Chapter

Uterine Fibroid Embolization

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Abstract

Uterine fibroids or leiomyomas are benign, hormone-dependent smooth muscle cell tumors that can be associated with menorrhagia, anemia, pelvic pain, urinary and/or intestinal symptoms, and dyspareunia. Traditionally, the mainstay of treatment has been surgical, consisting of hysterectomy or myomectomy. However, uterine artery embolization has become an increasingly utilized, minimally invasive treatment modality that can be offered as either sole therapy or as a staged, pre-operative measure to hysterectomy. A thorough knowledge of pelvic vascular anatomy and facility with specific embolotherapeutic techniques are required for safe and effective fibroid embolization.

Keywords: uterine artery embolization, uterine fibroid, embolic agent, menorrhagia, internal iliac artery

1. Introduction

Uterine fibroids (UF), or leiomyomas, are benign tumors arising from uterine smooth muscle. UF are common with reported lifetime prevalence rates approaching 70% in Caucasian women and over 80% in African American women [1]. Symptomatic fibroids—estimated to comprise less than 50% of all UF—are most commonly associated with menorrhagia and subsequent anemia in women of reproductive age [2]. As UF grow in volume, symptoms related to bulk effects, including constipation, bladder dysfunction, tenesmus, and chronic back and pelvic pain become problematic and may warrant intervention.

Controversy exists regarding the effect of UF on fertility. Several systematic reviews have reported evidence of increased rates of spontaneous abortion and decreased fertility [3, 4]. Because these reviews included numerous studies drawn from populations of women seeking reproductive assistance, the results presented may not be generalizable to all reproductive-aged women. A systematic review of studies drawn from general obstetric populations found no relation between risk of spontaneous abortion and presence of UF [5].

The traditional approach to UF management has been surgical. Hysterectomy remains the predominant intervention, with myomectomy an option for women desiring to maximize fertility. Uterine artery embolization (UAE) is a minimally invasive and uterine preserving procedure that has become an attractive therapeutic alternative over the last 20 years. Its efficacy and acceptable safety profile have helped establish the technique as a viable approach with minimal complications for women interested in retaining their uterus and avoiding invasive surgery [6]. The procedure involves percutaneous transarterial catheterization and embolization of the vessels perfusing the UF in an attempt to induce ischemic necrosis of the culprit lesion(s).

2. Risk factors and pathophysiology

The exact etiology of UF remains unclear. Several factors are thought to contribute to the overall risk of developing UF, including black race, nulliparity, advanced age prior to menopause, obesity, and hypertension [7, 8]. Menarche before age 10 and oral contraceptive use are also associated with increased risk [7, 9]. Bleeding and bulk symptoms associated with UF tend to ameliorate with menopause, suggesting that the persistence of UF depends on hormonal status [2]. There also exists a hereditary component, with first degree relatives of women affected by UF having a 2.5 fold higher risk of developing UF [10]. Recurrent chromosomal alterations and genetic mutations are found in a fraction of all UF [11, 12]. Protective factors include multiparity, a well-balanced diet, and progestin-only injectable contraception [7, 9, 13].

UF are classified based on their extent and location within the uterus. Broadly, submucosal fibroids are found immediately below the endometrium; subserosal fibroids beneath the serosal uterine surface; intramural fibroids within the myometrium; and pedunculated fibroids are suspended from the uterus by a stalk and may project into the peritoneal or uterine cavities. The International Federation of Obstetrics and Gynecology classification system describes UF localization on an eight-point scale with lower values denoting closer fibroid proximity to the endometrium and uterine cavity [14].

Submucosal fibroids carry an additional risk of endocavitary expulsion post-UAE [15]. Those with larger endometrial interface to maximum dimension ratio are even more likely to be completely or partially expelled into the uterine cavity. In general, larger masses are associated with higher complications rates, although the majority of endocavitary masses pass with few symptoms [15]. For women whose UF fit the above profile and wish to undergo UAE, explaining the risk and symptomatology of fibroid expulsion is essential to minimize post-procedural distress and ensure prompt engagement with their physician should expulsion manifest.

3. Imaging

Identification of UF is often incidental to pelvic examination or pelvic imaging. In patients with suggestive symptoms, trans-abdominal or trans-vaginal ultrasound is initially performed [16]. Color flow Doppler interrogation of the mass can help delineate the degree of vascularity of the UF. B-mode imaging can help delineate the location, depth, extent, and configuration of the UF. Further details of the uterine mass, including presence of potential malignancy, vascularization patterns and anastomoses, and the risk for passage of the infarcted mass, can be captured using contrast-enhanced MRI. Importantly, pre-procedural MRI provides a baseline measure of perfusion that can be tracked to measure the degree of infarction post-UAE [17–19]. It is important to note that imaging ought to be performed in coordination with a thorough gynecologic evaluation and examination including endometrial biopsy to rule out other etiologies. A multidisciplinary approach to patient care in close collaboration with colleagues in gynecology can lead to excellent outcomes [20].

