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Preservation of Fertility after Uterine Artery Embolization: A Review of Pregnancy Following Non-Surgical Intervention for Leiomyoma

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Methods: This literature review focuses on studies published within the last ten years which report on pregnancies after UAE in women treated for uterine fibroids.

Results: Of the nine studies included, there are increased rates of spontaneous abortion, pre-term delivery, post-partum hemorrhage and abnormal placentation in a subset of the studies. These results might be due to UAE or may perhaps be explained by the advanced maternal age of the subjects, or other subfertility factors not addressed in the studies.

Conclusion: The effects of UAE on subsequent pregnancy are still unclear. The paucity of large randomized controlled trials and the small number of reported cases of pregnancy (less than 200) limits the quality of the evidence. Until larger randomized trials are completed comparing myomectomy and UAE, myomectomy will continue to be the first line therapy for women who intend to become pregnant.

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Preservation of Fertility after Uterine Artery Embolization: A Review of Pregnancy Following Non-Surgical Intervention for Leiomyoma

by

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A Clinical Graduate Project Submitted to the Faculty of the

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The effects of UAE on subsequent pregnancy are still unclear. The paucity of large randomized controlled trials and the small number of reported cases of pregnancy (less than 200) limits the quality of the evidence. Until larger randomized trials are completed comparing myomectomy and UAE, myomectomy will continue to be the first line therapy for women who intend to become pregnant.

Keywords: leiomyoma, uterine artery embolization, pregnancy, fertility.

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Table of Contents

List of Tables

List of Figures and Pictures

List of Abbreviations

UAE……..……...…Uterine Artery Embolization

UFE.....Uterine Fibroid Embolization

LUAO……..……...……Laparoscopic Uterine Artery Occlusion

Preservation of Fertility after Uterine Artery Embolization: A Review of Pregnancy Following Non-Surgical Intervention for Leiomyoma

Introduction and Background

Uterine fibroids are a common benign tumor in women which increase in incidence with age. It is thought that nearly 70% of Caucasian women can be affected by age 50, and they occur even more frequently and earlier in life in African American women.[1] Abnormal uterine bleeding, pelvic pain and bloating, and urinary frequency are some of the predominant symptoms of leiomyomas, and if bleeding is excessive, anemia can result. Hemorrhage, associated with hypervascularization, is the most common complication of leiomyomas.[2] A uterus affected by fibroids can be the size equivalent of a uterus at 20 weeks of pregnancy. Little is known about the pathogenesis of leiomyomas, but the condition is thought to be influenced by genetic predisposition, steroid hormones and growth factors. Over time, they will grow or shrink without intervention, and normally when hormone levels wane during menopause, they will shrink permanently.

Leiomyomas develop in three distinct regions of the uterus: the internal wall of the uterus (submucosal) where they can project into the intra-uterine space, within the muscle wall of the uterus (intramural or transmural), and on the external wall of the uterus (subserous). Intramural leiomyomas are the most common type of uterine fibroid. The majority of leiomyomas are asymptomatic or will present with mild symptoms and do not require intervention. Symptoms are classified into three categories: increased uterine bleeding, bulk related symptoms (pelvic pressure and pain) and reproductive dysfunction.[3] If symptoms are troublesome, therapy is guided by the size and location of the myoma, the nature of the symptoms, the patient's age, obstetric history, and reproductive plans.

Fibroids themselves can contribute to infertility through several postulated mechanisms, and they account for between 1% and 2% of all cases of infertility.[3] The location of the fibroid within the uterus, not its size, is thought to be the most important factor in terms of effect on fertility. Leiomyomas which distort the internal cavity of the uterus, either submucosal or intramural, are associated with poor implantation, growth of the placenta over the myoma itself, rapid growth of fibroids in early pregnancy, and an increase in uterine contractility.[4] It is also thought that fibroids may contribute to abnormal local endocrine patterns, chronic endometrial inflammation, and abnormal vascularization.[5] The course of pregnancy is also adversely affected by the presence of submucosal or intramural fibroids, and is influenced by both size and location. There is an increased risk of spontaneous abortion, first-trimester bleeding, breech presentation, c-section and placenta abruptio, all of which are worsened when the placenta is positioned over the myoma within the uterus.[3]

Treatment for leiomyomas consists of several modalities: medical hormone treatment, which seeks to shrink the fibroid in size, surgery (myomectomy, hysterectomy), which is accomplished through several different approaches and seeks to excise the fibroid(s), and uterine artery embolization, which cuts off blood supply to the fibroid, resulting in infarction of the tissue. Myomectomy is the most common treatment for leiomyomas, but hysterectomy is considered the definitive treatment. Fifty percent of hysterectomies in African American women are due to leiomyoma.[3] If malignancy is suspected, surgery is indicated. Other possible treatments include endometrial ablation, surgical uterine artery obstruction, magnetic resonance-guided focused-ultrasound surgery, and myolysis.

