

Management of Fibroids for Patients desiring Pregnancy: UAE (Uterine Artery Embolization) versus Myomectomy-A review of the literature.

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Abstract

Background: A growing number of patients who desire future fertility, are presenting to IVF Units post-UAE (Uterine Artery Embolization) for fibroids. In most cases, the uterus remains unsuitable for gestation because of persistent fibroids, while others display endometrial or ovarian dysfunction. In all cases, these patients were advised by their gynaecologist to pursue UAE over myomectomy and referred for treatment.

Objective: To review the evidence regarding UAE versus myomectomy in women with fibroids who expressly seek future fertility.

Conclusions: UAE versus myomectomy for fibroids is associated with lower rates of pregnancy and livebirth with higher rates of miscarriage. UAE impairs ovarian reserve and is associated with significant post-intervention endometrial abnormalities. UAE offers no significant procedural risk reduction over myomectomy. In women with fibroids, expressly seeking future pregnancy, UAE should be reserved for women refusing or unsuitable for surgery.

Keywords: Uterine Artery Embolization (UAE), Myomectomy, Fibroids, Fertility.

Introduction

Uterine fibroids are the most common benign tumour affecting women. Lifetime prevalence is 50-60 %, rising to 70 % by age 50.[1] Management of symptomatic fibroids has traditionally fallen to surgical treatment, with medical management limited to 6-months due to the risks of osteoporosis.[2]

Fibroids and Fertility

Fibroids, except for sub-serosal location, are associated with lower pregnancy rates (RR = 0.697, P < 0.001) and higher miscarriage rates (RR = 1.678, P < 0.001). This includes intra-mural fibroids with no effect on the cavity. Sub-mucosal fibroids are associated with the lowest ongoing

In symptomatic patients, UAE vs hysterectomy offers comparable rates of satisfaction (78 % vs 87 %) for symptom relief.[3] It is controversial whether UAE should be offered to women still desiring future fertility. [4,5,6,7] It is about this group of women that this article is written.

Complication Rate associated with UAE and Surgery

UAE is seen as a means of reducing the surgical risk to patients. What is the evidence from RCT's?

Myomectomy vs UAE is associated with less early (15.9 % vs. 20.7 %), and late (8.1 % vs. 13.8 %) postprocedural complications.[5]

Hysterectomy versus UAE is showed fewer major complications: 2.7 % vs. 4.9 % (P-value = 0.68) and significantly fewer minor complications: 40 % vs. 58.0 %, RR= 1.45, (95 % CI: 1.04 – 2.02, P = 0.24).[11]

pregnancy rate (RR = 0.318, P < 0.001).[8] The pathophysiology of sub-fertility is related to endometrial receptivity and HOX gene expression [9], altered myometrial contractility and increased endometrial venous pressure.[10]

Uterine integrity following myomectomy remains a concern to gynaecologists for future pregnancy, especially in patients expressing the desire to deliver naturally.

In an unselected population, the prevalence of uterine rupture is 0.05 %, and 1.0 % following the previous caesarean section.[12] Meta-analysis shows uterine rupture in pregnancy following open vs. laparoscopic myomectomy remains low (0.4 % vs. 1.2 %, p = 0.119) while successful vaginal delivery in these groups is high 88 % vs. 93 %.[12]

UAE the Procedure

Uterine artery embolization was first described in the mid-'90s. The femoral artery is used as an entry site, to allow for catheterization of the uterine arteries and the injection of embolic particles: poly-vinyl alcohol

(PVA), PVA microspheres or gelatin-coated tris-acryl microspheres, which disrupt the blood supply of the fibroid (See figure 1 attached).