4. Indications and patient selection

Asymptomatic UF discovered incidentally can generally be managed non-operatively under the supervision of a gynecologist. Women experiencing symptomatic UF, however, are candidates for intervention and should be counseled regarding the

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options available to them. Numerous guidelines have described the best practices for UAE based on reported clinical evidence [21]. A consistent picture regarding the ideal candidate for UAE is presented across guidelines: a patient with symptomatic fibroids (bleeding, pain, mass effects) who wishes to avoid invasive surgery. Frequently reported absolute contraindications include viable pregnancy and active infection [21]. Commonly cited relative contraindications include immunocompromised status, hostile anatomy for endovascular intervention, renal impairment, contrast allergy, or previous uterine surgery.

Variability exists among guidelines regarding relative contraindications. Several guidelines recommend considering some UF as unsuitable for UAE based on the relative position of the mass in the uterus; with pedunculated, submucosal and subserosal fibroids variably suggested as being unsuitable for UAE [21–24]. Other guidelines make no such recommendations regarding UF positioning, leaving the anatomical suitability of a patient for UAE at the discretion of the treating physician [21, 25]. Patient desire to retain fertility is similarly divisive. Some guidelines cite a small reported advantage in fertility outcomes of women treated with myomectomy compared to UAE as rationale for recommending against UAE in women desiring future fertility [26, 27]. Other studies have demonstrated similar rates of fertility and complications associated with pregnancy in women treated with UAE when compared with the general population [28, 29]. Definitive evidence regarding the effects of UAE on fertility remains outstanding. It is our practice to recommend against UAE in patients wishing to maintain fertility [20].

Larger UF measuring greater than 10 cm or large uteruses greater than 24 weeks were once considered contraindications to UAE based on case reports detailing poor outcomes in women bearing these features [30]. Continued research and experience, however, has demonstrated the safety and efficacy of UAE for treatment of large UF and large uteruses [31, 32]. We currently do not recommend against UAE based on UF or uterine size alone [20].

The determination of the best treatment approach for a given patient with UF should begin with a consultation that covers a complete history and physical, a review of OB/GYN examination and assessment, the type and degree of symptoms, and a review of any available imaging. Ascertaining the patient's desire for future fertility and uterus preservation are important considerations in guiding intervention selection. In cases where UAE is indicated, explaining the risks associated with the procedure, including bleeding, infection, access site complications, possible negative effects on fertility and the potential need for surgical reintervention and hysterectomy, offers the patient a full account on which to base their decision.

Though rare, other indications for UAE include abnormal placental development, such as placenta previa, accreta, increta, and percreta. These conditions are commonly treated by emergency hysterectomy and carry a high risk of intrapartum hemorrhage, respiratory distress syndromes, kidney failure, and death. Hybrid prophylactic bilateral UAE and caesarian section has been described to increase the safety of fetus delivery and to minimize the risk of intrapartum hemorrhage from placental detachment [33]. In a hybrid operating room, bilateral uterine arteries are first cannulated and the infant is delivered. While the umbilical cord is clamped and the vaginal cavity is packed with the placenta in situ, both uterine arteries are embolized. In a series of 12 patients who underwent UAE-assisted cesarean section, 10 patients retained their uterus and 2 underwent hysterectomy [33]. There was no mortality, minimal blood loss and no post-operative infection. In these cases, the risk of low dose radiation to the fetus is considered negligible compared with baseline risks for all developmental abnormalities [34]. UAE may fall under the purview of multiple specialties, and a collaborative effort among gynecologists, interventional radiologists, and vascular surgeons is necessary to expand the availability of UAE and/or other surgical measures to more women [20].

5. Vascular anatomy of the female pelvis

It is vital to delineate the normal vascular anatomy and its variations for prevention of non-target embolization. In its most common configuration (77%), the internal iliac artery (IIA) bifurcates into two main stems, one anterior and one posterior. Other modes of IIA division include three-stem in 14%, four- or more-stem in 3%, and one main stem in 4% of cases. The anterior division branches include the obturator, umbilical/superior vesical, uterine, vaginal, inferior vesical, middle hemorrhoidal, inferior gluteal, and internal pudendal arteries. The posterior trunk gives rise to the iliolumbar, the lateral sacral, and the superior gluteal arteries. The superior gluteal artery is invariably the terminal branch. While the iliac bifurcation and the origin of the IIA is best visualized under contralateral anterior oblique projection, we have found ipsilateral anterior oblique projections to best demonstrate the origin and course of the uterine artery once the IIA has been adequately accessed and catheterized [35].

The diameter of the uterine artery varies from 2 to 5 mm and is usually largest during pregnancy and immediately after childbirth. It has a U-shaped course. It initially courses caudally against the pelvic wall, then horizontally across the ureter, and at last cranially along the uterus. Its three major terminal branches are the artery of uterine fundus, medial tubal branch, and medial ovarian artery. It is important to be aware of the medial ovarian branch coursing along the utero-ovarian ligament, as it anastomoses with a branch originating from the ovarian artery. The medial ovarian branch provides the total ovarian supply in 4% of the cases. Uterine artery branches are extensively anastomosed with the contralateral uterine artery, as well as with the ipsilateral ovarian and the inferior epigastric arteries. While the uterine artery provides most of the arterial supply of the uterus, the ovarian artery and the artery of the round ligament also contribute [36].