Therapy choices are determined by the size and type of fibroid, whether subserosal, intramural or submucosal. Myomectomy is the only therapy appropriate for subserosal fibroids. Uterine artery embolization (UAE) is not recommended in subserosal fibroids due to the risk of detachment from the uterus. If the fibroid is less than 10 cm in diameter, and is

either intramural or subserosal, then laparoscopic myomectomy is possible. Open (abdominal) myomectomy is needed if there are multiple myomas or if the diameter is greater than ten centimeters. Myomectomy is associated with a small increased risk of uterine rupture during pregnancy, particularly if the uterine cavity is entered during the procedure, or if the practitioner has limited experience with laparoscopic suturing. Hysteroscopic myomectomy is the approach used for submucosal fibroids.[1]

When preservation of fertility is a concern for the patient, there are limited treatment choices. Hormonal therapy is not appropriate during conception and pregnancy. Hysterectomy is not an option. Although myomectomy is the standard of care, there is an increased risk of miscarriage, uterine rupture, adhesion formation, intra-operative hysterectomy due to hemorrhage, and fibroid recurrence.[1] For women with cavity-distorting fibroids, myomectomy increases conception rate, and the patient can attempt conception relatively soon after the procedure.[3] Uterine artery embolization is an emerging alternative to myomectomy, but there is limited information as to fertility, with fewer than 200 documented cases of pregnancy following UAE.

Uterine Artery Embolization

Embolization as a general obstetric procedure was first developed in the 1970s as a means of achieving hemostasis in patients with post-partum hemorrhage. By 1995, uterine artery embolization was being explored as a less invasive alternative to surgery for leiomyomas.[2] Arteriography allows the radiologist to visualize the pelvic arterial tree and identify areas of tumor hypervascularization. The patient is sedated and given prophylactic ceftriaxone beforehand; the procedure takes between 60 and 90 minutes, and no sutures are required. Introducing particulate material into the arteries supplying the leiomyoma produces ischemic change to the fibroid without permanently damaging the uterus itself. As the fibroid dies, the blood supply to the uterus is maintained through collateral vascularization.[6]

An interventional radiologist, well-trained in the technique, performs the procedure. A catheter is passed into the common femoral artery (usually the right) and then into the contralateral internal iliac artery, and finally into the uterine artery. Particles of either polyvinyl alcohol microspheres (500-700 micrometers), gelatin-coated tris-acryl microspheres, or other embolic materials are administered until occlusion is achieved in the appropriate vessels. The ipsilateral uterine artery can be catheterized and embolized without withdrawing the catheter through the use of the Waltman's loop, a radiologic technique developed in the 1970s.[7] Occasionally, the arteries will spasm during the procedure, and this is relieved with antispasmodic boluses delivered intra-arterially.[7]

The risks of UAE include: pelvic pain, hematoma at the injection site, need for re-intervention (1 – 2.5%), chance of diminished ovarian reserve (1%),[8] ovarian failure with amenorrhea (as high as 15%, but primarily in women over age 45),[9] hemorrhage (0.15--0.75%), and life threatening event (0.2 -- 0.5%).[3] The rate for major complication is between 1 and 5%, which is comparable to both myomectomy and hysterectomy. The most common major adverse event is readmission to the hospital because of inadequately controlled post-procedural pain. There have been four reported deaths from complications after UAE, out of over 40,000 treated (this figure includes indications for UAE other than fibroids, such as post-partum hemorrhage, adenomyosis, etc). Two of these deaths were sepsis related, and two were due to pulmonary embolism.[6] Post Embolization Syndrome (PES) is a well-documented cluster of symptoms including pain, fever, malaise, nausea and vomiting. This phenomenon was more frequently seen in the past than it is today, mainly due to technical improvements to the procedure.[6]

There are certain situations where UAE would be contraindicated for leiomyoma. If a patient is immunosuppressed, suffers from severe vascular disease or has an allergy to contrast

media, they would not be a candidate for UAE. Other contraindications include pregnancy, malignancy or infection.[3]

One study reported that 1.1% of UAE patients go on to require a second surgical intervention within 30 days.[9] These re-interventions can include repeat embolization, myomectomy, hysterectomy, dilation and curettage, and oophorectomy. These risks are comparable to those of myomectomy.[3]

UAE is successful in relieving symptomatic menorrhagia in 85% of cases, and improving pelvic discomfort secondary to myoma compression in between 30-60% of cases.[9] Post-procedural patient satisfaction is comparable to myomectomy. Discharge and/or expulsion of the infarcted fibroid tissue can occur in either procedure.[3]

