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Radiological treatment of symptomatic uterine fibroids

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Uterine artery embolization (UAE) is a relatively new alternative treatment for symptomatic fibroids. Recent Level I evidence from two major randomized controlled trials has established UAE as a safe and effective alternative to hysterectomy. Technical aspects, choice of embolic agent, safety, contra-indications and complications of the procedure will be reviewed. The available data on the effects on ovarian function, fertility and pregnancy outcomes following UAE will be presented.

Key words: fibroid; uterine artery embolization; menorrhagia; interventional radiology.

Ravina et al[1] first described uterine artery embolization (UAE) as a treatment for uterine fibroids in 1995. Their work was stimulated by the observation of improvement in fibroid-related symptoms in patients undergoing UAE for postpartum haemorrhage. There has been increasing acceptance and evidence for this treatment modality in the intervening 12 years (National Institute of Health and Clinical Excellence, UK), although high-quality Level I evidence has only become available recently in the form of two randomized trials[2–6] comparing UAE with hysterectomy.

TECHNICAL ASPECTS

UAE is performed under X-ray guidance. As the treatment population is young and potentially fertile, the principle of effective treatment with minimum radiation exposure must be applied. For this reason, good angiographic equipment is required

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with the ability to minimize radiation exposure by a variety of techniques. The simplest way to minimize radiation exposure is to avoid angiographic runs, and rely on fluoroscopy instead.[7]

The currently accepted technique for UAE involves unilateral femoral artery access. The uterine arteries are catheterized selectively in turn and embolization is performed. A variety of catheters can be used for this, depending on the operator's preference. Micro-catheters can be useful when there are anatomical constraints such as marked tortuosity at the origin of the uterine artery or in small arteries. Some radiologists would advocate their use routinely to avoid spasm and ensure a good position for embolization. The use of bilateral femoral artery punctures has been described as a dose-reduction technique[8–10], and further measures to reduce dose include use of roadmaps rather than digitally acquired acquisitions and simultaneous embolization.

Antispasmodics, e.g. glyceryl trinitrate (GTN), can be administered if there is arterial spasm. The use of transdermal GTN has also been described.[11] There is evidence that success rates, fluoroscopy and procedural times are related to operator experience.[12] Antibiotic prophylaxis is widely used, although there is no evidence for this policy. Intra-uterine sepsis following UAE is rare and appears to be a sporadic occurrence; no specific risk factors have been identified.[13] Efforts should be made to ensure that there is no infection at the time of embolization. To this end, some have advocated that intra-uterine contraceptive devices should be removed prior to UAE, although this is not uniform practice.

Current standards of care aim for technical success rates of 96% (Table 1). Adverse factors affecting technical success include tortuosity and small calibre of the uterine artery and anatomical variants. However, on a second procedure, there can be technical success due to a number of factors, including pre-planning of approach, preselection of suitable catheters and possible hypertrophy of the remaining vessel.

There have been two small series[14,15] of outcomes following unilateral, and therefore technically inadequate, UAE. In one, a positive clinical outcome followed unilateral UAE due to technical failure in five patients, and supports the view that an initial conservative approach is reasonable before attempting sequential embolization of the remaining uterine artery. The second series reported seven patients, five of whom had repeat embolization within 2 months with a positive clinical outcome, compared with one of two patients treated conservatively. The same study reported three patients with congenital absence of the uterine artery, and one patient with previous ligation of the uterine artery. There was a positive response in the two patients with congenital absence of the uterine artery, and a poor response in the woman with previous ligation as ovarian collaterals had developed.

Table 1. Expected outcomes (CIRSE Quality Improvement Guidelines).

Technical success of embolization of both uterine arteries	96%
Leiomyoma size reduction	50–60%
Uterine size reduction	40–50%
Elimination of menorrhagia	>90%
Reduction in bulk symptoms	88–92%
Elimination of symptoms	85%
Recurrence	Unknown

There is evidence to support the use of contrast-enhanced magnetic resonance imaging (MRI) as a predictor of fibroid regrowth and likely symptomatic recurrence.[16–18] MRI is the modality of choice, especially where there are smaller areas of persistent fibroid vascularity. An interesting development is the potential application of contrast-enhanced ultrasound during the procedure to determine the endpoint of embolization or as follow-up.[19,20]

EMBOLIC AGENTS

There is a consensus that complete devascularization of all fibroids is mandatory for effective treatment.[18,21] Partial devascularization can result in a clinical improvement and volume reduction, but there is a higher recurrence rate in the long term.[14] An important cause of treatment failure is recanalization of one or both uterine arteries, minutes to hours after completion of the procedure.[22] This may be dependent on the type of embolization particle used. A variety of agents are available, but the main types used for UAE are particulate and gelatin sponge.

