

GENERAL GYNECOLOGY

Uterine fibroid embolization: a viable alternative to hysterectomy

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Uterine leiomyomata are the most common neoplasms found in gynecologic practice. According to the American College of Obstetrics and Gynecology (ACOG), fibroids occur in approximately 25-50% of all women, most commonly in those ages 30-40 years, and affect African American women in higher numbers than their white counterparts.¹ Fibroids are commonly the underlying cause of such symptoms as menorrhagia, pelvic pain, pressure and bloating, and severe dysmenorrhea; other associated complaints may include dyspareunia, leukorrhea, reduced fertility, miscarriage, acute or intermittent urinary retention, and/or constipation. Given the characteristics and severity of such symptoms, leiomyomata are likely to have a detrimental effect on quality of life.

Surgery has been the traditional treatment for fibroids. Myomectomy, surgical removal of leiomyomata without hysterectomy, is an option for women who wish to retain their uteri; however, intraprocedural bleeding may result in emergency hysterectomy. Additionally, myomectomy is associated with fibroid recurrence and further surgery in 23-51% of patients evaluated via ultrasound during a follow-up period of up to 5 years.²⁻⁴ Given these disadvantages, myomectomy is performed less often than hysterectomy, which has been considered the definitive treatment for fi-

Benign uterine fibroids, or leiomyomas, are the most common tumors found in gynecologic practice. Symptomatic fibroids present with menorrhagia, pelvic pain, leukorrhea, pressure and bloating, increased abdominal girth, and severe dysmenorrhea. Traditional treatment has relied on surgery because long-term medical therapies have demonstrated only minimal response. Uterine fibroid embolization (UFE) using particulate emboli to occlude the uterine arteries, thereby disrupting the blood supply to fibroids and leading to devascularization and infarction, has been reported to be effective in alleviating fibroid-related symptoms. UFE is a safe, effective, and durable nonsurgical alternative to hysterectomy.

Key words: alternative to hysterectomy, leiomyoma, uterine fibroid embolization

broids because there is no possibility of postprocedure recurrence.

More than 600,000 hysterectomies are performed in the United States each year, with uterine leiomyomata as the leading cause.⁵ Because it is classified as major surgery, hysterectomy for benign disorders has a number of drawbacks, not the least of which is an overall complication rate of 17-23% regardless of approach: abdominal, transvaginal, or laparoscopic.⁶ Hysterectomy is not appropriate for women who wish to retain their fertility; moreover, it has significant negative impact on psychosexual health compared with less invasive procedures, even in those who have no plans for future child-bearing.⁷

The Vaginal, Abdominal, Laparoscopic Uterine Excision study, undertaken to assess the rates of serious complications associated with hysterectomy in more than 37,000 women in the United Kingdom, found that individuals with symptomatic fibroids experience more intraoperative and postoperative complications than women with dysfunctional uterine bleeding.⁸ Trial researchers also observed that younger women are at most risk for experiencing severe complications with hysterectomy and recommended a less invasive alternative treatment for symptomatic fibroids in this patient group.⁸

Uterine fibroid embolization (UFE), also known as uterine artery embolization (UAE), is an emerging nonsurgical, minimally invasive therapy that, with accruing clinical experience, is gaining widespread acceptance in North America and Europe as a safe and effective treatment for reducing the symptoms of uterine leiomyomata. An estimated 200,000 UFEs have been performed worldwide since 1995,⁹ when this procedure was first utilized by Ravina et al.¹⁰

UFE involves the injection of particles, typically sized 500-900 μm , into the uterine arteries to cause occlusion, thereby disrupting the blood supply to fibroids and leading to devascularization and infarction. The result is improvement in fibroid-associated symptoms, preservation of the uterus, avoidance of general anesthesia, and obviation of the potential complications and lengthy recovery associated with surgery.

Selecting patients most likely to benefit

The Task Force on Uterine Artery Embolization and the Standards Division of the Society of Interventional Radiology recommend that UFE be offered only to women with symptomatic uterine leiomyomata who are of reproductive age but who are not interested in child-bearing.¹¹ In this patient subpopulation,