UF are not fed by a specific branch, but by a peri-myomatous plexus. In the presence of fibroids, the branches of the uterine artery are distorted and larger in caliber [16]. The superficial surface of UF are usually enveloped in a dense perifibroid arterial plexus whereas the core of the mass remains relatively hypovascular [16, 37]. The ovarian arteries contribute to UF arterial supply in 5–10% of the cases, especially in patients who have disturbed arterial networks secondary to prior pelvic surgery, tubal or ovarian pathologies or a large fundal fibroid. Round ligament arteries and lumbar arteries are rare sources of UF perfusion. Left–right uterine artery anastomoses are identified in roughly 10% of patients and ovarian-uterine artery anastomoses in 10–30% [16]. On the contrary, pedunculated fibroids are generally perfused by a solitary artery coursing through the fibrotic stalk. A proposed risk of necrosis and deterioration of the stalk with liberation of the mass into the peritoneal cavity has been used as a justification for classifying pedunculated fibroids as a relative contraindication to UAE [38]. Nevertheless, contrast-enhanced magnetic resonance imaging (MRI) of pedunculated fibroids treated with UAE found intact vascularization of the peduncle stalk with successful infarction of the mass and no complications related to UF location [38]. Other work has suggested that pedunculated fibroids are less likely to be completely infarcted following UAE although no clinical outcome data were reported [39]. The suitability of UAE in the treatment of pedunculated fibroids remains an outstanding issue. We currently do not recommend against UAE in patients with pedunculated UF configurations.

6. Choice of embolic agent

An array of embolic particles has been developed and employed in clinical practice. One of the earliest embolic materials used was non-spherical polyvinyl alcohol particles (nsPVA; Merit Medical, South Jordan UT). nsPVA are non-uniform in size and shape and are, therefore, dependent on thrombus formation to produce complete occlusion of the uterine artery lumen [40]. nsPVA also tends to occlude microcatheters and complicate delivery. MRI assessment of UF treated with UAE using nsPVA frequently showed recanalization of infarcted UF in a majority of women 6 months post-intervention, highlighting the need for newer embolic agents suited for UAE [41]. Thus, spherical polyvinyl alcohol (sPVA) particles were developed to address the size and shape variation of nsPVA; however, in practice, sPVA particles (Contour SE microspheres; Boston Scientific) produced inferior improvements in symptoms and smaller reductions in UF size post-UAE [42].

Gelatin sponge—a biodegradable agent derived from purified gelatin—has been used as an embolic agent in cases of hemorrhage, and has been employed successfully as an embolic agent in UAE [43]. Preparing the gelatin sponge agent from the stock material requires hand manipulation, which produces inconsistencies in size and shape thereby limiting quantifiable comparisons with other more consistently prepared embolic agents.

Particle size influences the degree of distal embolization and potential for non-target embolization [31]. The observed caliber of perifibroid arterial vessels is between 500 and 800 μm, which justifies the typical use of calibrated particles in the 500–700 or 700–900 μm range [44]. Employing smaller sized particles is associated with an increased risk of uterine necrosis and should therefore be avoided [45].

Tris-acryl gelatin microspheres (TAGM; Embospheres; Merritt Medical, South Jordan, Utah) are calibrated microspheres that come in sizes ranging from 40 to 1200 μm. When used for UAE, TAGM sized 500–700 μm are typically employed and have demonstrated distal penetration into the UF vasculature with minimal proximal aggregation that is observed with nsPVA [40].

A new entrant in the embolic material space is F-coated Hydrogel Microspheres Embozene; CeloNova BioScience, Newnan, Georgia. These microspheres are comprised of a hydrogel core of polymethylmethacrylate encased in a malleable polyphosphazene shell. These particles are biostable and are available in a range of sizes from 40 to 1300 μm [40]. Early experience with these agents has demonstrated safety and efficacy in the treatment of UF [46].

With the exception of greater symptomatic improvement with TAGM use as compared to sPVA, outcomes and complications of the other embolic agents generally suggests no clear evidence of superiority of TAGM [40, 42]. There is a need for better powered studies to differentiate among the different embolic agents.

7. Technical procedure

UAE is generally performed in a hybrid operating suite or catheterization suite under general or moderate sedation anesthesia. The latter requires ability and willingness of the patient to cooperate with positional and ventilatory instructions intraoperatively to maximize imaging quality as well as the accuracy of microcatheterization and embolic agent delivery. In the absence of contraindications, chemical and mechanical deep vein thrombosis prophylaxis via prophylactic dose of enoxaparin, graded stockings, and sequential compressive devices is administered before induction of anesthesia.

The single femoral artery approach is adequate to access both the ipsilateral and contralateral uterine arteries. The micropuncture technique is used for femoral arterial access. In young healthy women, clinically significant vasospasm is a serious consideration and must be monitored regularly. We suggest immediate availability of vasodilatory agents for intrarterial administration if necessary. In order to avoid arterial vasospasm, some interventionalists recommend ceasing GnRH analog treatment several weeks before treatment [20, 35].

Over a guidewire, a 5 F multisidehole catheter of choice is advanced into the midabdominal aorta. Flush aortography is performed looking for pelvic hypervascular neoplastic changes and dilation and tortuosity of the feeding UAs. Contralateral obliquity of the image intensifier facilitates visualization of the ipsilateral iliac bifurcation. Under roadmap guidance, selective catheterization of the IIA is performed using an angled guidewire and a 5 F C2 catheter (Merit Medical, South Jordan UT). Selective angiogram of the IIA in ipsilateral obliquity commonly facilitates visualization of the UA ostium. This image is then roadmapped. A coaxial microcatheter-based platform (Direxion; Boston Scientific, Marlborough, MA) is then developed over an 0.014 steerable guidewire, the tip of which can be curved manually before intrarterial insertion to help facilitate engagement of the target vessel ostium and to help overcome extreme arterial tortuosity.