Initially, non-spherical polyvinyl alcohol (PVA) particles were the main particulate embolic material used. However, variation in particle size and a tendency to aggregate leads to more proximal rather than distal vessel occlusion. This may lead to subsequent recanalization and continued supply to the fibroids via non-embolized distal small vessels. To this end, new particulate agents have been developed that do not aggregate.

Gelatin-coated trisacryl microspheres (Embospheres, Biosphere Medical, Rockland, MA, USA) were developed to offer the theoretical advantage of more uniform and targeted embolization of the perifibroid plexus.[23] These have been shown to result in more distal penetration on histological studies.[24] Embospheres have been followed by several other spherical agents.[25]

Whereas with non-spherical PVA particles, complete occlusion of the uterine artery was considered to be the endpoint of embolization, a new endpoint was proposed[26] with Embospheres; a limited embolization of uterine arteries resulting in a 'pruned-tree' appearance of the vasculature. However in a prospective, randomized study comparing non-spherical PVA particles and Embospheres[27], there was no difference in success rates by either imaging criteria (non-enhancement of all fibroids) or clinical outcome. Moreover, the intensity of pain and the complication rates were similar. Other trials are proceeding, but there is no definitive proof, to date, to support the use of one type of agent over another. In choosing between embolic agents with identical clinical outcomes, one needs to weigh the ease of handling, the total volume of particles required, the time for reaching the expected endpoint (with longer times being associated with higher radiation doses) and the cost of the agents.

The temporary embolic agent gelfoam has been used as an alternative agent to microparticles. Katsumori et al[28,29] reported favourable outcomes in 96 patients with both mid- and long-term follow-up, and concluded that gelatin sponge can achieve long-term symptom control for fibroids in the majority of cases. They recently demonstrated complete devascularization of fibroids in over 80% of patients assessed with contrast-enhanced MRI ($n = 27$).[30] Gelatin sponge is an inexpensive embolic agent, but currently lacks the wealth of data in comparison with PVA particles to support its widespread use.

ANALGESIA

Many analgesic protocols have been described varying from standard epidural anaesthesia in all patients, to extensive medication regimens with patient-controlled

analgesia in combination with non-steroidal anti-inflammatory drugs.[31,32] Even general anaesthesia has been advocated by some authors.[33]

The occurrence and intensity of pain are unpredictable[5,34], and pain should be assessed on a regular basis during admission to enable the administration of analgesics before progression to a level where pain control is virtually impossible.

There is disagreement regarding whether or not pain can be managed by a fixed pain medication protocol. Epidural anaesthesia does result in the lowest average pain scores[5], but the invasiveness, complexity and risks of the procedure restrict its use in daily practice. Opiates were administered in a high percentage (64%) of patients after UAE in the EMMY trial, although outpatient UAE has been advocated in some publications.[35–38] Pain during admission is lower after UAE compared with hysterectomy. Patient characteristics indicative for excessively high pain scores were not identified in this trial.

POSTEMBOLIZATION SYNDROME

Postembolization syndrome is characterized by low-grade pyrexia, discomfort and malaise. This is usually seen at postoperative days 3–7 and will settle with conservative measures. Postembolization syndrome is a recognized consequence of embolization procedures in a variety of territories. Although this may be deemed a complication if severe, requiring re-admission or prolonging admission, it can be argued that, in most reported cases, this is an expected side-effect of the procedure rather than a true complication.

EFFICACY

The overwhelming majority of published data about UAE for fibroids has been in the form of case series and prospective observational studies (Table 2). These series

Table 2. Results of observational studies of uterine artery embolization.