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TABLE 1

Recommendations for patient triage prior to UFE

1. Patients must undergo a gynecological examination within 1-2 months of scheduled procedure. Patients must have a recent negative Papanicolaou smear, negative cervical cultures for sexually transmitted diseases, and a negative evaluation for bacterial vaginosis and trichomonas.
2. An endometrial biopsy should be performed in women > 40 years of age and in those with risk factors for endometrial hyperplasia or malignancy. This biopsy should be performed at least 2-3 weeks prior to UFE to minimize risk of infection.
3. Preprocedural blood tests should include CBC with platelets, BUN and creatinine levels, PT, and PTT.
4. MRI of the pelvis with and without contrast is advised. Intracavitary fibroids, adnexal masses, or other uterine pathology may exclude UFE as an option, as may coexisting adenomyosis and extensive collateral circulation.
5. The procedure should be scheduled within the first 2 weeks of the menstrual cycle, with negative results from a pregnancy test on the day of the procedure.
6. It is preferable that patients are not receiving GnRH agonist therapy at the time of UFE because this makes it difficult to accurately assess the response to UFE. It is hypothesized that the caliber of the uterine arteries may diminish, making it technically difficult to perform UFE. When possible, perform UFE after resumption of menstrual cycles if GnRH therapy was previously used.
7. Discontinue all nonsteroidal and herbal products at least 3-4 weeks prior to the procedure, to diminish the risk of puncture site bleeding.
8. The physician should provide extensive patient education including handouts, technical explanations, and the web addresses for medical web sites to augment informed consent.
9. Patients should be advised to use contraception after the procedure.
10. Informed consent must be obtained by the interventional radiologist.
11. Ideally, patients should maintain a working relationship with a gynecologist before and after procedure for referral and follow up.

BUN, blood urea nitrogen; *CBC*, complete blood count; *GnRH*, gonadotropin-releasing hormone; *MRI*, magnetic resonance imaging; *PT*, prothrombin time; *PTT*, partial thromboplastin time; *UFE*, uterine fibroid embolization.

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UFE is indicated for individuals with clinically documented fibroids and fibroid-related symptoms who wish to avoid surgery, particularly hysterectomy,¹¹ who refuse blood transfusion for health or religious reasons and/or who have failed medical or surgical therapy. Contraindication to general anesthesia may be another consideration.

Of the numerous treatment options available, patient selection for UFE is generally based on such factors as bulk symptoms, bleeding symptoms, and desire for future fertility or uterine preservation.⁹

A patient's ultimate choice among available fibroid therapies may depend on the fibroid-related impact on her health-related quality of life (HRQoL), the length of convalescence that is acceptable to her, and the importance she assigns to tolerable invasiveness and symptom resolution.⁹

Preprocedure evaluation

A cooperative relationship between the obstetrician/gynecologist (Ob/Gyn) and interventional radiologist (IR) is essential for effective diagnosis, treatment,

and follow-up of patients who are potential candidates for UFE, and the combined efforts of these specialists contribute to the establishment of optimal clinical guidelines for patient care and long-term follow-up.⁹ Collaboration begins with the screening and selection of patients because both specialists must contribute their skills when choosing appropriate candidates.

Preoperative consultation with an Ob/Gyn is necessary to confirm the diagnosis of fibroids, to ensure a patient's overall gynecologic health, to diagnose any preexisting infection, and to exclude other conditions that mimic fibroid symptoms or that may require surgical intervention. The presence of atypical symptoms or an unusual pattern of bleeding may necessitate additional gynecologic assessment. See **Table 1** outlining recommendations for patient triage prior to UFE.

Diagnosis and diagnostic imaging

Subsequent to symptom evaluation, leiomyoma are often detected initially by an Ob/Gyn via bimanual palpation of an enlarged mobile uterus with irregular contours. Additional diagnostic testing,

in the form of imaging studies, is indicated for patients with suspected fibroid tumors.

A number of imaging methods are used in the detection, evaluation, and mapping of uterine fibroids: transvaginal sonography (TVS); 3-dimensional saline-infusion sonohysterography (SHG), which uses a saline contrast medium in combination with TVS; hysteroscopy; and magnetic resonance imaging (MRI). Each method has both advantages and disadvantages for evaluating leiomyomata.

Although a systematic review of common diagnostic imaging tests found inconsistent sensitivity (21-100%) and specificity (53-100%) for TVS,¹⁴ its low cost, availability, and noninvasive quality make it a first-line choice for the identification of fibroid disease.^{15,16} However, TVS may fail to detect small fibroids and subserosal myomas and, particularly in the presence of a large uterus or multiple fibroids, has a limited capability for localization mapping.¹⁵

In comparison with TVS, both hysteroscopy and SHG are more accurate in detecting submucosal fibroids: the

former with a sensitivity and specificity of 53-100% and 97-100%, respectively, and the latter with a sensitivity and specificity of 57-100% and 96-100%, respectively.¹⁴ SHG is an office-based procedure that, although more invasive than TVS does not require anesthesia; it demonstrates more sensitivity and specificity than TVS in detecting submucosal myomas and focal endometrial lesions.¹⁴ In a systematic review of 7 studies, a clinically significant positive likelihood ratio of 29.7 was shown for SHG.¹⁴