Superselective microcatheterization of the UA is then performed with advancement of the catheter to the proximal-most branches of the uterine artery feeding the fibroid. Use of power injector for angiography is essential as manual contrast infusion through the small caliber, high resistance microcatheter platform can be difficult and lead to suboptimal imaging. Once the satisfactory positioning of microcatheter tip is confirmed on angiography, the system is copiously flushed with heparinized saline in preparation for the delivery of embolic agent [20].

The embolic agent is delivered in bursts through the microcatheter under fluoroscopic guidance with intermittent heparin saline flush. Extreme care is taken to avoid reflux of the embolic agent particularly toward the end of each session when greater resistance to flow is encountered. The system is then gently flushed with heparinized saline to irrigate out the residual embolic content within the microcatheter. This must be performed under fluoroscopic visualization to prevent nontarget embolization. Adequate devascularization of the UF from the accessed side is then confirmed on completion angiography of the ipsilateral IIA through the 5 F C2 catheter after removing the microcatheter coaxial platform.

Up-and-over technique is used to similarly catheterize the contralateral UA and deliver embolic agent as described previously. Completion aortoiliac angiogram is performed to ensure adequate UF devascularization and to rule out nontarget embolization.

Alternative techniques have been reported. Bilateral femoral puncture with sequential UA catheterization and simultaneous embolization is associated with reduced fluoroscopy time, reduced procedure time, and no added complication risk when compared to unilateral femoral puncture [47]. Transradial access (TRA) has been employed successfully in percutaneous coronary interventions for years, and studies exploring the suitability of TRA for UAE have been promising [48, 49]. In those patients with sufficient collateral perfusion of the hand and suitable radial artery anatomy, TRA may have 100% technical success rate with no immediate complications [49]. Patients usually enjoy fewer restrictions in positioning and movement following the procedure and report satisfaction with the freedom offered by TRA.

8. Outcomes and complications

Accumulated evidence over decades has supported the use of UAE in the treatment of uterine masses in a safe and efficacious manner. Expected outcomes following UAE include a 50–60% reduction in UF size, an 88–92% reduction in bulk symptoms associated with UF, 90% reduction in bleeding associated symptoms,

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and a patient satisfaction rate of 80–90% [25, 26]. Reduction in UF size can be visualized within weeks of UAE and continues for 3–12 months following the procedure. Histopathological analysis of successfully infarcted UF is characterized by coagulative or hyaline necrosis [50]. The degree of UF infarction as captured by contrast enhanced MRI 24–72 hours post-UAE has been reported to predict the magnitude and durability of symptomatic improvement as well as risk for reintervention [51]. Women exhibiting 100% infarction on post-operative imaging enjoyed a 0% reintervention rate after 24 months, whereas women with almost complete (90–99%) or partial (<90%) infarction experienced reintervention rates of 20 and 50%, respectively.

Interventional success is generally defined as reducing blood flow through the UA to near stasis and causing complete infarction of the UF [6]. Gradual revascularization of the myometrium occurs in the weeks following UAE while the UF ideally remains infarcted and regresses. Failure rates range from 20 to 28%, most likely due to incomplete embolization of the UF vasculature, recanalization of the UF vasculature, or the persistence and engorgement of collaterals feeding the UF post-UAE [6, 52]. Identification of collateral blood supply to the UF, either before UAE using an aortogram or MRI, or peri-procedurally using cone-beam CT angiography, will inform the embolization procedure and ensure all vessels supplying the UF are targeted [6, 53]. In cases where the ovarian artery is found to supply the UF, either independently or via a utero-ovarian anastomosis, embolization of the ovarian artery is required to ensure complete infarction of the UF. Despite the risk of ovarian compromise following ovarian artery embolization in this scenario, reports studying the effects of ovarian artery embolization in conjunction with UAE have found no evidence of menopause precipitation, nor worsening of menopausal symptoms [52]. This is in contrast to prior work that reported roughly 40% of women over the age of 45 experienced ovarian failure following UAE without ovarian artery embolization [54]. Among women under the age of 45, no cases of ovarian failure were observed. These observations suggest that, should UAE negatively affect the ovarian capacity, the extent of ovarian function compromise is related to the patient's age at the time of the procedure.

Post-embolization syndrome, involving pelvic pain, low-grade fever, nausea, loss of appetite, and malaise, is almost inevitable following UAE. The treatment is supportive, consisting of antipyretic, fluids, analgesia, and anti-inflammatory medication. Over 90% of women undergoing UAE report pain following the procedure, making pain management an important consideration in caring for these patients [55]. Admitting patients for a 24-hour observation period allows for pain management under the direct care of their physician. [20] Several approaches have been reported that aim to reduce post-procedural pain and opioid use in these patients. Peri-procedural superior hypogastric nerve block using a 0.75% ropivacaine solution is effective in minimizing post-procedural pain and significantly reduces total opioid usage [55]. A single pre-procedural dose of intravenous dexamethasone can also improve patient pain scores and reduce markers of inflammation. However, the total opioid use in these patients has been found not to be significantly different from those not receiving pre-procedural dexamethasone [56].