Reference	*n*	Mean duration of follow-up (months)	Menorrhagia improvement (%)	Bulk symptom improvement (%)	Mean fibroid volume reduction	Complications
Hutchins[40] (1999)	305	12	92	92	48	Puncture site haematoma 4 Hysterectomy 1 Re-admission for pain 2
Spies[43] (2001)	200	21	90	91	60	Endometrial infection 2 Fibroid expulsion 1 PE 1, DVT 1
Walker[44] (2002)	400	16.7	84	79	64	Hysterectomies for infection 3 Amenorrhoea 26 Fibroid expulsion 9 Chronic vaginal discharge 13
Pron[41] (2003)	538	3	83	77	42	Amenorrhoea 21

PE, pulmonary embolism; DVT, deep vein thrombosis.

report remarkably consistent results. UAE relieves fibroid-related symptoms in the vast majority of patients.[12,39–44] Menorrhagia is controlled in 85–95% of patients, and bulk-related symptoms are controlled in 70–90% of patients. Symptom recurrence in the short term appears to be low.

There have been a number of comparative studies between UAE and other procedures. These include a retrospective comparison of UAE and myomectomy at a single teaching centre[45], a small single-centre randomized trial of UAE and hysterectomy[46], and two large prospective cohort studies comparing UAE with myomectomy.[47,48] All show similar results and support the findings from the case series (Table 3).

High-quality Level 1 evidence has only become available recently in the form of two randomized trials[2–6] comparing UAE with hysterectomy. Recently, a small ($n = 30$ in each group) randomized trial has compared myomectomy with UAE[49], but as myomectomy is the main surgical comparator which preserves the uterus, a major RCT is required. A pilot trial has been completed at the authors' institution (FUME – Fibroids of the Uterus; Myomectomy vs Embolization), and analysis of the results is in progress.

The results of recent trials are summarized below.

REST trial (Randomized controlled trial of Embolization vs Surgical Treatment for fibroids)

This was a pragmatic, multicentre, Government-funded randomized controlled trial comparing UAE and surgery (hysterectomy or myomectomy) in women with symptomatic uterine fibroids. The primary endpoint was quality of life at 1-year follow-up as measured by the Medical Outcomes Study 36-item Short-Form General Health Survey (SF-36). The initial power calculation was for 200 patients (90% power to detect a 10-point change in SF-36). One hundred and fifty-seven patients were recruited, with a reduction in power to 80%. Secondary outcomes were Euro-QOL, hospital stay, 24-h pain score, return to normal activities, symptom score, complications and need for further invasive treatment. A health economic analysis was also performed. One hundred and six patients underwent UAE and 51 underwent surgery (43 hysterectomy, eight myomectomy).

There was no difference in the mean SF-36 scores between the two groups at 1 year. There was a highly significant reduction in hospital stay and 24-h pain score, and an earlier return to daily activities with UAE. There were 50 minor complications in 36 patients (34%) in the UAE group, and 16 minor complications in 10 patients in the surgery group (20%). The most common minor complications in the UAE group and the surgery group were postembolization syndrome (52%) and sepsis (25%), respectively.

There was only one major complication in the UAE group during the initial hospital admission compared with eight in the surgery group. However, 12 major adverse events were documented in the UAE group in the first year, compared with two in the surgery group. This equates into a major adverse event rate within the first year of 12% in the UAE group compared with 20% in the surgery group ($P = 0.22$). Within the UAE group, complications classed as major included vaso-vagal attack and two cases of breast cancer, in addition to expulsion of infarcted fibroids. One patient (1/95) failed to resume menses in the UAE group compared with none of the eight women who underwent myomectomy.

Table 3. Results of comparative studies of uterine artery embolization (UAE) vs hysterectomy/myomectomy.

Reference	*n* (UAE/ hysterectomy or myomectomy)	Study type	Menorrhagia improvement	Hospital stay	Complications	Quality of study
Razavi[45] (2003)	67/44	Retrospective observational UAE vs myomectomy	92% for UAE vs 76% myomectomy. Bulk symptoms −64% improvement with UAE vs 91% for myomectomy	UAE 0 days vs 2.9 days for myomectomy. Return to activities 8 days for UAE vs 36 for myomectomy	At least one complication in 25% after myomectomy vs 11% after UAE ($P < 0.05$)	Retro-spective
Pinto[46] (2003)	40 /20	RCT UAE vs hysterectomy	31/36 = 86% UAE	4 days shorter with UAE, $P < 0.001$	25% minor complications after UAE vs 20% major complication rate after myomectomy	Small numbers with significant cross-over between groups
Goodwin[47] (2006)	149/60	Prospective multicentre cohort vs myomectomy	No significant difference	UAE 1 day vs 2.5 days myomectomy. Return to work 10 days for UAE vs 37 days myomectomy	Less adverse events with UAE	Assessment by validated questionnaire, non-randomized
Mara[49] (2006)	30/33	RCT UAE vs myomectomy	Lower, non-significant reduction in relief of symptoms for UAE	Significant reduction in hospital stay and return to activities	Higher re-intervention rate for UAE.No difference in complications	Small study
Siskin[48] (2006)	77/69	Prospective multicentre cohort vs myomectomy	Reduction in tumour-related symptoms 88.3% for UAE vs 75.4% for myomectomy. Median UFS-QOL score higher after UAE ($P = 0.041$) at 6, 12 and 24 months		42% in myomectomy group vs 26% in UAE group ($P < 0.05$)	UFS-QOL used. Non-randomized