Although hysteroscopy, with or without biopsy, is considered the gold standard for evaluating the uterine cavity, it is an invasive procedure that entails moderate to severe discomfort for the patient.¹⁵ A prospective, blinded, comparison study of SHG vs hysteroscopy in a cohort of 117 women found a statistically significant lower medication pain score for SHG (1.6 on the Mann-Whitney test) than for hysteroscopy (3.2).¹⁷

MRI is a powerful and noninvasive technique with a sensitivity (100%) and specificity (91%) that equal or surpass those of TVS, hysteroscopy, and SHG in the assessment of submucosal fibroids.¹⁵ For patients who are interested in UFE, pelvic MRI with and without intravenous gadolinium contrast is the diagnostic method of choice.¹³ Fibroid size, number, and location are critical in determining a patient's candidacy for UFE; MRI depicts these variables, which are predictors of the success and safety of the procedure, more accurately and with less intraobserver variability than ultrasound and identifies those patients who will benefit most.¹² Additionally, following the procedure, post-UFE contrast-enhanced MRI reliability detects fibroid viability and tissue perfusion (enhancement), which is predictive of procedure success or failure.

Although the majority of leiomyomata can be treated with UFE, exceptions include exophytic subserosal fibroids with a stalk of less than 2 cm or submucosal intracavitary pedunculated fibroids that may detach and lodge in the uterine cavity or abdominal cavity after embolization and single dominant fibroids larger than 10 cm, which are gen-

erally associated with greater procedural failure rates.¹²

Assessing the morphology of these relative contraindications to UFE is more practicable with the use of MRI.¹² MRI is also efficient in detecting the presence of possible coexisting pathologic and anatomic factors, such as adenomyosis, coexisting tuboovarian pathology, or large fundal leiomyomata with aberrant ovarian or collateral blood supply, that would predispose patients to treatment failure with UFE.¹² In fact, reported data have shown that the initial diagnosis and subsequent treatment plan for 18% of cases being evaluated for UFE were changed following MRI.¹²

General side effects and complications

A number of general side effects are expected with UFE. These include self-limiting nonpurulent vaginal discharge, transient vasomotor symptoms (hot flashes) that are likely related to the temporary interruption of normal ovarian hormone production common to many gynecologic interventions, constipation, cramping, spontaneous fibroid tissue expulsion not requiring assistance, and postembolization syndrome (PES).¹⁸⁻²⁰ PES occurs with embolotherapy in any solid organ as part of the immune response; it presents with transient low-grade fever, pain, nausea, and fatigue lasting from a few hours to a few days.^{18,20} The transient fever is generally no higher than 101°F and is usually associated with leukocytosis.

Therapeutic infarction of uterine fibroids begins immediately following UFE and generally causes several hours of moderate to severe pelvic pain, cramping, and nausea. Pain may be best managed with aggressive sustained treatment with a nonsteroidal analgesic beginning 1-2 hours prior to UFE and the use of a patient-controlled analgesia pump afterward, generally for 6-12 hours, after which most patients can be transitioned to oral medications.

Antiemetics are also helpful in reducing post-procedural nausea. Aggressive early use of the triad of nonsteroidal analgesics, narcotic pain medication, and antiemetics facilitates early hospital dis-

charge and forestalls unnecessary readmissions. Although some physicians discharge patients on the day of the procedure without incident,²¹ most admit patients to the interventional radiology service for overnight hospitalization to ensure optimal control of pain.

Overall, the rate of complications associated with UFE is very low, and most complications are transient. Transcervical leiomyoma tissue passage is the most common complication requiring surgical intervention; it occurs in approximately 2.5% of patients.^{20,22} The most serious complication associated with UFE is endometritis/uterine infection, with a reported incidence of approximately 2%.^{18,20}

The rate of hysterectomy subsequent to UFE ranges between 0.25% and 1.6% and is generally attributable to infection, pain, and bleeding.²⁰ Uterine necrosis, a rare complication (fewer than 10 reported cases to date) following this procedure, also necessitates hysterectomy and treatment with antibiotics to prevent bacteremia, sepsis, and death.²⁰ Patients should be made aware of possible emergency hysterectomy should such severe complications arise.

A study of 400 consecutive patients undertaken by Spies et al,²⁰ published in 2002, found that, based on ACOG definitions, perioperative complications occurred in only 5% of UFE procedures for symptomatic fibroids. Such complications included allergic reaction to contrast medium; accidental injury to the femoral nerve or uterine artery; groin hematomas; endometritis; pulmonary embolism; and arterial thrombosis.²⁰

A current and much larger study involving more than 450 patients, completed in 2007 at the Cleveland Clinic in Cleveland, OH, found a more substantial rate of minor complications (61 complications in 53 patients, or 11% of the cohort) following UFE (Table 2), although the associated morbidity rate was still very low.²² Office hysteroscopy, was utilized liberally to evaluate post-UFE complaints such as leukorrhea and abnormal vaginal bleeding. Researchers reported that the factors most likely to increase the risk for developing complications included prior myomectomy and the use

