy compared with abdominal hysterectomy.* A prospective, randomized, multicenter study concluded that laparoscopic-assisted hysterectomy offered the benefits of less-invasive surgery without increased risk (100). Eighty women with uterine size of between 280 and 700 g (considered a contraindication to vaginal hysterectomy) were included in the study. Laparoscopy-assisted vaginal hysterectomies, with the laparoscopic portion of the procedure concluded before ligation of the uterine arteries (type I according to the Munro and Parker classification) were compared with the standard abdominal approach (101). Estimated blood loss, postoperative day 1 hemoglobin, postoperative pain (as measured by a visual analog scale), and postoperative hospital stay were all significantly better for the laparoscopy-assisted hysterectomy group. The abdominal hysterectomy group had seven postoperative complications: one woman with a cuff hematoma who required transfusion, one with delayed bleeding requiring reoperation and transfusion, and five other women with fevers. The only complications in the laparoscopic group were postoperative fevers in two women.

A retrospective cohort study compared laparoscopic hysterectomy in 34 women who had uterine weights of >500 g (range, 500–1,230 g) with the case of 68 women who had uterine weights of <300 g (102). The investigators found no difference in complications rate, blood loss, hospital stay, or postoperative recovery, but operating times were significantly shorter in the women with smaller uteri. No patient required conversion to laparotomy. Therefore, in experienced hands, the benefits of laparoscopic hysterectomy may also be extended to women who have large myomas.

**Conservative surgery for uterine sarcoma** Hysterectomy is the treatment of choice when leiomyosarcoma is found. However, a small number of young women who desired to retain fertility have been offered uterine preservation when sarcoma was found incidentally at the time of a presumed myomectomy and when no evidence of residual disease was found on postoperative ultrasound, hysteroscopy, abdominal and pelvic magnetic resonance imaging (MRI) or computed tomography scan, or chest roentgenogram. In a review of the available data, including their own cases, Lissoni et al. (103) reported that 27 such sarcomas were managed by observation, with a mean follow-up of 42 months (range, 11–92 mo). Nine women had subsequent surgery, and 3 had evidence of residual disease. Among the 18 women who were observed, only 1 had a recurrence, and 9 women had subsequent pregnancies that went to term.

## NEW APPEARANCE OF MYOMAS

Although new myomas may grow after myomectomy, most women will not require additional treatment. If the first surgery is performed in the presence of a single myoma, only 11% of women will have subsequent surgery. If multiple myomas are removed during the initial surgery, only 26% will have subsequent surgery (mean follow-up, 7.6 y) (104). Individual myomas, once removed, do not grow back. Myomas detected after myomectomy, often referred to as recurrence, either are the result of persistence of myomas left at the time of surgery or are newly developed myomas. Perhaps this circumstance is best designated as new appearance of myomas.

Studies reporting new appearance of myomas should be carefully evaluated. Methodological problems, including incomplete follow-up, insufficient length of follow-up, the use of either transabdominal or transvaginal sonography (with different sensitivity), or other inconsistent methods being used to confirm new appearance confound many studies. Data analysis also may confound results. Life table analysis is the optimal method for calculation of new appearance rates; that is, the group lost to follow-up is assumed to have had similar outcomes as the group that has been followed (105, 106).

Reports of new appearance may be measuring persistence, likely related to the thoroughness of the surgeon in removing myomas initially present. Sonography found that 29% of women had persistent myomas 6 months after myomectomy

(107). In addition, the background formation of new myomas in the general population should be considered. As noted elsewhere, a hysterectomy study found myomas in 77% of specimens from women who did not have a preoperative diagnosis of myomas (108).