EMMY[3] (2006)	88/89	RCT vs hysterectomy	No significant difference in symptomatic improvement (SF-36). Technical failure in 17.2%, hysterectomy in 23.5% of UAE group at 2 years	Highly significant reduction in hospital stay, return to daily activities and 24-h pain score with UAE	4.9% major complications in UAE group vs 2.7% in hysterectomy arm. Higher re-admission rate after UAE	High technical failure rate — multicentre, different levels of expertise, ?small uterine arteries in this population
REST[2] (2006)	106/51	RCT vs hysterectomy (or myomectomy in eight)	No significant difference in mean SF-36 scores at 1 year. Ten underwent repeat intervention in UAE group in the first year	Highly significant reduction in hospital stay, return to daily activities and 24-h pain score with UAE	12% (9/106) major complications in first year in UAE group vs 20% in hysterectomy group — includes breast cancer ($n = 2$) and expulsion fibroids in UAE group	RCT
HOPEFUL[50,51] (2007)	649/459	Retrospective cohort study	95% experienced relief of symptoms in hysterectomy group vs 85% after UAE ($P < 0.0001$), although more women would recommend UAE to a friend		Less complications after UAE (19 vs 26%, $P = 0.001$), 23% required further treatment for fibroids after UAE (mean FU = 4.6 years)	Retrospective study

RCT, randomized control trial.

The technical failure rate for UAE was 3.0% (3/101). Within the first year, 9.4% (10/106) of women in the UAE group required re-intervention. Two underwent hysterectomy during their hospital stay due to technical failure of UAE, four underwent subsequent hysterectomy, and four underwent repeat UAE. Economic analysis of total costs over the first year calculated the cost of those randomized to UAE as £1751 compared with £2702 for those randomized to surgery.

The REST trial demonstrated that UAE is a safe and effective alternative for women not wishing to undergo surgery. The faster recovery time needs to be balanced with the need for re-intervention for persistent symptoms at around 10% at 1 year. The incidence of complications was similar in both groups, although the temporal profile was different, with the majority of complications following UAE seen following discharge.

EMMY trial (EMbolization vs hysterectoMY for symptomatic uterine fibroid disease)

This was a prospective randomized, multicentre trial, designed to assess non-inferiority of UAE compared with hysterectomy with 2-year follow-up. The primary endpoint was the prevention of hysterectomy in 75% of cases. Secondary endpoints included hospital stay, complications/re-interventions, reduction in fibroid volume, quality of life (SF-36) measures and costs. There were 177 patients, 88 of whom were randomized to embolization and 89 were randomized to hysterectomy. Nineteen of 81 (23.5%) patients underwent hysterectomy after embolization at 2 years (including four initial complete technical failures) which, according to the study definition, concludes that UAE is non-inferior to hysterectomy. There were no significant differences in improvement compared with baseline in pain and bulk-related symptoms.

Bilateral failure of UAE occurred in four patients (4.9%) and all required hysterectomy. Unilateral UAE was achieved in 10 (12.3%) patients. Re-interventions other than hysterectomy occurred in four patients: two hysteroscopic procedures for removal of necrotic fibroid tissue, one incisional hernia repair following hysterectomy and one diagnostic hysteroscopy. Therefore, the total re-intervention rate following UAE in this trial was 28.4% (23/81). In the surgical arm, six (8.0%) further re-interventions were required following hysterectomy: four laparoscopies/laparotomies for pain, one incisional hernia repair and one repair of vesico-vaginal fistula.