TABLE 2
Complications following UAE for symptomatic uterine leiomyomata

Complication	n (%)	95% CI (%)
Perforation	1 (0.2)	0.04 (1.2)
Hematoma	3 (0.7)	0.2 (1.9)
Allergic reactions	5 (1.1)	0.5 (2.6)
Febrile morbidity	10 (2.2)	1.2 (4)
Vaginal discharge	10 (2.2)	1.2 (4)
Nausea/vomiting	4 (0.9)	0.3 (2.2)
Pain	6 (1.3)	0.7 (3.1)
Urinary retention	3 (0.7)	0.2 (1.9)
Paraesthesias of right leg S/P UAE access via right femoral artery	1 (0.2)	0.04 (1.2)
Urinary tract infection	3 (0.7)	0.2 (1.9)
Endometritis	5 (1.1)	0.5 (2.6)
Menopause	3 (0.7)	0.2 (1.9)
Prolapsing submucosal fibroids	5 (1.1)	0.6 (2.6)
Small bowel obstruction	1 (0.2)	0.04 (1.2)
Sepsis with subsequent hysterectomy and death	1 (0.2)	0.04 (1.2)

There were a total of 61 complications in 53 patients. CI, confidence interval; S/P, status post; UAE, uterine artery embolization. Adapted from, Park AJ et al.²²

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of embolic particles 355-500 μg in size (ie, smaller than the typical 500-900 μm).²²

Through 2007, there have been only 4 reported fatalities related to UFE. Pulmonary embolism was the cause of death in 2 cases; the other 2 deaths were a result of septicemia and disseminated intravascular coagulation.⁹

Postprocedure results

Reported clinical success rates of UFE range from 81% to 94%.²³⁻²⁵ Symptoms of menorrhagia improve in 83-92% of patients, pain in 77-79%, and bulk-related symptoms in 79-92%.²³⁻²⁷ Leiomyomata continue to shrink for up to 1 year following embolization, and the re-

ported percentage of uterine or fibroid volume reduction varies according to the length of follow-up.

Short- and midterm outcomes

At 3 months subsequent to UFE, the reported mean decrease of uterine volume ranges from 27% to 46%²⁷⁻³⁰ and the reported mean decrease of fibroid volume is 40-44%.^{27,29,30} After 6 months, the reported mean reduction of leiomyoma volume is 31%-59%,^{28,31-33} and, after 12-14 months, 37%-66%.^{28,31-34} Patient satisfaction with UFE treatment outcomes over short- and midterm follow-up was high, ranging from 91% to 97%.^{25,27,28}

Long-term outcomes

Long-term data from the Fibroid Registry for Outcomes Data (FIBROID), the Embolization vs Hysterectomy (EMMY) trial, and other studies of UFE with 5- to 7-year patient follow-up experience have provided clear evidence that UFE results in durable symptom relief and improvement in HRQoL.^{5,35-39}

The goals of the FIBROID registry were to assess the efficacy and safety of UFE in improving leiomyoma-related symptoms and to determine the durability of these improvements.⁵ This multicenter longitudinal study involved 2112 women with symptomatic leiomyomata who participated in a 3-year follow-up.⁵ Comparison with baseline data found that symptom scores were significantly better at 3 years than at 6 months or 1 year, with an improvement of 41.41 points ($P < .001$).⁵ The change in HRQoL score was similar, improving 41.47 points over baseline at 3 years.⁵

Other sizable prospective studies of UFE with 5-7 years postprocedure follow-up found continued symptom control in 72-73% of patients^{37,38} and a high rate of patient satisfaction³⁷⁻³⁹ (surprisingly, even in women who needed an additional intervention).³³ These investigations also revealed that 87-91.4% of patients treated with UFE would recommend the procedure to others.^{18,39}

Treatment failure

Although the risk of fibroid recurrence following embolization has not yet been thoroughly defined, there are a number

of possible reasons for UFE failure. Because this procedure causes shrinkage of fibroids but preserves normal uterine tissue, it may be possible for new fibroids to develop and symptoms to recur. A prospective study by Marret et al³⁹ used transvaginal ultrasound to assess patients at a median of 30 months following UFE; results reported the appearance of new fibroids in 7 or the cohort of 85 (8.2%).