### Clinical Follow-Up

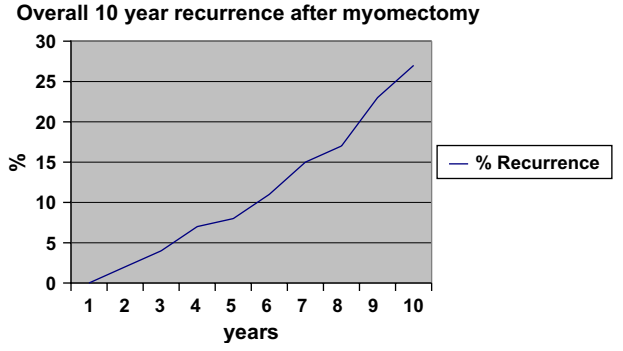
Clinical exam alone may not be effective in assessing the incidence of new appearance of myomas, because women who return to the gynecologist are more likely to have gynecologic problems associated with new myomas than are women who remain asymptomatic. Also, enlargement of the uterus may result from adenomyosis or misdiagnosis of an adnexal mass. Clinical symptoms, such as abnormal bleeding or pelvic discomfort, ascertained by phone or written survey, may overstate new appearance rates, because these symptoms may result from unrelated causes. However, self-reported diagnosis based on symptom questionnaires has reasonably good correlation with sonographic or pathologic confirmation of myomas and may be the most appropriate method of gauging clinical evidence of new appearance (109). One study of 622 patients, who were 22–44 years of age (average, 33 y) at the time of surgery and were followed over 14 years, found the cumulative new appearance rate to be 27%, on the basis of clinical examination followed by ultrasound confirmation (Fig. 4) (110). An excellent review of life table analysis studies found a cumulative risk of clinically significant new appearance of 10%, 5 years after abdominal myomectomy (106).

### Sonographic Follow-Up

Routine ultrasound follow-up is sensitive but detects many clinically insignificant myomas. One hundred forty-five women with mean age of 38 years (range, 21–52 y) were followed after abdominal myomectomy, with clinical evaluation every 12 months and transvaginal sonography at 24 and 60 months (or sooner, with clinical suspicion) (107). No lower size limit was used for the sonographic diagnosis of myomas. The cumulative probability of new appearance was 51% at 5 years. A study of 40 women who had a normal sonogram 2 weeks after abdominal myomectomy found that the cumulative risk of sonographically detected new myomas of >2 cm was 15% over 3 years (111).

**FIGURE 4**

Overall 10-year recurrence after myomectomy. Reproduced from BJOG Vol. 98, Candiani GB, Fedele L, Parazzini F, Villa L, Risk of recurrence after myomectomy, pp. 385–9, 1991, with the permission of the Royal College of Obstetricians and Gynaecologists.




*Parker. Management of uterine myomas. Fertil Steril 2007.*

### Need for Subsequent Surgery

Meaningful information for a woman with myomas considering treatment is her approximate risk of developing symptoms that would require yet additional treatment. A study of 125 women followed by symptoms and clinical exam after a first abdominal myomectomy found that a second surgery was required during the follow-up period (average, 7.6 y; range, 5–10 y) for 11.1% of women who had one myoma removed initially and for 26.3% of women who had multiple myomas removed (104). Crude rates of hysterectomy after myomectomy vary from 4.3%–16.8% over 5 years (48, 112, 113).

### Prognostic Factors Related to New Appearance of Myomas

**Age** Studies show conflicting results, with one study showing an increased risk (107) of new appearance with increasing age and another showing decreased risk (114). Given that the incidence of myomas increases with increasing age, 4.3 per 1,000 woman-years for 25- to 29-year-olds and 22.5 per 1,000 woman-years for 40- to 44-year-olds, new myomas would be expected to form as age increases, even after myomectomy.

**Subsequent childbearing** One study found that pregnancy with delivery subsequent to myomectomy was the only factor that influenced the new appearance rates: the 10-year clinical new-appearance rate for women who subsequently gave birth was 16%, but for those women who did not give birt, the rate was 28% (110).

**Number of myomas initially removed** Risk of new appearance increases with number of myomas removed, representing either persistence caused by increased difficulty of removing all myomas initially or predisposition to the development of new myomas (104, 107, 110). After ≥5 years of follow-up, 27% of women who had a single myoma removed initially had clinically detected new myomas, and 59% of women with multiple myomas initially removed had new myomas (104).