Previous uncontrolled series report hysterectomy rates between 1.5 and 4.5%. Pinto et al[46] found a clinical failure rate of 14%, with three of 40 (7.5%) of patients requiring hysterectomy. There are a number of possible explanations for the low rate of efficacy of UAE in the EMMY trial, including severity of presenting symptoms and the high technical failure rate. This may be due to the multicentre design of this trial, including sites relatively inexperienced in the technique.

The EMMY trial showed no significant difference in the major complication rate for each technique (4.9% in UAE arm vs 2.7% in hysterectomy arm) and no difference in the minor complication rates (64.2% vs 56.0%, respectively). UAE patients were re-admitted more often following treatment, but hospital stay was significantly shorter in UAE patients (mean 2.5 vs 5.1 days, $P < 0.001$). UAE patients returned to daily activities more quickly, and pain was less severe following UAE in the first 24 h. Thus, allowing for the lower efficacy rate in this trial, the reduction in pain, shorter hospital stay and faster return to daily activities demonstrate that UAE is a serious alternative to hysterectomy.

HOPEFUL trial (Hysterectomy Or Percutaneous Embolization For Uterine Leiomyomata)

This study[50,51] was a retrospective cohort study looking at outcomes following hysterectomy and UAE in the UK. Data were collected from 459 women who had undergone hysterectomy and 649 women who had undergone UAE in the preceding 7 years. Ninety-five percent of women experienced relief of symptoms in the hysterectomy group compared with 85% after UAE ($P < 0.0001$). Fewer complications were seen after UAE (19 vs 26%, $P = 0.001$). Twenty-three percent of women required further treatment for fibroids after UAE with a mean follow-up of 4.6 years. An interesting observation was that fewer complications were seen in patients receiving antibiotics prior to UAE, but the authors concluded that this did not imply causation.

Economic analysis demonstrated that UAE was less expensive than hysterectomy (£2536 vs £3282), even when costs of subsequent re-intervention following UAE were taken into account. Overall, quality adjusted life-years were not significantly different between the two groups, although they did become so when the value of retention of the uterus was factored into the calculations.

LONG-TERM OUTCOMES

There have been three recent reports of prospective studies assessing outcomes of UAE at 5-year follow-up. Spies et al[52] reported outcomes on a cohort of 200 patients. Initial symptom improvement was seen in 87% at 1 year, reducing to 85%, 83%, 79% and 73% at annual intervals up to 5 years of follow-up. Subsequent major re-interventions including hysterectomy ($n = 25$), myomectomy ($n = 6$) or repeat UAE ($n = 3$) were required in 20% of cases.

Katsumori et al reported 5-year outcomes in 96 patients.[28] Follow-up at 4 years was available for 49 patients, and 16 patients at 5 years. Symptom control was reported at 3, 4 and 5 years at 89.5%. Treatment failures remained constant at 12.7% at 3 years of follow-up, and no increase in this rate was seen at 4 or 5 years.

Walker and Barton-Smith[53] reported outcomes from a cohort of 258 women treated 5–7 years previously. One hundred and seventy-two (67%) women responded to a questionnaire at this time. Seventy-five percent of women had experienced a return to normal or an improvement in menstrual flow. Fibroid-related symptoms were improved in 80% of women. Satisfaction rates were high, with 88% of women satisfied 5–7 years following treatment. Twenty-eight (16%) women underwent additional interventions: nine hysterectomies, six myomectomies, nine hysteroscopic resection of fibroids and three hysteroscopy for vaginal discharge.

The results from all these studies demonstrate that the majority of women will have sustained symptom control following UAE.

RECURRENCE FOLLOWING UAE

Hysterectomy is the only definitive cure for symptomatic fibroids. In women wishing to retain their uterus, fibroid recurrence may occur following myomectomy or UAE. A study of long-term imaging and outcomes demonstrated that incompletely infarcted fibroids are a cause of treatment failure.[18] A study of cases ($n = 24$) of repeat UAE[54] found that most cases had a combination of uninfarcted fibroids from the initial

procedure and new fibroids. In this study, two patients had new fibroids as the only apparent cause of recurrent symptoms.

A number of studies have identified large dominant fibroid volumes as being more likely to recur in the long term.[52,55,56] However, a study by Marret et al[55] found that multiple fibroids are predisposed to recurrence, whereas the opposite finding (fewer, larger fibroids) was found in the registry data.[56] At present, there are no reliable data on predictors of outcome based on fibroid size, number and location.