Incomplete fibroid infarction, which is most often associated with the technical aspects of embolization, may result in regrowth of fibroids despite an initial reduction in uterine volume.⁴⁰⁻⁴² Particularly for patients who receive unilateral embolization owing to arterial spasm, vessel dissection, and/or anatomic obstacles, such as hypoplastic, atretic, or absent vessels, the rate of hysterectomy during 5 year follow-up is 2.19 times higher than that in women with successful bilateral embolization.⁴³

The degree of fibroid infarction, as determined by enhanced MRI following UFE, is also related to long-term clinical outcomes.⁴³ In a retrospective study of 290 patients, individuals were divided into 3 groups according to infarction rates: those with 100% infarction, those with 90-99% infarction, and those with less than 90% infarction. At 5 years, the cumulative rates of symptom control for each group were 93%, 71%, and 60%, respectively.⁴³

Research by Spies et al³⁷ and Katsumori et al⁴⁴ identified factors associated with long-term failure of UFE. Evaluation of patients who had not yet failed treatment at 1 year found that those who had not improved symptomatically at this juncture were 5 times more likely to fail in the long term.³⁴ Those with larger than median baseline leiomyomas and those with less than median leiomyoma shrinkage were 3 times more likely and 2.4 times more likely, respectively, to fail long term.³⁸

To date, studies designed to assess the effect of baseline uterine characteristics on the likelihood of treatment failure have demonstrated conflicting results, with several reporting no link between uterine or fibroid size and the risk of failure^{31,45,46} and others reporting that fi-

broids larger in size and greater in number were significant predictors of failure^{5,47,48} In addition, 2 of these studies noted a significantly increased risk of UFE failure in patients with a history of prior surgery for fibroids.^{31,46}

Fertility/pregnancy after UFE

Although there is some valid concern regarding the effect of UFE on women who wish to retain fertility, pregnancy after this procedure is well documented.

A retrospective analysis by Walker and McDowell found 56 completed pregnancies in a series of 1200 patients who had UFE performed by a single IR.⁴⁹ This cohort included 108 women attempting pregnancy, of whom 33, or 30.5%, were successful.⁴⁹ The mean age in this patient subgroup was extremely high (for conception) at 37.44 years; 39.5% had some form of investigation for infertility before embolization.⁴⁹ The authors particularly noted that 14 of the women with a successful pregnancy outcome had failed myomectomy and had been offered hysterectomy as their only option before undergoing UFE.⁴⁹

Data from this analysis demonstrated a significant increase in cesarean section (72.7%) and increases in preterm delivery (18.2%), postpartum hemorrhage (18.2%), and miscarriage (30.4%) for the subgroup of women who became pregnant compared with the general obstetric population.⁴⁹ Investigators observed that these results could be only partly explained by the demographics of the study population, which was atypical and had additional risk factors for pregnancy and delivery complications.⁴⁹

A large, prospective, multicenter Canadian study undertaken by Pron et al⁵⁰ evaluated pregnancies that occurred in 555 women who had undergone UFE. Because the study was not originally designed to assess fertility or pregnancy outcomes, reproductive histories were not obtained and other fertility factors were not investigated; furthermore, the denominator of women attempting to achieve pregnancy was not optimally defined.⁵⁰ Before UFE, 164 women expressed a desire for pregnancy; however, only 35 women reported trying to conceive 1 year later.⁵⁰ These circumstances

precluded the calculation of the percentage of successful pregnancies.

At the 2 year follow-up, 21 women, with an average age of 34 years, had conceived (3 conceived twice); 13 were previously nulliparous.⁵⁰ Twenty-three of the 24 pregnancies were spontaneous (1 woman had in vitro fertilization) and resulted in 18 live births (14 full term, 4 preterm), 4 spontaneous abortions (16.7%), and 2 elective terminations.⁵¹ Three women, all nulliparas, experienced abnormal placentation.⁵⁰ Two of these patients (of 24 total) developed complete placenta previa,⁵⁰ an incidence much higher than the 2.8 cases per 1000 births recorded in the general obstetric population.⁵¹ The third patient developed a placenta membranacea with accreta that resulted in cesarean hysterectomy.³⁸ All 3 patients experienced postpartum hemorrhage.⁵⁰

The study authors concluded that women are able to conceive after UFE and that the majority of such pregnancies result in full-term deliveries; however, they recommended conservative management of pregnancies occurring after UFE until more is known about delivery outcomes.⁵⁰ They also advised close monitoring of placental status to facilitate transfer of care to an appropriate treatment center if abnormalities are detected.⁵⁰

Rare, instances of premature menopause have been reported in 2-3% of patients under the age of 45 years and in approximately 8% of women aged 45 years and older following UFE.^{25,27} Decrease in ovarian reserve and nontarget ovarian embolization has also been reported.⁵² For all these reasons, pregnancy rates after UFE may be decreased and fertility compromised compared with women who have undergone myomectomy.

Randomized controlled clinical trials

To date, randomized controlled clinical trials (RCTs) directly comparing outcomes of UFE with those of surgical treatments have been few. Recruitment for such trials has been problematic owing to patients' unwillingness to be randomized between a major surgical procedure and minimally invasive UFE.