**Gonadotropin-releasing hormone agonists** Preoperative treatment with GnRH-a decreases myoma volume and may make smaller myomas harder to identify during surgery, increasing the risk of persistence. A randomized study compared 16 women who had immediate myomectomy with 8 women who were treated with GnRH-a for 3 months, followed by myomectomy (107). Three months after surgery,

all women had normal clinical exams, but 5 (63%) of the women in the GnRH group had myomas of size <1.5 cm detected sonographically, whereas only 2 (13%) untreated women had myomas detected.

**Laparoscopic myomectomy** Reoperation rates may not differ for women having laparoscopic, as opposed to abdominal, myomectomy. Eighty-one women randomized to either laparoscopic or abdominal myomectomy were followed with transvaginal sonography every 6 months for ≥40 months (115). Myomas of >1 cm were detected in 27% of women after laparoscopic myomectomy, compared with in 23% in the abdominal myomectomy group. However, no woman in either group required reoperation or other intervention for myomas during the study period.

### Reducing New Appearance After Myomectomy

Treatment with GnRH-a after myomectomy may reduce new myoma growth. A nonrandomized study compared 25 women who were given GnRH-a after myomectomy with 40 women who chose not to be treated after surgery. Gonadotropin-releasing hormone agonist was given monthly for 3 months, then 1 month per year for 3 years (111). Sonographic evaluation was performed 2 weeks after the initial surgery and then every 6 months during the study period. Nine (22.5%) of the 40 untreated women had new appearance of myomas of >2 cm, but only 1 (4%) of the 25 GnRH-a–treated women had new myomas. No other studies have been performed to confirm these results.

## UTERINE ARTERY EMBOLIZATION

Uterine artery embolization appears to be an effective treatment for selected women with uterine myomas. Presently, the effects of UAE on premature ovarian failure, fertility, and pregnancy are unclear. Therefore, many interventional radiologists advise against the procedure for women considering future fertility. Appropriate candidates for UAE include women who have symptoms severe enough to warrant hysterectomy or myomectomy. Although very rare, complications of UAE may necessitate life-saving hysterectomy. Therefore, women who would not accept hysterectomy under any circumstance should not undergo UAE.

Contraindications to treatment of myomas with UAE include active genitourinary infection, genital tract malignancy, reduced immune status, severe vascular disease limiting access to the uterine arteries, contrast allergy, or impaired renal function. Relative contraindications include submucous myomas, pedunculated myomas, recent GnRH-a treatment or previous iliac or uterine artery occlusion, or postmenopausal status (116).

Few new applications of an established procedure have been studied and documented as deliberately as UAE. The Society for Interventional Radiology developed and validated a myoma-specific quality-of-life questionnaire and established a national prospective, multicenter registry collecting baseline, procedural, and outcome data on UAE patients (117). Despite these commendable efforts, randomized trials comparing UAE with myomectomy have not been organized. The American College of Obstetricians and Gynecologists recommends that women considering UAE have a thorough evaluation with a gynecologist to help facilitate collaboration with the interventional radiologist and that protocols establish the responsibility of caring for the patient at all times (118).

### Technique for UAE

Percutaneous cannulation of the femoral artery is performed by a properly trained and experienced interventional radiologist (119). Embolization of the uterine artery and its branches is accomplished by injecting gelatin sponges, polyvinyl alcohol particles, or tris-acryl gelatin microspheres via the catheter until occlusion, or slow flow, is documented. Total radiation exposure, approximately 15 rads, is comparable to that in one to two computed tomography scans or barium enemas (120).