For patients who are pursuing treatment for leiomyoma, there are some factors that drive the choice towards UAE and away from myomectomy. Patients who wish to avoid intra-abdominal surgery do well with UAE, as do patients who have undergone prior myomectomy. Previous abdominal surgery can leave extensive pelvic adhesions making subsequent myomectomy technically difficult. Patients with large fibroid uteri (greater than 20 weeks gestational size) are at increased risk for hemorrhage or hysterectomy and can benefit from a 2 step treatment. Initially UAE is performed to decrease uterine volume, followed by myomectomy.[10] A main advantage of embolization over myomectomy rests in the fact that in one procedure, all fibroids are treated. Myomectomy treats only individual fibroids, and regrowth of fibroids after surgery is common.[11]

As described in Up To Date, "the relationship between leiomyomas and infertility is controversial. Couples should complete a full infertility evaluation before addressing the role of leiomyomas in their infertility."[3] They recommend that women with asymptomatic myomas not postpone pregnancy, because both myomas and advancing maternal age can adversely affect fertility. If the infertile patient has asymptomatic myomas that alter the shape of the

uterine cavity, however, myomectomy is recommended. There are several retrospective observational studies which have concluded that removal of obstructing fibroids improves fertility.[5] If the fibroids do not affect the uterine cavity, other causes of infertility should be addressed before pursuing myomectomy.[3]

Managing fibroids during pregnancy can be a problem in itself. Some fibroids increase in size during pregnancy, and large fibroids (>3 cm) are associated with adverse pregnancy events. Surgical removal of fibroids during pregnancy is to be avoided due to risk of hemorrhage. If the patient has had prior myomectomy or UAE, Up To Date recommends managing them as a prior cesarean patient.[3]

Purpose of the study

The purpose of this study is to clarify the effectiveness of uterine artery embolization in fertility preservation for women who undergo treatment for leiomyoma. Among women whose fertility is a concern, current treatment guidelines for leiomyoma recommend myomectomy.[3] UAE is an alternative with shorter hospital stays, shorter recovery periods, and comparable rates of symptom reduction. It is also a significantly less invasive procedure which makes it more appealing to patients. Worldwide, estimates of UAE are around 40,000 for all indications, but the majority of these have been performed on women who are past their childbearing years.[6] The aim of this literature review is to analyze and update information concerning this procedure with respect to fertility preservation. There are fewer than 200 reported cases of pregnancy after UAE, and these deserve analysis in the interest of guiding therapeutic recommendations for women with leiomyoma who still wish to have children.

Methods

A comprehensive literature search was performed using the keywords: leiomyoma, uterine artery embolization, pregnancy, fertility, embolization – therapeutic, leiomyoma – therapy, fertility, uterine neoplasms – therapy, and fibroid. Medline, CINAHL, Evidence-

Based Medicine Review Multifile, and Web of Science were the databases used. Multiple databases were used in the interest of thoroughness, and literature was reviewed and included only if it held relevance to the topic. As a procedure, UAE was only first described in 1995, and fertility results prior to 2000 are few. In studies with serial results released every few years concerning a given patient population, only the most recent published articles were chosen in the interest of being as current as possible. The results were then compiled and analyzed. The inclusion criteria were English language articles that addressed issues of fertility after UAE in premenopausal women. Papers were excluded if UAE had been used to treat conditions other than uterine fibroids (such as adenomyosis, uterine arteriovenous malformation, gestational trophoblastic disease, placenta accreta, etc). Studies which focused only on outcomes of UAE not related to fertility, were likewise excluded. The articles were reviewed and graded on the following criteria: randomization, control group/intervention group, sample size, population, and outcomes reported. Stronger studies gave details of maternal age, pregnancy history, time from UAE to pregnancy, outcome of pregnancy, gestational time, infant weight, and birth complications.

Results

A total of 9 articles are included, with publishing dates ranging from 2000 to June 2009. Publishing dates are generally several years after the date of embolization. The time needed for a patient to conceive and deliver imposes a long timeline on this research, and several of the studies plan to publish as more pregnancies occur. There was only one prospective randomized study (Mara et al, 2008), which compared UAE and myomectomy in randomized groups; the rest were retrospective or prospective studies. One study compared patients receiving UAE with patients receiving laparoscopic uterine artery obstruction (LUAO), a procedure which cuts the artery medial to its origin from the hypogastric artery after either ultrasonic or bipolar

cauterization (Holub et al), but it was not randomized. There were no studies comparing UAE with a group receiving no intervention.