The Pinto trial

Perhaps in response to recruitment difficulties, 1 of 2 RCTs comparing UFE with hysterectomy used the controversial Zelen randomized-consent design, in which patients who were allocated to the hysterectomy arm were not informed of the study or the possibility of alternative treatment with UFE.^{53,54} This trial, undertaken by Pinto et al, was small, with only 57 women enrolled, and applied stratified randomization 2:1 in favor of UFE.^{53,54} The primary outcome measure was length of hospital stay.

Outcomes between the study arms were compared on an intent-to-treat basis; however, owing to crossover between the treatment arms, efficacy and safety were assessed based on the actual treatment received.^{53,54} Results of this trial found that hospital stays were significantly shorter in the UFE arm than in the hysterectomy arm: 1.71 days (\pm 1.59) vs 5.85 days (\pm 2.52), a difference of 4.14 days.⁵³ The percentage of patients visiting the emergency department after the procedure was 25% in the UFE group vs 20% in the hysterectomy group, but complications in the former group were minor (PES, pelvic pain, urinary tract infection), whereas those in the latter group were major (abscess at site of surgical incision, intraabdominal abscess plus anemia, urinary retention).⁵³

The EMMY trial

The multicenter, randomized, noninferiority EMMY trial, conducted in The Netherlands, compared the postprocedure experience of 177 patients in 28 Dutch hospitals who underwent either hysterectomy or UFE for treatment of uterine fibroids and menorrhagia.³⁵ Randomization was 1:1 for each procedure, and outcomes were compared on an intent-to-treat basis.³⁵

Results at 24 months were similar in both patient groups for improvement in pain and bulk-related complaints.³⁵ Eighty-four of UFE patients (9%) reported at least moderate improvement of pain compared with 78.0% of hysterectomy patients; bulk-related complaints improved 66.2% in the former group and 69.2% in the latter.³⁵ Hospital stay was significantly shorter for the UFE

arm compared with hysterectomy, with a mean of 2.5 days vs 5.1 days ($P < .001$), respectively.³⁵

UFE met the study's primary endpoint, avoiding hysterectomy in 76.5% of cases.³⁵ Study authors observed that this success rate is much lower than those of earlier uncontrolled series that reported hysterectomy subsequent to UFE in only 1.5% and 4.5% of cases, depending on the length of follow-up.³⁵ The investigators added that such discrepancies underscore the need for RCTs.³⁵

Overall, EMMY trial results demonstrated that, on the basis of efficacy and HRQoL, UFE is a good alternative to hysterectomy.^{35,36} However, the researchers noted that, for patients seeking certainty in the cessation of menorrhagia, hysterectomy remains the treatment of choice.³⁵

The Mara trial

Midterm results of an RCT comparing the safety, efficacy, and reproductive results of UFE and myomectomy over a mean follow-up duration of 24.9 months were reported by Mara et al.⁵⁵ A cohort of 121 patients with reproductive plans who presented with intramural fibroid(s) larger than 4 cm were randomized into 2 groups: 58 for UAE and 63 for myomectomy.⁵⁵ Periprocedural results were analyzed on an intent-to-treat basis.⁵⁵

In most parameters of early postprocedure results and in frequency of early complications, there were no significant differences between the 2 study groups.⁵⁵ UFE patients underwent a significantly shorter procedure and required a shorter hospital stay and recovery period compared with the myomectomy arm.⁵⁵ Subjects in the former group also demonstrated significantly lower serum concentrations of C-reactive protein (an acute phase marker) on the second day following the procedure.⁵⁵ Myomectomy and UFE were found to be comparable in terms of technical success rate, safety, and efficacy in reducing symptoms; however, reproductive results differed significantly in favor of myomectomy.⁵⁵

Although reproductive data may have been partly influenced by the short dura-

tion of follow-up and the variance in the number of patients trying to conceive in each group (40 after myomectomy and only 26 after UFE), statistically significant differences were observed in the number of successful deliveries (19 for the myomectomy group and only 5 in the UFE group) and in the number of early pregnancy losses (6 in the former group and 9 in the latter; in all cases spontaneous or unnoticed miscarriage in the first trimester).⁵⁵ These results favored the surgical procedure over UFE.⁵⁵

The trial investigators stated: "The fact that the rate of [spontaneous] abortions after UAE was higher than 60% (in contrast with 23% after myomectomy) is the most alarming result of the study to date . . ." Existing studies from other authors^{9,50,56} reported post-UFE abortion rates at 27%, 16.7%, and 24%, respectively, in contrast to this RCT's findings.⁵⁵ The authors concluded that whereas UFE is less invasive and is as safe and effective as myomectomy for symptoms related to uterine fibroids, myomectomy appears to have superior reproductive outcomes in the first 2 years following treatment.⁵⁵

The REST trial

The multicenter Randomized Trial of Embolization vs Surgical Treatment (REST) trial recruited 157 women with symptomatic fibroids who were randomly assigned in a 2:1 ratio to either UFE or surgery, with 106 patients randomized to the UFE arm and 51 to the group undergoing surgery (43 hysterectomies and 8 myomectomies, all performed through abdominal incision).¹⁹ Study authors acknowledged difficulties in recruitment that reduced the trial size from a planned 200 to 157 participants.