Postprocedural pain, the result of hypoxia, anaerobic metabolism, and formation of lactic acid, usually requires 1 night of pain management in the hospital. Most women are discharged the next day and may need to take nonsteroidal anti-inflammatory medications for 1–2 weeks. Many women can return to normal activity within 1–3 weeks, although about 5%–10% of women have pain for >2 weeks. About 10% of women will require readmission to the hospital for postembolization syndrome, which may be characterized by diffuse abdominal pain, nausea, vomiting, low-grade fever, malaise, anorexia, and leucocytosis. This process is treated with IV fluids, continued nonsteroidal anti-inflammatory medications, and pain management and usually resolves within 48–72 hours. Persistent fever is managed with antibiotics, but failure to respond to antibiotics may indicate sepsis, which needs to be aggressively managed with hysterectomy.

### Outcomes of UAE

One study used a myoma-specific quality-of-life questionnaire to evaluate 305 women, 3 months after UAE. Overall patient satisfaction was 92% (121). A study of 400 women with longer follow-up (mean, 16.7 mo) reported 26% clinical failures with no improvement of symptoms (122). The largest prospective study reported to date includes 555 women, 18–59 years of age (mean, 43 y), 80% of whom had heavy bleeding, 75% of whom had pelvic pain, 73% of whom had urinary frequency or urgency, and 40% of whom had required time off work as a result of myoma-related symptoms (123).

Telephone interviews 3 months after UAE found that menorrhagia improved in 83% of women, dysmenorrhea improved in 77%, and urinary frequency improved in 86%. Mean myoma volume reduction of the dominant myoma was 33% at 3 months, but improvement in menorrhagia was not related to preprocedural uterine volume (even volume of >1,000 $cm^3$) or to the degree of volume reduction obtained. Of note, two women (2/555, 0.4%) had continued uterine growth and worsening pain and were found to have sarcomas. The complication-related hysterectomy rate was

1.5%; 2 women had infections, 4 had persistent postembolization pain, 1 had a prolapsed myoma, and 1 had continued vaginal bleeding. Whereas 3% of women who were <40 years of age had amenorrhea, 41% of women >50 years of age had amenorrhea within the follow-up period.

Although many women pursuing UAE desire uterine conservation, some investigators suggest that UAE is more appropriately compared with hysterectomy in that both procedures are appropriate only for women who do not desire to conceive (124). A prospective, randomized trial comparing hysterectomy and UAE in 177 women with symptomatic myomas found that major complications were rare, with one pulmonary embolus in each group. No woman had a blood transfusion after UAE, whereas 10 (13%) had a transfusion after hysterectomy. Hospital stay was significantly shorter for UAE (2 vs. 5 d), but UAE was associated with more readmissions (9 vs. 0) for pain or fever, or both, in the 6-week postoperative period. After the procedure, in the UAE group, 1 woman had pneumonia, 1 required resection of a submucous myoma, and 1 had sepsis. After hysterectomy, 1 woman had a vesicovaginal fistula.

To date, five deaths have been reported after UAE: in two women, from septic shock; in one woman, from a pulmonary embolus; and in two, from uncertain causes. Estimates suggest that >50,000 UAE procedures have been performed worldwide. Therefore, the estimated mortality rate of 1/10,000 compares well with the mortality rate of approximately 3/10,000 for a similar group of women who were <50 years of age and did not have malignancy or compromised immunity and were having a hysterectomy (125).

The risk of premature ovarian failure after UAE needs further study. Transient amenorrhea has been reported in $\leq$15% of women. Ovarian arterial perfusion, as measured by Doppler sonography immediately after UAE, showed that 35% of women had decreased ovarian perfusion and 54% had complete loss of perfusion (126). Normal FSH, $E_2$, ovarian volume, and antral follicle counts have been documented in most women after UAE (127). However, there are no data that demonstrate the ability of these tests to predict the onset of menopause. Younger women, whose ovaries contain a large number of follicles, are likely to maintain a normal FSH despite destruction of a significant number of follicles. However, loss of follicles may cause ovarian failure at an earlier age than would otherwise occur (Vogelzang R, personal communication). Long-term follow-up of women who have UAE will be necessary to answer this important question.