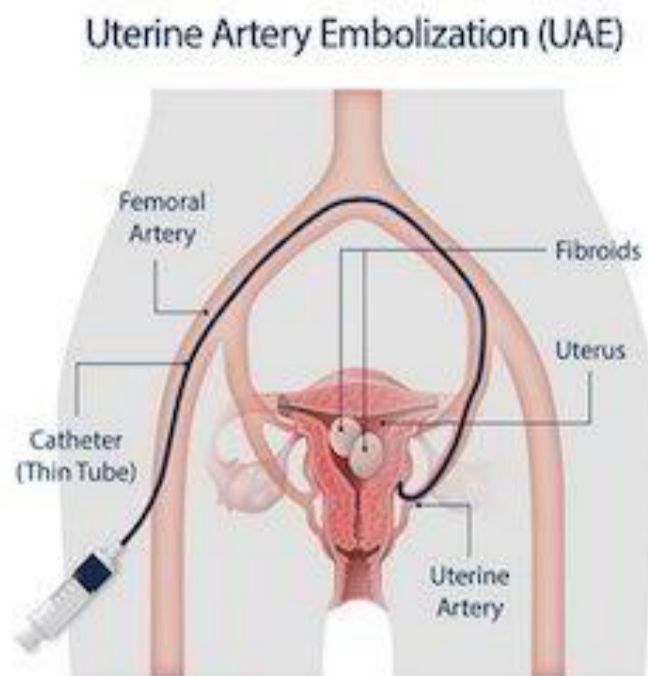


Figure 1

UAE and Ovarian Reserve

Fibroids derive their blood supply from both sides in almost all cases. Bilateral uterine artery embolization, where occlusion or marked reduction in blood flow in both uterine arteries is achieved, is considered a technical success. The recommended threshold for bilateral uterine artery embolization is 96 %.[4]

Angiography in patients undergoing UAE showed ovarian-uterine artery anastomosis in 21.7 %. The uterine artery was the major blood supply to the ovary in 6.6 % of patients.[13]

In patients undergoing hysterectomy following UAE, histology confirmed the presence of embolic particles in the fallopian tube or ovary in all patients with evidence of utero-ovarian anastomosis at the time of the procedure.[14] (See Figure 2 attached).

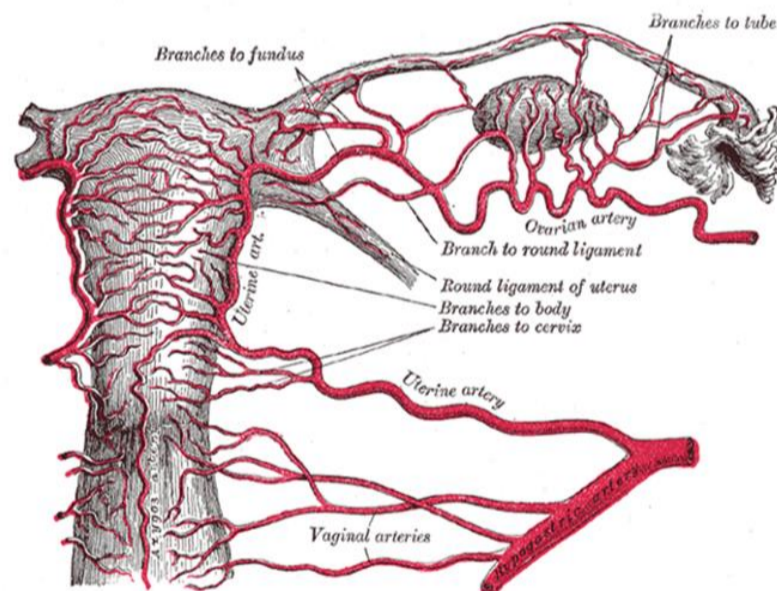


Figure 2

Analysis of AMH (Anti-Mullerian Hormone) and AFC (Antral follicle count) shows a reduction in ovarian reserve post-UAE. Women aged < 40 years show the greatest ability to recover, however, baseline levels of ovarian function are not recovered, with permanent deficit.[15] Up to 7 % of women develop permanent amenorrhoea following UAE. [16] Post-procedural ovarian reserve testing following UAE vs. supra-cervical hysterectomy in premenopausal women, showed the averaged percentage

changes in AFC and AMH, to be -63.4 % vs -8.4 % and -61.9 % vs -3.5 %, respectively. UAE is associated with significant ($p < 0.001$) deleterious changes in all measures of ovarian reserve.¹⁷ The reduction in ovarian reserve following UAE is more than that seen at hysterectomy.[18]

UAE and the Myometrium

UAE is associated with a 50 % volume reduction in most patients.¹⁹ Volume reduction is progressive, 46 %, 61 % and 66 % at 3, 6 and 12

months, respectively.[20] The relationship of volume to diameter is not linear, rather it is governed by the formula: $\text{Volume} = \frac{4}{3}\pi r^3$. This

implies a 50 % volume reduction of a fibroid does not translate into a 50 % reduction in diameter. If you have 3 fibroids of diameter 10, 8 and 5cm before UAE, and all undergo a 50 % volume reduction, you are left with fibroids of diameter 8, 6.4 and 4cm respectively.