This trial was conducted in 27 hospitals in the United Kingdom, with the primary outcome measure being quality of life, as evaluated at 12 months after the procedure on the Medical Outcomes Study 36-Item Short-Form General Health Survey (SF-36).¹⁹ Secondary outcomes included an assessment of results on the EuroQol-5D questionnaire, an instrument used to measure patient preferences in certain health-

related outcomes, including those for hysterectomy.¹⁹

Although the UFE arm had significantly greater improvement in scores for the physical function, social function, and physical-role components of the SF-36 at 1 month, at 12 months, there were no statistical differences between the study arms for any of the eight components of this instrument.¹⁹ Both the median hospital stay and the median time until patients could resume all recorded activities of daily living were significantly shorter in the UFE group compared with the surgery group.

Thirteen major adverse events (AEs) occurred in the UFE arm (12%) and 10 in the surgery arm (20%) during the first year of follow-up; for the most part, these events were related to the procedures.¹⁹ Study authors noted that 3 of the major AEs in the UFE group were cancers detected within 2 months following the intervention and were highly unlikely to be related to treatment.¹⁹ However, 10 of the 106 women in the UFE arm required a secondary intervention at 1 year to treat recurrent or persistent symptoms; after the 1 year benchmark, 11 additional women from this group were admitted for the same indication.¹⁹

Secondary outcomes showed that symptom scores at 1 and 12 months after the procedure were significantly better in the surgery arm.¹⁹ At 1 year, the number of women who reported that they would recommend their treatment to a friend was high in both treatment groups, with a slight advantage to the surgery group compared with the UFE group (93% vs 88%, respectively).¹⁹

Based on their findings, the trial investigators concluded that for women with symptomatic fibroids, the faster recovery following UFE must be weighed against the necessity of further treatment in a minority of patients.¹⁹

Comparison of UFE vs myomectomy

A recent multicenter prospective cohort study by Goodwin et al⁵⁷ compared the postprocedure outcomes of 149 women who underwent UFE with outcomes of 60 women who underwent myomectomy. The primary endpoint in this study was an improvement in the uterine

TABLE 3

Total regression adjusted direct medical care costs and indirect costs for absenteeism and disability days associated with the treatment of uterine fibroids

Treatment or procedure	Total direct operative costs at 1 y ^a (adjusted for confounders)	Average absenteeism/disability days and estimated indirect costs per person (adjusted for confounders)	Total direct and indirect costs
Hysterectomy	\$17,390 ^b	92.0 d (\$14,169-\$25,229) ^c	\$31,559-\$42,619
Myomectomy	\$18,674 ^d	72.8 d (\$11,532-\$20,533) ^e	\$30,206-\$39,207
UFE/UAE	\$20,634 ^f	48.9 d (\$8,671-\$15,439) ^g	\$29,305-\$36,073
Endometrial ablation	\$13,019 ^h	45.3 d (\$7,702-\$13,716) ⁱ	\$20,721-\$26,735
No surgical treatment	\$8,257 ^j	38.1 d (\$6,735-\$11,992) ^k	\$14,992-\$20,249

UAE, uterine artery embolization; UFE, uterine fibroid embolization.

Data extracted from, Carls GS et al. What are the total costs of surgical treatment for uterine fibroids? *J Womens Health (Larchmont)* 2008.⁶⁰

^a Includes preoperative, perioperative, and postoperative expenditures; ^b n = 19,629; ^c n = 497; ^d n = 1743; ^e n = 93; ^f n = 373; ^g n = 25; ^h n = 1115; ⁱ n = 25; ^j n = 14,214; ^k n = 372.