### Surgical Evaluation Before UAE

The use of UAE before myomectomy or hysterectomy is not proven, adds significant expense, and increases risk. An early study used surgical evaluation, including laparoscopic and hysteroscopic biopsies of myomas before UAE, presumably to rule out the presence of uterine sarcoma (94). However, general anesthesia is required for laparoscopy, and one assumes the cumulative risks and expense of three procedures. Sarcomas are very rare in premenopausal women and are heterogenous tumors, so directed biopsies may not be adequate to make a diagnosis (128). Therefore, these procedures are not included in the preoperative evaluation (129).

### Fertility and Pregnancy After UAE

Potential fertility after UAE is uncertain, because an analysis has not been performed of women who actively attempt and achieve pregnancy after UAE. Nor have fertility rates after UAE been compared with rates after myomectomy or with those of untreated women who have similar myomas. And although the risk appears to be low for women <40 years of age, premature ovarian failure would be devastating in this setting.

Nevertheless, pregnancies have been reported after UAE. Of 34 pregnancies subsequent to UAE, 32% of women had a spontaneous abortion (130). In a report of 164 women desiring future fertility before UAE, during 24 months of follow-up, 21 women achieved pregnancy, 4 (24%) had a spontaneous abortion, 2 had elective terminations, and 18 had live births (131).

For women achieving pregnancy, one study reported that 6% had postpartum hemorrhage, 16% had premature delivery, and 11% had malpresentation (130). Another study reported 8 term and 6 preterm deliveries, but 2 women had placenta previa, and 1 woman had a membranous placenta. It is not clear whether this apparent high incidence of abnormalities is related to an effect of UAE on endometrium or a placental problem that is inherently found in women with uterine myomas. As a result, some investigators recommend early pregnancy sonography to look for placenta accreta (131).

Although women achieve pregnancy and deliver healthy infants after UAE that is performed to treat postpartum hemorrhage, subsequent healing and tensile strength of otherwise normal myometrium is likely to be different than with infarcted myomas (132). Uterine rupture has not been reported during pregnancy after UAE; however, uterine wall defects, necrosis, and fistula have been reported, and integrity of the uterine wall remains unknown (133–135). Therefore, outcomes for UAE treatment of postpartum hemorrhage should not be extrapolated to UAE treatment of myomas before pregnancy.

### Uterine Artery Occlusion

Alternative methods of uterine artery occlusion have been developed that are both more and less invasive than UAE, including laparoscopic uterine artery occlusion and nonincisional transvaginal uterine artery occlusion. Laparoscopic occlusion has similar short-term results as UAE but requires general anesthesia, is invasive, and requires a skilled laparoscopic surgeon. Transvaginal occlusion is performed by placing a specially designed clamp in the vaginal fornices and, guided by Doppler ultrasound auditory signals, positioning

it to occlude the uterine arteries. The clamp is left in place for 6 hours and then removed. Results are preliminary, but this technique may develop into an alternative, noninvasive method for decreasing myoma size (136, 137).

### Magnetic Resonance Imaging–Guided Focused Ultrasound

Ultrasound energy can be focused to create sufficient heat at a focal point so that protein is denatured and cell death occurs. Concurrent MRI allows precise targeting of tissue and monitoring of therapy by assessing the temperature of treated tissue (138). The advantages of this procedure are a very low morbidity and a very rapid recovery, with return to normal activity in 1 day. Presently, the procedure is not recommended for women who desire future fertility. Although initial studies had treatment limited by the US Food and Drug Administration to approximately 10% of myoma volume, pathologic examination of planned hysterectomy specimens documented necrosis in an area that was three times the treated area (138). A 15% reduction in myoma size was reported 6 months after treatment, but only a 4% reduction was noted at 24 months. An evaluation of clinical outcomes found that 6 months after treatment, 71% of women had significant symptom reduction, but at 12 months, about 50% still had significant symptom reduction, and 23 (28%) of 82 evaluable patients had undergone subsequent hysterectomy, myomectomy, or UAE (139). Also, women actively sought out MRI–guided focused ultrasound, and no control group was included (sham MRI–guided focused ultrasound), so placebo effect cannot be ruled out. One woman had a sciatic nerve injury caused by ultrasound energy, and 5% had superficial skin burns. It remains to be seen whether increases in treatment areas will be associated with any increased risks. As the technology continues to develop, further studies will be needed to evaluate the risks and efficacy of MRI–guided focused ultrasound in the treatment of uterine myomas.