Mara et al (2008) examined the reproductive results in a study which randomized 121 women with "fibroids and unfinished reproductive plans" to either UAE (n=58) or myomectomy (n=63) between 2001 and 2005.[12] Out of 17 pregnancies in the UAE group, 5 were completed at term, and the infants were of normal size. The spontaneous abortion rate in the UAE group was 64% compared to 23% in the myomectomy group. 42% of the participants in the study had another subfertility factor other than myoma, making the results difficult to interpret. There was one instance of postpartum hemorrhage, but no other complications were recorded.[12]

Firouznia et al (2009) reported on 15 pregnancies in Iran after UAE for uterine fibroids. Of the 23 women treated who were seeking to become pregnant, 14 succeeded, with one subject being pregnant twice. Two miscarriages occurred, both in women 41 years of age, and one infant was low birthweight, but this conception was only 2 months after UAE. All 13 births were by ceasarian delivery. There was one case of postpartum hemorrhage caused by retained placental tissue.[13]

Holub et al (2008) did a prospective cohort-controlled study in the Czech Republic which compared pregnancies after two different procedures for fibroids – UAE and LUAO (laparoscopic uterine artery occlusion). In the UAE group, there were 28 pregnancies in 20 women after a total of 112 underwent UAE, and 38 pregnancies after 225 LUAO procedures. Although total group numbers were small, they found a 56% rate of spontaneous abortion in the UAE group, compared to 10.5% in the LUAO group, and both groups had increased risk of preterm birth and c-section. Laparoscopic uterine artery occlusion is performed through the abdominal wall, placing vascular clips, sutures or using bipolar coagulation and working

external to the arteries, as opposed to working intravascularly to embolize the arteries as is done in UAE.[14]

Pabon et al (2008) reported on 11 pregnancies in 10 women after UAE in 57 women wishing to preserve fertility. In this group, where there had been no prior births, there were 8 live births, and 3 spontaneous abortions. Four were delivered vaginally, and four by c-section. Seven infants were of normal size and were delivered at term, 1 macrosomic infant was born pre-term at 33 weeks.[15]

Walker et al (2006) report in the largest study to date, on 56 completed pregnancies after 1200 UAEs with one interventional radiologist performing all the procedures between 1996 and 2005. There were 33 successful live births in 27 different women in this UK study. Spontaneous abortions occurred in 30.4% of these pregnancies, and there were increased rates of c-section, preterm delivery, and postpartum hemorrhage compared to the general obstetric population. Nineteen of those who became pregnant had prior subfertility, and there were 35 first conceptions in this group. 81.8% of deliveries were at term, the rest were pre-term. The average maternal age was 37.4 in this study.[16]

Pron et al (2005) report on 24 pregnancies in 21 different women after 555 underwent UAE in Canada. There were three cases of abnormal placentation (two with placenta previa, one with partial accreta) and another with placenta membranacea with accreta which resulted in cesarean hysterectomy. There were three postpartum hemorrhages, all secondary to placental abnormalities, and four small for gestational age infants (less than 5th percentile), two of which were complicated with gestational hypertension.[17] This study compared embolization and myomectomy, but the differences between the groups were found to be not statistically significant in a review article published in 2006.[10]

Price et al (2005) contributed 2 cases of pregnancy after UAE in the UK, both c-section deliveries, one due to obstructing fibroids and one due to breech presentation.[18]

McLucas et al (2001) report on 17 pregnancies in 14 women after UAE in 400 women, 139 of whom expressed an interest in future fertility. Women who were over 40 were excluded from the group included in the study, an unusual precedent in studies like this. There were 10 deliveries, and two on-going pregnancies at the time of publication.[8]

Ravina et al (2000) report on 12 pregnancies in 9 women after UAE in a very early study reporting on pregnancy after UAE in France. The mean maternal age was 38.[19]

From Table 2 (page 23), it is evident that compared to the general obstetric population, risks are elevated in pregnancy after UAE for spontaneous abortion, cesarean delivery, pre-term delivery, and postpartum hemorrhage. Malpresentation is not well reported in the literature, except when rates are high. There was one study which had increased rates of small for gestational age infants. Mean maternal age in these studies is higher than the general obstetric population, ranging from 32.2 to 38.5 compared to 27.4. The sum total of pregnancies after UAE included here is 185, and the sum total of deliveries is 106. Spontaneous abortion, elective termination, ectopic pregnancy, and pregnancies that were ongoing at the time of study publication account for the difference in these figures.

Discussion

The primary goal of this study was to identify trends in fertility after uterine artery embolization based on a review of current medical literature. This discussion will focus on the outcomes reported, but due to the low quality of evidence, a limited number of reported cases, and a lack of homogeneity among study participants, no statistically significant trends are identified.

The rate of spontaneous abortion in patients after UAE is elevated across the board in these studies, ranging from 0 – 56%. Interpreting these results is difficult, especially given the other possible factors contributing to spontaneous abortion. The risk of spontaneous abortion is known to increase with age, from 9-17% in women between 20 and 30 years of age, to 20% at

age 35, 40% at age 40, and 80% at age 45.[20] The average maternal age in the included studies ranges between 32.2 and 38.5. Given the demographics of the population studied, the results are less surprising.