The most commonly reported long-term complication associated with UAE is permanent amenorrhea. Women over 45 years of age are reported more likely to experience permanent amenorrhea following UAE (20–40%) than women under 45 (0–3%) [25]. Transient amenorrhea following UAE is often observed and may be a consequence of non-target ovarian artery embolization although this is not considered a major complication. Other observed complications include persistent vaginal discharge, transcervical expulsion of infarcted tissue, prolonged and intractable pain, and infection [25]. Very rare cases of deaths have been reported following

UAE as a result of pulmonary embolization, sepsis, and embolization of occult leiomyosarcoma [31].

Reintervention is indicated, should UF related symptoms return secondary to resumed growth of the primary UF or growth of a new UF. Reported reintervention rates range from 14 to 35% [26, 57]. Reinterventions may include repeat UAE, hysterectomy, or myomectomy. Patients undergoing UAE should be counseled regarding the risks of reintervention. Fostering long-term relationships with patients undergoing UAE allows for tracking of outcomes and early intervention should symptoms re-emerge [25].

While several guidelines cite preservation of fertility as a relative contraindication to UAE, uncertainty remains regarding fertility outcomes following the procedure [21]. Published case series following pregnancies in women attempting to conceive following UAE found an overall pregnancy rate of ~30% [58]. As compared to the general obstetric population, women treated with UAE have similar or increased rates of obstetric complications, with specifically increased rates of miscarriage and cesarean section deliveries [58, 59]. Notably in the majority of these studies, women with UF treated by UAE were older than the general obstetric population and carried additional risk factors, which may explain some of the observed increases in complication rates. For women with complex UF pathology who desire to retain their uterus and avoid invasive surgery, UAE may be presented as an option that preserves some chance of conception in the future.

9. Comparison with hysterectomy and myomectomy

The traditional approach to the treatment of symptomatic fibroids has been surgical, with hysterectomy being the most common [60]. Complete removal of the uterus is a definitive treatment for UF that precludes recurrence and may be a suitable recommendation for women who have completed child bearing. Though rates of hysterectomy are decreasing, the lifetime prevalence among U.S women as of 2012 was 45%, with nearly one-third of all hysterectomies performed as treatment of UF [60]. While laparoscopic hysterectomy has become more commonplace, open hysterectomies remain most frequently employed.

Myomectomy is a uterine sparing surgical intervention best suited to the removal of one to three fibroids in an anatomically accessible location [31]. Like hysterectomy, myomectomy may be done laparoscopic or open, with the laparoscopic approach associated with fewer complications and quicker recovery [61]. For women with submucosal fibroids projecting into the intrauterine cavity, hysteroscopic myomectomy is a suitable option that is associated with quick recovery and return to daily living [2].

Laparoscopic management of UF, either by hysterectomy or myomectomy that employs power morcellation for specimen removal, has been associated with a risk of dissemination of occult sarcoma [31]. Histopathological analysis of hysterectomy specimens shows a 0.4% rate of unsuspected malignancy in uteruses treated for UF [62]. Under these circumstances, patients should be informed of the risk of occult malignancy dissemination.

Growing clinical experience and promise of UAE in the treatment of UF motivated the design and execution of several randomized clinical trials (RCTs) comparing medium- and long-term outcomes and patient satisfaction with UAE compared with surgical interventions. The embolization versus hysterectomy (EMMY) trial recruited women with symptomatic UF and assigned them 1:1 to either UAE or hysterectomy [63]. Patient satisfaction rates and quality of life scores were similar between UAE and hysterectomy out to 10 years [64]. The study reported a 69% success rate with UAE while 31% of UAE treated patients experienced refractory or relapsing symptoms requiring definitive treatment by hysterectomy. Of note was the observation that women with BMI >25 and a history of smoking at baseline were more likely to require reintervention following UAE. The reported 69% clinical success rate is notably lower than other reported rates ranging 80–90% [31]. The authors attributed the lower UAE success rate to the fact that eligible candidates recruited to the study suffered severe bleeding symptoms, and the trial required a much longer 10-year follow-up window that is only used in tracking outcomes [64].

The REST trial grouped women treated with myomectomy with women treated with hysterectomy in order to expand the UAE comparison to surgical intervention [65]. Women treated with either UAE or surgery enjoyed similar satisfaction rates and quality of life improvements at 5 years. Differences in reintervention rates were noted, however, as 32% of women treated with UAE required further intervention within 5 years as compared to 4% of women in the surgery group. A study directly comparing UAE to myomectomy found symptom improvement in 88.3% of UAE women compared to 75.4% in myomectomy at 2 years post-intervention [66]. Bearing the risks of reintervention in mind, the above trials affirm UAE as a safe procedure that enjoys rates of satisfaction and symptom improvement similar to those observed in hysterectomy and myomectomy. A Cochrane review of published RCTs comparing UAE to surgical interventions reaffirms this view and shows that UAE is associated with shorter hospital stays, less disability, and similar satisfaction rates when compared to surgical intervention [26].