SAFETY

The published literature suggests that embolization for control of postpartum or post-myomectomy haemorrhage does not interfere with uterine function, ovarian function or fertility.[57] Regarding embolization specifically for fibroids, hundreds of cases have been published in series of varying sizes. Three series alone report an aggregate of over 1200 patients. All these series demonstrate peri-procedural complication rates in the range of 1–4%, with most of the complications being minor. While there have been severe complications after UAE[58–75], they have been rare. Significant or severe complications, including 30-day mortality, are less common after UAE than surgery[76,77] (see Table 3).

One major complication specifically related to UAE is uterine sepsis which may require hysterectomy. This complication is fortunately rare and there is no real predictor for its occurrence. Postembolization syndrome is common and will usually settle with conservative measures. Following embolization, submucosal fibroids may slough and be passed vaginally[78,79], or, if large, need extraction with hysteroscopy.[80] Expected outcomes (CIRSE Quality Improvement Guidelines) and complication rates are summarized in Tables 1 and 4. Contra-indications to UAE are summarised in Table 5.

OVARIAN FUNCTION

Embolic material can be found histologically in the ovary following UAE.[81] Early studies of ovarian function after UAE found that transient or permanent amenorrhoea developed in 14% (mostly $>$ 45 years of age) of women.[82] The impact of UAE on ovarian function and subsequent fertility on younger patients is less well known. Pron et al[41] found a 3% rate of amenorrhoea in patients under 40 years of age in their large multicentre observational study. Other smaller studies have shown no significant rise in follicle-stimulating hormone (FSH) on day 3 or menstrual disturbance in younger women undergoing UAE[83–85], although the overall numbers have been small. Ovarian

Table 4. Complication rates for uterine artery embolization (CIRSE Quality Improvement Guidelines).

	Reported rate (%)	Suggested threshold (%)
Transient amenorrhoea	5–10	10
Permanent amenorrhoea $>$ 45 years	7–14	15
Permanent amenorrhoea $<$ 45 years	0–3	3
Transcervical fibroid expulsion	0–3	5
Non-infectious endometritis	1–2	2
Endometrial or uterine infection	1–2	2

Table 5. Contra-indications to uterine artery embolization.

Absolute contra-indications	Relative contra-indications
Viable pregnancy	Coagulopathy
Active infection	Severe contrast reaction
Suspected malignancy	Renal impairment
	Immunocompromise[120]
	Previous pelvic radiotherapy
	Partially treated pelvic infection
	Wish to maintain fertility[100,110,121]
	Concurrent use of gonadotrophin-releasing hormone[122]
	Adenomyosis[94,95]
	Pedunculated subserosal fibroid[123]

function does not seem to be differentially affected by hysterectomy, myomectomy or UAE.[86] Utero-ovarian anastomoses appear to be relatively common (44%[87]), and their presence has been associated with a rise in FSH levels and particle penetration histologically[88], although their overall significance is less clear.

ADENOMYOSIS

Adenomyosis is a condition characterized by the presence of ectopic endometrial glands and stroma in the myometrium. It is a common condition that presents in women during their reproductive life with pelvic pain and menorrhagia.

Symptoms related to adenomyosis are non-specific and similar to those from uterine fibroids. Hence, such women may undergo UAE. Treatment failure due to undiagnosed adenomyosis in centres where pre-procedure MRI was not available has been described in the initial experience of UAE for symptomatic fibroids. Goodwin et al[39] described three patients requiring hysterectomy after UAE for symptomatic fibroids, where postoperative pathological examination revealed undiagnosed adenomyosis. Some initial reports have demonstrated promising short-term outcomes[89–93], but longer-term outcomes are poor at 2 and 3 years.[94,95]

FERTILITY, FIBROIDS AND UAE

Although subfertility is multifactorial, fibroids have been proposed as a contributory factor (see chapter by Khaund and Lumsden for a detailed review of the impact of fibroids on reproductive function). There are a number of postulated mechanisms by which fibroids may impair fertility. Theories include mechanical blockage of the tubal ostia impairing sperm or embryo transport, abnormal vascularization, abnormal endometrial development, chronic intracavitary inflammation and increased uterine contractility.[96–98] Thus removal/shrinkage of the fibroid could theoretically improve fertility.