In addition to maternal age, fibroid disease of the submucosal type as an independent disease entity increases the risk of spontaneous abortion. It has been found that fibroids distorting the uterine cavity are more apt to produce this effect.[21] The authors in the group reporting the highest rate of spontaneous abortion (56%) noted that the extent of fibroid disease, and the quality of myometrial perfusion are key factors in future pregnancies.[14] These factors are not controlled for in these studies, and are therefore confounding variables.

The rate of cesarean delivery was also elevated across all the studies (47-100%) when compared to the normal obstetric population (31%). There are several factors which play into this finding. Current recommendations regarding pregnancy management after either UAE or myomectomy suggest managing this population in the same way as patients with prior cesarean section.[3] Surgical myomectomy can weaken the uterine wall in the areas where fibroids are removed, a situation which is comparable to prior cesarean where the uterine wall is weakened at the incision site and confers an increased risk of rupture with subsequent pregnancies. Given this obstetric strategy after myomectomy, it is appropriate that a similarly conservative approach is used in pregnancies after UAE, which is a relatively new and untried therapy. It is therefore accurate to say that cesarean section often follows UAE, but is not caused by it.

Pre-term delivery appears to be nearly consistent with the normal obstetric population, as does the frequency of small for gestational age neonates. These findings are reassuring given early fears that vascular supply to the developing fetus would be inadequate after embolization. Neonates who were not premature met the CDC's averages for birthweight. Three of the nine studies showed elevated rates of preterm delivery, two matched the normal rates, and there were 4 that fell below average.

Postpartum hemorrhage is elevated (between 0 and 20%) in some of the studies, when compared to the normal obstetric population (8%). It is worth noting that while these studies report on a given number of pregnancies, many do not progress to birth. Therefore, in a study such as the Mara study with 26 pregnancies, there were only 5 births, and of these, there was one person with post-partum hemorrhage, which as a percent is expressed as 20%. The Holub study also reports a 20% rate, but this represents only two out of ten deliveries. Four of the studies report a 0% risk of hemorrhage, but clearly the numbers are too small to be conclusive.

Malpresentation and abnormal placentation are phenomena not well reported in the literature reviewed, except in studies where they were found to be noteworthy. Many of the studies simply do not report on them. Conclusions are not possible because of the small numbers of patients, and the inconsistency in the reporting on these variables. Furthermore, as Holub notes, there are other "known risks for abnormal placentation [which] include advanced maternal age, multiparity, smoking, and prior cesarean delivery."[14] The Pron study makes the recommendation that placental status is closely monitored in these patients as a general precaution.[17]

All of these reported complications discussed above have multiple possible causes, UAE being only one. Studies have shown that fibroid disease itself increases the risk of certain pregnancy complications even in untreated disease. Risks of placental abruption, breech presentation, dysfunctional labor, and an increased risk of cesarean delivery have been documented, and risks are greatest when the placenta is implanted over the myoma within the uterus.[3] Whether this relationship is causative, or the result of confounding factors is still unknown. Thus, comparing pregnancy outcome after UAE to the general obstetric population, does not take into account the effects of the underlying disease.

Limitations of Study

Although pregnancy provides a good measurable endpoint and a strong gauge of fertility, the pregnancy results in these studies are not interpretable in terms of pregnancy rate. In studies of fertility and infertility, pregnancy rate is defined as the success rate for pregnancy, expressed as a percentage of all attempts that lead to pregnancy per menstrual cycle. We do not know what future pregnancies these patients might achieve, nor how many women actually tried to become pregnant between the date of their embolization and the publication date of the study. A subset of the articles mention how many subjects stated an interest in having a baby at some point in the future, and still fewer address the number of study participants who were actively trying to conceive. To measure fertility, given these constraints, is problematic: we can say pregnancy is possible after UAE, but the data is insufficient to quantify in terms of fertility.

The lack of homogeneity among subjects is another problem for interpretation. Many of the women in these studies are already burdened with subfertility factors other than myoma.[12] The degree of fibroid disease, prior obstetric history, advanced maternal age, possible spousal infertility, etc, are not controlled for, and are therefore confounding factors.

The study sample sizes range from 2 to 56, with a total of 185 pregnancies and 106 deliveries reported. This number is lamentably small, and results in under-powered information, and limited statistical significance. The studies with only one exception are either prospective or retrospective cohort studies, generally Level II-2 evidence.