## CONSIDERATIONS FOR MANAGEMENT OF UTERINE MYOMAS

A woman's individual circumstance, including myoma-related symptoms and their effect on quality of life, desire (or not) to preserve fertility, and her desires regarding care should be considered before recommending therapy. Multiple treatment options often exist, and on the basis of this review, the following points may be considered.

For an asymptomatic woman who desires fertility, evaluation of the uterine cavity with saline infusion sonography, hysteroscopy, or MRI provides useful information regarding the potential impact of myomas on fertility. If the cavity is not deformed, myomas need not be treated, and conception may be attempted. If the cavity is deformed, myomectomy (hysteroscopic or abdominal) can be considered. Laparoscopic myomectomy may be offered by experienced laparoscopic surgeons who have the ability to perform multilayered myometrial closures.

For an asymptomatic woman who does not desire fertility, observation (watchful waiting) should be considered. If there is concern that the uterus may be near at least one ureter at the pelvic sidewall, renal ultrasound or intravenous pyelography should be considered to rule out significant hydronephrosis. Perhaps more frequently than once per year, an office visit can be scheduled to review the patient's symptoms and to perform a pelvic examination to evaluate uterine size. If necessary, sonographic evaluation of the ovaries can be performed.

For a symptomatic woman who desires future fertility and has abnormal bleeding as her primary symptom, a baseline hemoglobin is useful because accommodation to anemia can occur. If indicated, further evaluation of the endometrium with endometrial biopsy or with dilatation and curettage can be performed. Evaluation of the uterine cavity with saline-infusion sonography, hysteroscopy, or MRI can help determine the appropriate treatment options. If the cavity is deformed, myomectomy (hysteroscopic or abdominal) should be considered. Laparoscopic myomectomy may be offered by experienced laparoscopic surgeons. If the symptoms of pain or pressure (bulk symptoms) are present, and if the uterine cavity is not deformed, myomectomy (abdominal or laparoscopic) can be considered. If the cavity is deformed, myomectomy by abdominal route should be considered. Laparoscopic myomectomy may be offered by experienced laparoscopic surgeons.

For a symptomatic woman who does not desire future fertility, observation (watchful waiting) can be considered if no treatment is desired at the time. A symptomatic perimenopausal woman may desire observation until menopause, when symptoms often diminish. If there is concern that the uterus may be compromising the ureters, renal ultrasound or intravenous pyelography should be performed. The presence of significant hydronephrosis indicates the need for treatment. Symptoms suggestive of uterine sarcoma (irregular bleeding, pelvic pain, and uterine growth) can be evaluated with MRI-gadolinium and lactate dehydrogenase (140).

If metrorrhagia is present, evaluation of the endometrium with sonography, endometrial biopsy, or dilatation and curettage should be considered. If the endometrium is normal, a levonorgestrel intrauterine system or hysteroscopic myomectomy and/or endometrial ablation may be appropriate treatment. Myomectomy (abdominal or laparoscopic), hysterectomy (vaginal, laparoscopic or abdominal), or UAE can be considered. For a woman with primarily myoma-related pain or pressure symptoms (bulk symptoms), myomectomy, hysterectomy, UAE, or focused ultrasound (presently limited by size and number of myomas) may be considered. For a woman who chooses hysterectomy and who is not at high risk of ovarian cancer, ovarian conservation should be considered (141).

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