10. New generation of devices

Magnetic resonance-guided high intensity focused ultrasound (MR-g HIFU) is a non-invasive intervention that works to thermally ablate UF via the delivery focused ultrasound waves [67]. Rounds of sonification and heating lasting 30 seconds are interleaved with 90-second cooling-off periods; the target tissue temperatures reach 60–85°C, thereby provoking coagulative necrosis of the targeted mass [68]. FDA guidelines regarding MR-g HIFU limit the total and percent volumes of uterine mass subject to thermal ablation to confine the sonification to the fibroid. Prospective studies tracking symptom severity scores and quality of life indices in women, whose UF were treated with MR-g HIFU, found significant improvement of both measures after at least 2 years of follow-up [67, 68]. In a direct comparison with UAE, however, women who underwent MR-g HIFU reported smaller improvements to quality of life scores after treatment [69]. MR-g HIFU also fared worse in terms of reintervention rates, with women undergoing UAE experiencing a 6.7% reintervention rate compared to a 30% reintervention rate in the MR-g HIFU group at mid-term follow up [69]. Potential explanations for the different outcomes are that MR-g HIFU treats only a single mass whereas UAE targets all masses in the uterus, and that MR-g HIFU ablates only a fraction of the total mass volume whereas UAE completely infarcts UF.

11. Conclusion

As the rates of hysterectomy fall and patient desire for less invasive management of uterine fibroid rises, uterine artery embolization has become increasingly prominent. Two decades of experience have validated the procedure as safe and effective with continued advancement in procedural techniques, equipment and imaging, embolic agents, pain management, and operator experience lending to improved outcomes. There remain outstanding questions regarding UAE. Well-controlled investigations of fertility outcomes in women undergoing UAE or surgery for UF are needed. As new embolic agents become available, comparison trials to gauge efficacy and safety among the different agents are necessary. Continued delineation of patient anatomy that suggest susceptibility to ovarian insufficiency post-UAE is also important to ensure patients are well-counseled regarding their risks. The potential for further advancement leaves UAE well-positioned to continue its expansion in clinical practice.

Abbreviations

EMMY	embolization versus hysterectomy
F	French
MR-g HIFU	magnetic resonance-guided high intensity focused ultrasound
MRI	magnetic resonance imaging
nsPVA	non-spherical polyvinyl alcohol
RCT	randomized clinical trials
SPRM	selective progesterone receptor modulators
sPVA	spherical polyvinyl alcohol
TAGM	tris-acryl gelatin microspheres
TRA	transradial access
UAE	uterine artery embolization
UF	uterine fibroid
UPA	ulipristal acetate

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References

[1] Baird DD et al. High cumulative incidence of uterine leiomyoma in black and white women: Ultrasound evidence. American Journal of Obstetrics and Gynecology. 2003;**188**(1):100-107

[2] Stewart EA. Clinical practice. Uterine fibroids. The New England Journal of Medicine. 2015;**372**(17):1646-1655

[3] Pritts EA, Parker WH, Olive DL. Fibroids and infertility: An updated systematic review of the evidence. Fertility and Sterility. 2009;**91**(4):1215-1223

[4] Sunkara SK et al. The effect of intramural fibroids without uterine cavity involvement on the outcome of IVF treatment: A systematic review and meta-analysis. Human Reproduction. 2010;**25**(2):418-429

[5] Sundermann AC et al. Leiomyomas in pregnancy and spontaneous abortion: A systematic review and meta-analysis. Obstetrics and Gynecology. 2017;**130**(5):1065-1072

[6] Kohi MP, Spies JB. Updates on uterine artery embolization. Seminars in Interventional Radiology. 2018;**35**(1):48-55

[7] Marshall LM et al. A prospective study of reproductive factors and oral contraceptive use in relation to the risk of uterine leiomyomata. Fertility and Sterility. 1998;**70**(3):432-439

[8] Medikare V et al. The genetic bases of uterine fibroids: A review. Journal of Reproduction and Infertility. 2011;**12**(3):181-191

[9] Wise LA et al. Reproductive factors, hormonal contraception, and risk of uterine leiomyomata in African-American women: A prospective study. American Journal of Epidemiology. 2004;**159**(2):113-123

[10] Vikhlyaeva EM, Khodzhaeva ZS, Fantschenko ND. Familial predisposition to uterine leiomyomas. International Journal of Gynaecology and Obstetrics. 1995;**51**(2):127-131

[11] Makinen N et al. MED12, the mediator complex subunit 12 gene, is mutated at high frequency in uterine leiomyomas. Science. 2011;**334**(6053):252-255

[12] Ligon AH, Morton CC. Genetics of uterine leiomyomata. Genes Chromosomes and Cancer. 2000;**28**(3):235-245

[13] Wise LA et al. Intake of fruit, vegetables, and carotenoids in relation to risk of uterine leiomyomata. The American Journal of Clinical Nutrition. 2011;**94**(6):1620-1631

[14] Munro MG et al. The FIGO classification of causes of abnormal uterine bleeding in the reproductive years. Fertility and Sterility. 2011;**95**(7):2204, 2208 e1-2208, 2208 e3

[15] Verma SK et al. Submucosal fibroids becoming endocavitary following uterine artery embolization: Risk assessment by MRI. American Journal of Roentgenology. 2008;**190**(5):1220-1226

[16] Pelage JP et al. Uterine fibroid vascularization and clinical relevance to uterine fibroid embolization. Radiographics. 2005;**25** (Suppl 1):S99-S117

[17] Keung JJ, Spies JB, Caridi TM. Uterine artery embolization: A review of current concepts. Best Practice and Research. Clinical Obstetrics and Gynaecology. 2018;**46**:66-73

[18] Fleischer AC et al. Three-dimensional color Doppler sonography before and after fibroid embolization.