The Mara et al (2008) study done in Ireland, was the only randomized study which placed fibroid sufferers into either a myomectomy group or an embolization group. There were 40 pregnancies after 63 myomectomies, with a pregnancy rate of 63% compared with 26 pregnancies after 58 embolizations, and a pregnancy rate of 45%. The authors concluded that among women who plan to get pregnant shortly after their fibroid treatment, myomectomy is

the better procedure.[12] A post-procedural waiting period of 6 months to a year is recommended after UAE for women attempting to conceive in order to allow fibroids to shrink and the uterus to revascularize.[13]

Although leiomyoma are associated with between one and two percent of cases of infertility, there are no randomized controlled trials which demonstrate that myomectomy improves fertility in these women.[5] There are many retrospective observational studies which support this view, however. To properly analyze the effect of UAE (or myomectomy) on fertility, it would need to be compared to a control group, matched both in terms of age and extent of fibroid disease. Whether this type of study could attract participants is questionable in a randomized controlled trial. Women seeking help with fertility and significant fibroid disease are probably not willing to be left untreated in a control group. Another difficulty in conducting research is the inherent variability of fibroid disease: size, location and number of fibroids are interacting contributors to outcome. Matching patients in terms of these variables is difficult within the structure of research design.

Conclusion

Leiomyoma confer a fertility burden on the female population of childbearing age in and of themselves. Myomectomy is a procedure which, in select patients, decreases infertility, but it has a few grave risks which threaten fertility such as hemorrhage and hysterectomy. In choosing a treatment designed to improve fertility, the patient actually risks complete infertility. Finding alternative treatments for fibroids is clearly a valuable pursuit, but any new treatment must be measured against myomectomy, and proven to be as good or better. There is only one RCT comparing UAE and myomectomy to date, and the small population size limits the power of this study.

With fewer than 200 documented cases of pregnancy following UAE and only 106 live births, the safety of the procedure cannot be established with respect to subsequent pregnancy.

The studies show higher rates of miscarriage and preterm delivery after UAE, but the interpretation of the data is limited because of the small number of patients, and advanced maternal age. Larger studies with age-matched controls are needed before conclusions can be made regarding the possibility and safety of pregnancy after UAE.

A subset of the studies report postpartum hemorrhage and abnormal placentation as two complications of pregnancy which may be of concern after UAE. Conservative management of these pregnancies is recommended while awaiting further research. A conservative approach to pregnancies results in an increased rate of cesarean deliveries.

Medical therapy for hormonal management of leiomyomas in women attempting to become pregnant is not recommended, and current recommendations favor myomectomy over UAE in this population, except in certain circumstances. For women at high surgical risk, for example, those with extensive uterine leiomyomas presenting considerable surgical challenge, or those with previous abdominal laparotomy, UAE is the recommended procedure.[3]

For many patients, the symptoms of leiomyoma intensify over time, and treatment may not even be considered until after the reproductive years are past. In this population, there are many treatment options, and definitive treatment is tailored to the needs of the individual. The patient who anticipates a reproductive future has fewer choices, however, and until more research is completed, first line treatment will continue to be myomectomy.

Table 1. Literature review matrix

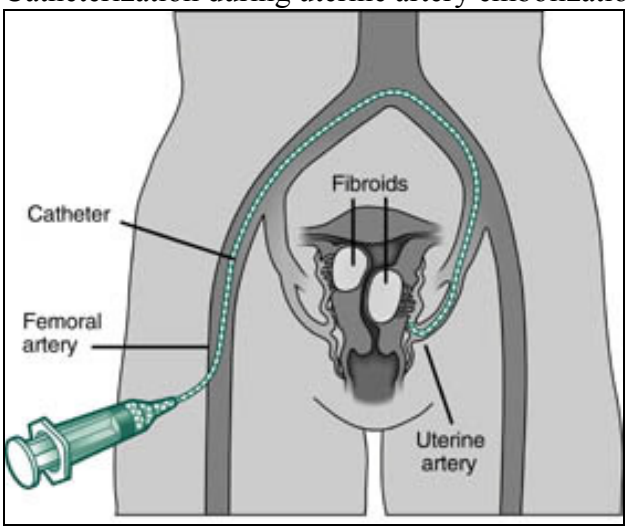
Paper	Study design	Number of subjects/Population	Inclusion criteria	Results/Comments/Conclusions
Firouznia 2009 Iran	Prospective cohort study	UAE in 102 women, 23 with a stated interest in fertility	Women seeking treatment for fibroid disease. Desire to preserve fertility was not an exclusion criterion	15 pregnancies in 14 women UAE "can serve as a substitute for invasive operations" Need for RCTs and more studies
Mara et al 2008 Ireland	Prospective Randomized Study	UAE in 58 women, Myomectomy in 63 women	Fibroids > 4 cm in diameter All subjects have desire to preserve fertility	26 pregnancies in 26 women Level I evidence The spontaneous abortion rate in the UAE group was 64% compared to 23% in the myomectomy group 42% of the subjects had at least one other subfertility factor
Pabon 2008 Spain	Prospective cohort study	UAE in 100 women, 57 with a stated interest in fertility	Women seeking treatment for fibroid disease. Desire to preserve fertility was not an exclusion criterion	11 pregnancies in 10 women Need for larger studies
Holub 2008 Czech Republic	Prospective multicenter cohort study	UAE in 112 women, LUAO in 225 women (laparoscopic uterine artery occlusion) No randomization; treatment decision based on patient/doctor decision, of which no details are given	Women seeking treatment for fibroid disease.	28 pregnancies in 20 women in the UAE group Increased risk of spontaneous abortion in UAE group (56%) compared to LUAO group (10.5%) Compared with pregnancies following LUAO, there were more cases of postpartum hemorrhage and malpresentation in the UAE group, but these were not statistically significant
Walker 2006 United Kingdom	Retrospective cohort study	UAE in 1200 women	Women seeking treatment for fibroid disease.	56 pregnancies Increased risk of cesarean section, spontaneous abortion, preterm delivery, and postpartum hemorrhage compared to normal obstetric population
Pron 2005 Canada	Prospective multicenter cohort study	UAE in 555 women	Women seeking treatment for fibroid disease.	24 pregnancies in 21 women Recommendation to monitor placental status throughout pregnancy High maternal age (average 36 yrs) a confounding factors
Price 2005 United Kingdom	2 case reports Retrospective cohort	Pregnancy reported in 2 women after UAE	Women seeking treatment for fibroid disease. Prior UAE	2 healthy infants in 2 primigravid women