Bradley. Uterine fibroid embolization: a viable alternative to hysterectomy. *Am J Obstet Gynecol* 2009.

quality of life questionnaire score (UFQoLs) of 5 points or more; 6-month secondary endpoints included comparison of change in UFQoLs between the UFE and myomectomy groups; overall quality-of-life scores; AEs; change in size of dominant fibroid (UFE cohort only); uterine volume change, menstrual bleeding changes; hospitalization days; time to return to normal daily activities and work; and relationship between dominant fibroid size change and UFQoLs (UFE cohort only).⁵⁷

Although both groups experienced significant improvements in reduction in menstrual bleeding scores, uterine volume reduction, UFQoLs, and overall quality-of-life scores, there were no statistically significant differences found between the UFE patients and the myomectomy patients.⁵⁷ However, there were statistically significant differences in favor of UFE compared with myomectomy in the mean duration of hospital stay (23.8 hours vs 61.6 hours; $P \leq .0001$), number of days for return to daily activities (14.6 days vs 44.4 days [$P \leq .05$]), and the mean number of missed work days (9.9 days vs 37.0 days; $P \leq .001$).⁵⁷ Of the 149 UFE patients, 33 (22.1%) experienced at least 1 AE compared with 24 (40%) of the 60 myomectomy patients.⁵⁷

A separate study by Siskin et al was designed as a third arm of the study by Goodwin and colleagues⁵⁸ described above. Its dual purpose was to evaluate the safety and efficacy of polyvinyl alco-

hol microspheres in patients undergoing UFE and to compare the long-term changes in HRQoL following UFE (77 patients) and following myomectomy (69 patients).⁵⁸ Study results were similar to those of Goodwin and colleagues⁵⁸; however, median quality-of-life scores at 6 months were found to be significantly higher in the patients treated with UFE vs those who underwent myomectomy.

The RCT by Mara et al⁵⁵ comparing UFE and myomectomy is discussed more fully in the *Randomized controlled clinical trials* section of this article. Results showed that whereas UFE is less invasive and as safe and effective as myomectomy for symptoms related to uterine fibroids, myomectomy appears to have superior reproductive outcomes in the first 2 years following treatment.^{53,56}

Total costs of uterine fibroid treatment

Eight published studies have analyzed the cost and cost-effectiveness of standard surgical management vs UFE for uterine fibroids.⁵⁹ Of these, 5 reported lower hospital costs for UFE, largely owing to a shorter length of stay, which compensated for higher imaging costs and physician fees associated with surgery.⁵⁹ Four cost-effectiveness analyses found UFE to be more cost effective than surgery, even when repeat procedures were necessary and/or complications arose subsequent to UFE.⁵⁹

In an objective analysis of health care economics, Carls and colleagues⁶⁰ investigated both direct and indirect costs associated with surgical and nonsurgical treatments for uterine fibroids, using data obtained from the MarketScan Commercial Claims and Encounters databases for the years 1999-2004. Total direct operative costs at 1 year, which included preoperative, perioperative, and postoperative expenditures, adjusted for confounders, were \$20,634 for UFE, \$18,674 for myomectomy, and \$17,390 for hysterectomy (Table 3).⁶⁰ However, when indirect costs for absenteeism and disability days were calculated at 1 year and added to direct costs, the totals, adjusted for confounders, ranged from \$29,305 to \$36,073 for UFE, \$30,206 to \$39,207 for myomectomy, and \$31,559 to \$42,619 for hysterectomy (Table 3).⁶⁰ The average adjusted number of absentee/disability days experienced during the study period were 92.0 for women who had undergone hysterectomy, 72.8 days for those who had undergone myomectomy, and 48.9 days for those who opted for UFE (Table 3).⁶⁰

Conclusion

UFE has several potential advantages over hysterectomy and myomectomy. Compared with surgery, UFE is a percutaneous procedure that involves no general anesthesia, no surgical incision, and no blood loss or risk of blood transfusion. Recovery and time to return to work and activities of daily living is

weeks shorter than recovery from hysterectomy and open (abdominal) myomectomy. Patient satisfaction is high among UFE patients.

Two multicenter studies with combined cohorts totaling more than 2200 patients recently reported long-term follow-up data for UFE-treated symptomatic leiomyomata.^{5,61} Both support the conclusion that UFE is effective and safe, with durable symptom control, few complications, and improved HRQoL.^{5,61} Results of the EMMY trial, discussed earlier in this article, also led to the conclusion that, based on HRQoL, UFE is a good alternative to hysterectomy.^{35,36}

In view of the number of procedures performed worldwide to date and in comparison with complications associated with myomectomy and hysterectomy, the rarity of serious complications demonstrates the intrinsic safety of UFE.⁹

For women with symptomatic fibroids, UFE can be construed as a safe, effective, and durable alternative to classic surgery. UFE carries high success and low complication rates that are sustained in the long term, and in features of quality-of-life and patient satisfaction, UFE equals or surpasses surgery. However, for women who are actively trying to conceive, the role of UFE remains unclear. At present, myomectomy to enhance fertility may be a better choice.

UFE is an option that all physicians may wish to discuss with all patients presenting with uterine fibroids who are being offered hysterectomy of myomectomy. A collaborative and multidisciplinary practice between gynecologists and interventional radiologists represents state-of-the-art care for women with fibroids. With such an approach, our patients can be given a truly informed consent. ■

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