UAE and the Endometrium

Hysteroscopy reveals endometrial abnormalities in 59.1% of women following UAE. This included tissue necrosis (40.9 %), intra-cavity

UAE and Pregnancy

When pregnancy outcomes are compared, UAE vs Myomectomy is associated with lower pregnancy rates (50% vs. 78%, $P < 0.05$), lower livebirth rates (19 % vs. 48 %, $P < 0.05$) and higher miscarriage rates (64 % vs. 23 %, $P < 0.05$).[5]

Women following UAE vs. Myomectomy have a RR = 2.22 (95 % CI: 1.11 – 4.44) not to get pregnant and a RR = 2.79 (95% CI:1.25 – 6.22) to abort.

Systematic review of UAE vs. Myomectomy showed higher miscarriage (27.4 % vs. 19.0 %, $P < 0.001$) and lower livebirth rates (60.6 % vs. 75.6 %, $P < 0.001$). [7]

Following UAE in women of average age 35.9, rates of miscarriage were 28 %, equivalent to women with untreated fibroids.[22]

Fertility Assessment before UAE

Fibroids often co-exist with other pathology, such that while 5-10 % of women present with infertility and fibroids, in only 1 - 2.4 % of cases, are the fibroids the sole cause of infertility.[25] Pre-intervention AFC or AMH levels provide only a prognostic measure of expected ovarian response to stimulation (egg number).

The age-associated embryo aneuploidy rates [26], and averaged percentage chance of LBR (live birth rate) per mature oocyte retrieved (MOR) need to be communicated to patients to place the egg number into context. In the general IVF population (ages 23 – 43 years), LBR / MOR = 3.8 %.[27]

Conclusions

Untreated fibroids reduce pregnancy rates and increase miscarriage rates. UAE for fibroids is associated with significantly lower pregnancy rates, higher miscarriage rates and lower live birth than if managed by myomectomy. Myomectomy offers acceptable uterine integrity in subsequent pregnancy and the ability for a natural delivery, with no significantly increased procedural complication rate over UAE. Fertility

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Randomized comparison of UAE vs. myomectomy showed a reintervention rate of 32.8 % vs 3.2 %, $P < 0.0001$. The main indication for surgical reintervention was the persistence of a large fibroid (> 5cm) at 6 months post-UAE. [5]

myoma protrusion (35.4 %), intra-cavity adhesions (10.2 %), and fistulae between intra-mural myomas and the cavity (6.3 %). [21]

Follow-up of 31 women of average age 37.3, post-UAE, all actively seeking pregnancy with normal ovarian reserve tests, showed a single pregnancy which ended in miscarriage after a total of 33.4 months. (This included the transfer of 22 embryos in own-egg IVF cycles and 8 embryos from donor-egg transfers). This equates to a monthly fecundability rate of 0.1 %, (95 % CI 0 – 0.3 %).[23]

The American College of Obstetrics and Gynaecology (ACOG) lists the express desire for future fertility as a relative contra-indication to UAE. There is a recommendation that patients be adequately counselled regards the reproductive implications before UAE.[24]

If considering fertility preservation prior to UAE, oocyte freezing places further demand on egg number. In comparison, to fresh oocytes, vitrified oocytes are associated with lower fertilization (77.9 % vs. 90.5 %, 95 % CI: 0.80 – 0.93), cleavage (90.0 vs. 99.2 %, 95 % CI: 0.87 – 0.96) and blastulation rates (34.8 % vs. 50.8 %, 95 % CI: 0.54 – 0.86), meaning less embryos from a given number of frozen eggs. [28]

Fertility assessment and discussion of its preservation fall outside the scope of the interventional radiologist and the generalist gynaecologist. Not involving a fertility specialist in the decision-making process around UAE in women desiring future pregnancy will ensure uninformed consent.

evaluation of a couple is complex and best performed at a fertility unit, without which the patient makes an uninformed decision. The desire for a future pregnancy is a relative contraindication to UAE for fibroids. Patients need to be well informed of the potential adverse effects of UAE and fertility outcomes.

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