McLucas 2001 USA	Prospective Cohort Study	UAE in 400 women, 139 women with stated interest in fertility	Women selected for UAE fibroid treatment, only women <40 years old were included in study, a total of 52 women	17 pregnancies in 14 women 10 normal term deliveries 2 women still pregnant at publication time states no growth retardation, but no infant weights reported "Effect on fertility is comparable to myomectomy"
Ravina 2000 France	Prospective Cohort Study	12 pregnancies in 9 women following UAE after 184 embolizations	Women selected for UAE fibroid treatment	Preliminary study of fertility after UAE. Author was the first to describe UAE for fibroids in the literature Pregnancies were serendipitous due to uncertainties of fertility, average maternal age 38 Earliest UAE in this study was performed in 1988 for unknown indication, pt became pregnant 2 yrs later, but advanced AIDS and streptococcal septicemia at 28 wks complicated the pregnancy, she went into pre-term labor, and infant died. Patient died a few mos later.

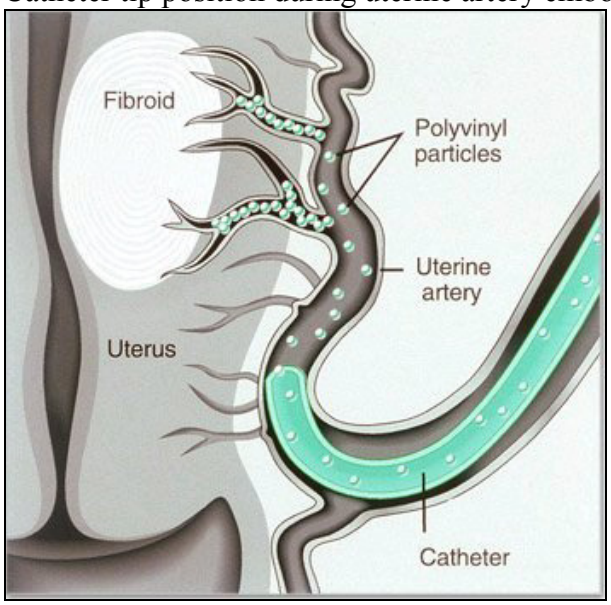
Table 2. Pregnancy outcomes reported by study