Journal of Ultrasound in Medicine. 2000;**19**(10):701-705

[19] Pelage JP et al. Uterine fibroid tumors: Long-term MR imaging outcome after embolization. Radiology. 2004;**230**(3):803-809

[20] Nassiri N et al. An academic tertiary referral center's experience with a vascular surgery-based uterine artery embolization program. Annals of Vascular Surgery. 2018;**52**:90-95

[21] Chen HT, Athreya S. Systematic review of uterine artery embolisation practice guidelines: Are all the guidelines on the same page? Clinical Radiology. 2018;**73**(5):507 e9-507 e15

[22] Vilos GA et al. The management of uterine leiomyomas. Journal of Obstetrics and Gynaecology Canada. 2015;**37**(2):157-178

[23] Carranza-Mamane B et al. The management of uterine fibroids in women with otherwise unexplained infertility. Journal of Obstetrics and Gynaecology Canada. 2015;**37**(3):277-285

[24] Marret H et al. Therapeutic management of uterine fibroid tumors: Updated French guidelines. European Journal of Obstetrics, Gynecology, and Reproductive Biology. 2012;**165**(2):156-164

[25] Dariushnia SR et al. Quality improvement guidelines for uterine artery embolization for symptomatic leiomyomata. Journal of Vascular and Interventional Radiology. 2014;**25**(11):1737-1747

[26] Gupta JK et al. Uterine artery embolization for symptomatic uterine fibroids. Cochrane Database of Systematic Reviews. 2014;**12**:CD005073

[27] Goldberg J et al. Pregnancy outcomes after treatment for fibromyomata: Uterine artery embolization versus laparoscopic myomectomy. American Journal of Obstetrics and Gynecology. 2004;**191**(1):18-21

[28] Pisco JM et al. Pregnancy after uterine fibroid embolization. Fertility and Sterility. 2011;**95**(3):1121 e5-1121 e8

[29] Mohan PP, Hamblin MH, Vogelzang RL. Uterine artery embolization and its effect on fertility. Journal of Vascular and Interventional Radiology. 2013;**24**(7):925-930

[30] Pelage JP et al. Fibroid-related menorrhagia: Treatment with superselective embolization of the uterine arteries and midterm follow-up. Radiology. 2000;**215**(2):428-431

[31] Silberzweig JE et al. Management of uterine fibroids: A focus on uterine-sparing interventional techniques. Radiology. 2016;**280**(3):675-692

[32] Berczi V et al. Safety and effectiveness of UFE in fibroids larger than 10 cm. Cardiovascular and Interventional Radiology. 2015;**38**(5):1152-1156

[33] Li Q et al. Prophylactic uterine artery embolization assisted cesarean section for the prevention of intrapartum hemorrhage in high-risk patients. Cardiovascular and Interventional Radiology. 2014;**37**(6):1458-1463

[34] Patel SJ et al. Imaging the pregnant patient for nonobstetric conditions: Algorithms and radiation dose considerations. Radiographics. 2007;**27**(6):1705-1722

[35] Varghese K, Adhyapak S. Uterine artery embolization for bleeding due to fibroids. In: Therapeutic Embolization. Cham: Springer International Publishing; 2017. pp. 83-92

[36] Boyer L et al. Uterine fibroid embolization (UFE). In: Chabrot P, Boyer L, editors. Embolization. London: Springer London; 2014. pp. 323-340

[37] Goodwin SC, Spies JB. Uterine fibroid embolization. The New England Journal of Medicine. 2009;**361**(7):690-697

[38] Smeets AJ et al. Safety and effectiveness of uterine artery embolization in patients with pedunculated fibroids. Journal of Vascular and Interventional Radiology. 2009;**20**(9):1172-1175

[39] Lacayo EA et al. Leiomyoma infarction after uterine artery embolization: Influence of embolic agent and leiomyoma size and location on outcome. Journal of Vascular and Interventional Radiology. 2017;**28**(7):1003-1010

[40] Das R et al. Comparison of embolic agents used in uterine artery embolisation: A systematic review and meta-analysis. Cardiovascular and Interventional Radiology. 2014;**37**(5):1179-1190

[41] Das R et al. MRI assessment of uterine artery patency and fibroid infarction rates 6 months after uterine artery embolization with nonspherical polyvinyl alcohol. Cardiovascular and Interventional Radiology. 2013;**36**(5):1280-1287

[42] Rasuli P et al. Spherical versus conventional polyvinyl alcohol particles for uterine artery embolization. Journal of Vascular and Interventional Radiology. 2008;**19**(1):42-46

[43] Katsumori T, Kasahara T, Akazawa K. Long-term outcomes of uterine artery embolization using gelatin sponge particles alone for symptomatic fibroids. American Journal of Roentgenology. 2006;**186**(3):848-854

[44] Siskin GP et al. Leiomyoma infarction after uterine artery embolization: A prospective randomized study comparing tris-acryl gelatin microspheres versus polyvinyl alcohol microspheres. Journal of Vascular and Interventional Radiology. 2008;**19**(1):58-65

[45] Pelage JP et al. Uterine artery embolization in sheep: Comparison of acute effects with polyvinyl alcohol particles and calibrated microspheres. Radiology. 2002;**224**(2):436-445