At present, guidelines suggest that UAE should be avoided in women wishing to retain future fertility due to the lack of data on outcomes. Data on pregnancy following UAE are in the form of case reports and limited case series.[99–106] Goldberg et al[107]

analysed pregnancy outcomes following treatment for fibroids by UAE or laparoscopic myomectomy. They concluded that those patients treated by UAE were at an increased risk of preterm delivery and malpresentation. However, there were significant demographic differences between the two groups in this analysis, with the group treated by UAE being significantly older and with larger fibroids.

There have been concerns of abnormal placentation following UAE. Low-lying placenta was seen in 26% in the initial series from Carpenter and Walker[99] of 26 pregnancies. Another study has reported two cases of placenta previa and one case of placenta accreta in their series of 18 patients.[101] Larger studies are needed to assess whether these results from small initial reports are more generally applicable. All studies to date have consistently shown an increased rate of caesarean section, from 50% to 90%. This may reflect increased vigilance in these potentially high-risk patients. The overall rate has fallen with increasing experience of managing these patients.

There is no evidence that previously fertile women become infertile following pelvic embolization for other indications.[57] Ultrasound and MRI following embolization demonstrate that there is normal revascularization of the normal myometrium with a normal appearance of the endometrium at 6 months.[108] This is felt to reflect the rich collateral supply within the pelvis. This is supported by the lack of evidence for any significant uterine ischaemia, as no elevation in serum markers of muscle ischaemia has been demonstrated following UAE.[109]

The effects of UAE on the strength and integrity of the endometrium are unknown, although histopathological studies on failed embolization have shown that the adjacent myometrium is spared.[81] However, there is a theoretical risk that UAE may increase the rate of uterine rupture, although there are insufficient data available to answer this question at present. Only two cases of a rupture following embolization have been reported previously.[101] One patient had two previous myomectomies prior to embolization. In the other case[100], the patient had had a previous normal live delivery by caesarean section following UAE.

At present, due to the lack of supporting evidence, UAE is performed for patients who wish to retain their fertility if they are thought unsuitable for myomectomy or hysteroscopic resection. These patients are therefore likely to have large and multiple fibroids with a pronounced effect on cavity distortion.[110] There are no data to directly assess whether treatment by UAE can increase fertility rates, or to compare fertility rates following myomectomy against UAE.

NOVEL THERAPEUTIC MODALITIES

Recently, preliminary safety and feasibility reports[111–113] of the use of high-intensity focused ultrasound to treat fibroids have been published. This novel technique allows non-invasive deep tissue ablation without harming overlying skin or organs. This has been combined with high-resolution MRI guidance[114–116], allowing accurate targeting and real-time thermal mapping. The disadvantage of this technique is that it is a focal treatment, rather than global as in UAE. The advantage is that it may be performed as a day-case procedure, without the requirement for introduction of any needle into the patient. Use of MRI guidance may be prohibitive in terms of cost compared with the established modalities.

Alternative methods of ablation include MRI-guided laser ablation[117] and radio-frequency ablation[118,119], which entail image-guided placement of a probe(s) into the fibroid. As with all the ablative techniques, they achieve focal treatment.

Practice points

- menorrhagia improvement is expected in 85–95% of patients following UAE
- improvements in bulk symptoms are seen in 70–90% of patients, although women with very large fibroids may find absolute volume reduction disappointing
- there is Level 1 evidence that UAE can achieve similar symptom control compared with hysterectomy
- overall costs are reduced compared with hysterectomy, even when costs of further intervention following UAE are included
- postembolization syndrome is common and should be viewed as an expected side-effect of the procedure rather than a true complication
- the majority of complications occur following discharge (expulsion of fibroids, uterine sepsis), and local protocols for the management of these patients should be established
- recurrence of symptoms is in the range of 15–20% at 5 years
- transient or permanent amenorrhoea is seen in 3–14% of women over 45 years of age
- the long-term effects of UAE on ovarian function and subsequent fertility are not known
- limited data are available regarding pregnancy outcomes following UAE
- current guidelines are that UAE should be considered in all women with menorrhagia and associated fibroids if they wish to retain their uterus and/or avoid surgery

Research agenda

- evaluate the long-term effect of UAE and myomectomy on ovarian function and fertility
- evaluate the long-term recurrence rates of fibroids after UAE or myomectomy
- evaluate the psychosexual impacts of UAE and myomectomy
- develop a staging system to stratify patients for prediction of outcomes

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