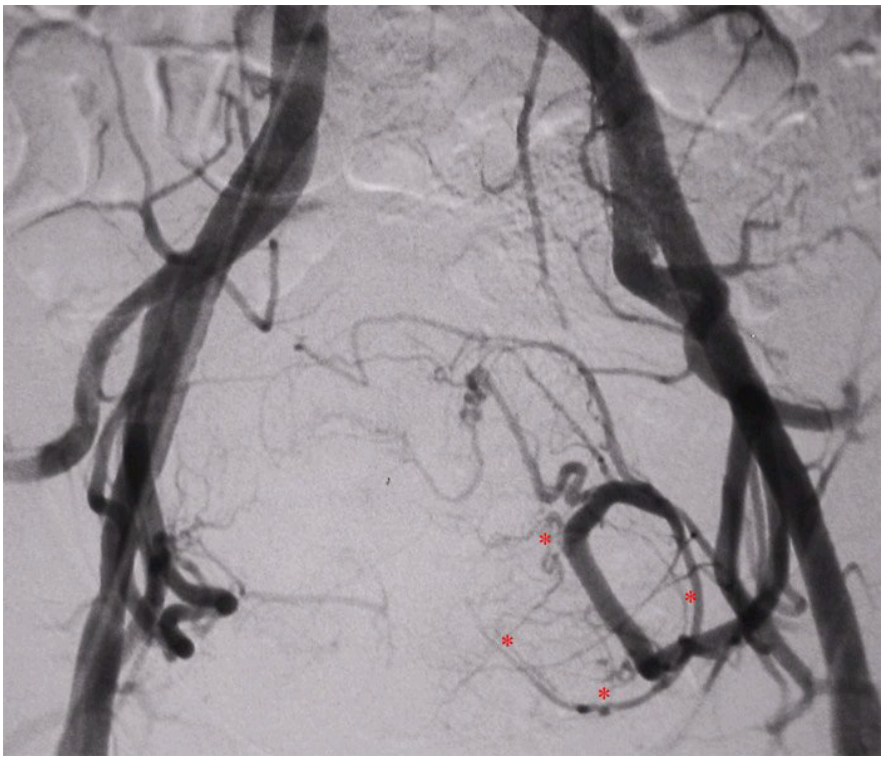
Lead author n = # of reported pregnancies Publication date	CDC data general obstetric population [20]	Firouznia (n=15) 2009	Mara (n=26) 2008	Pabon (n=11) 2008	Holub (n=28) 2008	Walker (n=56) 2006	Pron (n=24) 2005	Price (n=2) 2005	McLucas (n=15) 2001	Ravina (n=12) 2000
Mean maternal age	27.4	33.8	32.2	35.3	33.6	37.44	36	38.5	Not reported	38
Mean neonate weight (kg)	3.298	3.274	3.042	3.225	3.015	3.53 Premies 1.692	3.161 Premies 2.009	3.283	Not reported	2.906
Spontaneous abortion	10-15%	13%	64%	27%	56%	30%	17%	0%	33%	42%
Delivery complications (expressed as a % of total deliveries)										
Preterm delivery	12.7%	0%	0%	13%	20%	18.2%	22%	0%	7%	12%
Cesarean delivery	31%	100%	60%	50%	80%	73%	50%	100%	47%	62%
Postpartum hemorrhage	4-6%	8%	20%	0%	20%	18%	16%	0%	0%	0%
Malpresentation	6%	Not reported	Not reported	Not reported	20%	Not reported	Not reported	50%	20%	Not reported
Small for gestational age	10%	8%	0%	0%	10%	3%	22%	0%	0%	0%
Abnormal placentation	Not reported	Not reported	Not reported	0%	0%	3%	12.5%	0%	7%	0%

Catheterization during uterine artery embolization

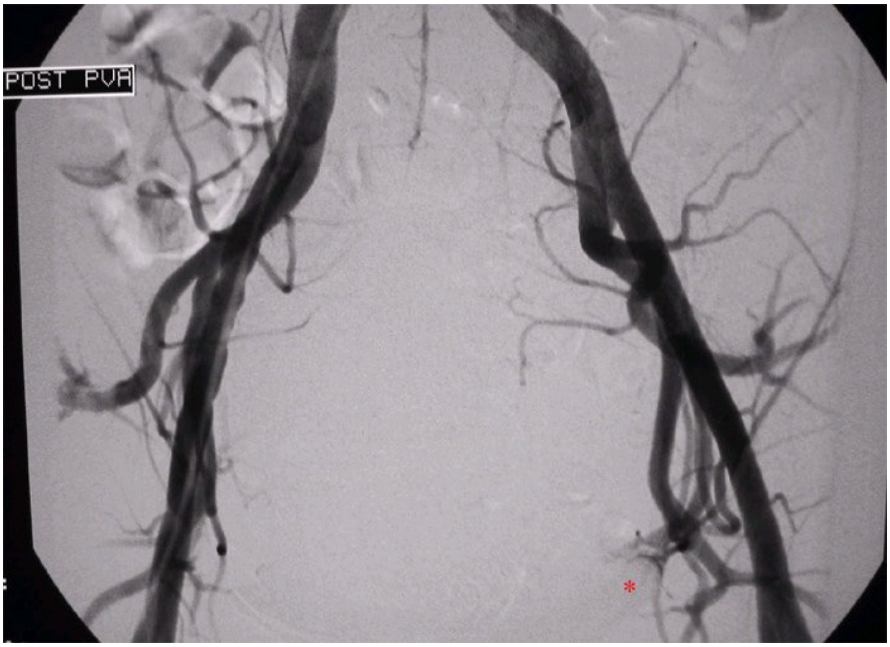


Catheter tip position during uterine artery embolization





Pre-embolization angiogram of a patient with fibroids (Reprinted with permission from Madison Radiology)



Post-embolization angiogram of the same patient (Reprinted with permission from Madison Radiology)

Endnotes

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