[46] Smeets AJ et al. Embolization of uterine leiomyomas with polyzene F-coated hydrogel microspheres: Initial experience. Journal of Vascular and Interventional Radiology. 2010;**21**(12):1830-1834

[47] Costantino M et al. Bilateral versus unilateral femoral access for uterine artery embolization: Results of a randomized comparative trial. Journal of Vascular and Interventional Radiology. 2010;**21**(6):829-835. quiz 835

[48] Fischman AM, Swinburne NC, Patel RS. A technical guide describing the use of transradial access technique for endovascular interventions. Techniques in Vascular and Interventional Radiology. 2015;**18**(2):58-65

[49] Resnick NJ et al. Uterine artery embolization using a transradial approach: Initial experience and technique. Journal of Vascular and Interventional Radiology. 2014;**25**(3):443-447

[50] Weichert W et al. Uterine arterial embolization with tris-acryl gelatin microspheres: A histopathologic evaluation. The American Journal of Surgical Pathology. 2005;**29**(7):955-961

[51] Kroencke TJ et al. Uterine artery embolization for leiomyomas: Percentage of infarction predicts

clinical outcome. Radiology. 2010;**255**(3):834-841

[52] Hu NN et al. Menopause and menopausal symptoms after ovarian artery embolization: A comparison with uterine artery embolization controls. Journal of Vascular and Interventional Radiology. 2011;**22**(5):710-715 e1

[53] Alabdulghani F, O'Brien A, Brophy D. Application of cone-beam computed tomography angiography in a uterine fibroid embolization procedure: A case report. Case Reports in Radiology. 2018;**13**(1):130-134

[54] Chrisman HB et al. The impact of uterine fibroid embolization on resumption of menses and ovarian function. Journal of Vascular and Interventional Radiology. 2000;**11**(6):699-703

[55] Binkert CA et al. Superior hypogastric nerve block to reduce pain after uterine artery embolization: Advanced technique and comparison to epidural anesthesia. Cardiovascular and Interventional Radiology. 2015;**38**(5):1157-1161

[56] Kim SY et al. The effects of single-dose dexamethasone on inflammatory response and pain after uterine artery embolisation for symptomatic fibroids or adenomyosis: A randomised controlled study. BJOG-An International Journal of Obstetrics and Gynaecology. 2016;**123**(4):580-587

[57] Sandberg EM et al. Reintervention risk and quality of life outcomes after uterine-sparing interventions for fibroids: A systematic review and meta-analysis. Fertility and Sterility. 2018;**109**(4):698-707 e1

[58] Carpenter TT, Walker WJ. Pregnancy following uterine artery embolisation for symptomatic fibroids: A series of 26 completed pregnancies. BJOG-An International Journal of Obstetrics and Gynaecology. 2005;**112**(3):321-325

[59] Walker WJ, McDowell SJ. Pregnancy after uterine artery embolization for leiomyomata: A series of 56 completed pregnancies. American Journal of Obstetrics and Gynecology. 2006;**195**(5):1266-1271

[60] Stewart EA, Shuster LT, Rocca WA. Reassessing hysterectomy. Minnesota Medicine. 2012;**95**(3):36-39

[61] Jin C et al. Laparoscopic versus open myomectomy—A meta-analysis of randomized controlled trials. European Journal of Obstetrics, Gynecology, and Reproductive Biology. 2009;**145**(1):14-21

[62] Takamizawa S et al. Risk of complications and uterine malignancies in women undergoing hysterectomy for presumed benign leiomyomas. Gynecologic and Obstetric Investigation. 1999;**48**(3):193-196

[63] Volkers NA et al. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids: 2 years' outcome from the randomized EMMY trial. American Journal of Obstetrics and Gynecology. 2007;**196**(6):519 e1-519 11

[64] de Bruijn AM et al. Uterine artery embolization vs hysterectomy in the treatment of symptomatic uterine fibroids: 10-year outcomes from the randomized EMMY trial. American Journal of Obstetrics and Gynecology. 2016;**215**(6):745 e1-745 e12

[65] Moss JG et al. Randomised comparison of uterine artery embolisation (UAE) with surgical treatment in patients with symptomatic uterine fibroids (REST trial): 5-year results. BJOG-An International Journal of Obstetrics and Gynaecology. 2011;**118**(8):936-944

[66] Siskin GP et al. A prospective multicenter comparative study between myomectomy and uterine artery embolization with polyvinyl alcohol microspheres: Long-term clinical outcomes in patients with symptomatic uterine fibroids. Journal of Vascular and Interventional Radiology. 2006;**17**(8):1287-1295

[67] Kim HS et al. MR-guided high-intensity focused ultrasound treatment for symptomatic uterine leiomyomata: Long-term outcomes. Academic Radiology. 2011;**18**(8):970-976

[68] Funaki K, Fukunishi H, Sawada K. Clinical outcomes of magnetic resonance-guided focused ultrasound surgery for uterine myomas: 24-month follow-up. Ultrasound in Obstetrics and Gynecology. 2009;**34**(5):584-589

[69] Froeling V et al. Midterm results after uterine artery embolization versus MR-guided high-intensity focused ultrasound treatment for symptomatic uterine fibroids. Cardiovascular and Interventional Radiology. 2013;**36**(6):1508-1513