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REVIEW ARTICLE

Pregnancy success and outcomes after uterine fibroid embolization: updated review of published literature

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ABSTRACT

Females with symptomatic leiomyomas (fibroids) wishing to maintain fertility are faced with difficult treatment choices. These include uterine fibroid embolization (UFE), myomectomy, hormonal therapy, MRI high intensity focused ultrasound, and myolysis. This review focuses on UFE, one of the most commonly accepted minimally invasive procedural choices among patients with symptomatic fibroids wishing to retain the option of becoming pregnant in the future, and makes comparisons to myomectomy which has historically been the surgical choice for fertility-preserving fibroid treatment. Pubmed and Google Scholar searches using keywords such as: uterine artery embolization, uterine fibroid embolization, pregnancy, complications, infertility were performed between Jan 1, 2019 and May 10, 2019. Publications were chosen based on their inclusion of information pertaining to fertility or pregnancy after UFE without being limited to single case reports.

Randomized controlled trials comparing myomectomy and UFE are limited due to study size and confounding variables, but through registry data and familiarity with referring clinicians, UFE has gained wide acceptance. Healthy pregnancies following UFE have been sporadically reported but the actual fertility rate after UFE remains uncertain. Conversely, low birth weight, miscarriage and prematurity have been associated with UFE. Despite inherent risks of possible fertility issues after UFE, the procedure remains an option for females with clinically symptomatic fibroids who desire pregnancy. However, additional research regarding rates of conception and obstetrical risks of infertility following UFE is necessary.

INTRODUCTION

The first surgical myomectomy was performed in the 1840s. More recently, myomectomy has been shown to result in fertility rates of approximately 53.6–55.9%. Ravina et al¹ reported the first uterine artery embolization in France in 1995, followed with early reports by Pelage et al^{2–5} showing a low complication rate and effectiveness.

Uterine artery embolization (UAE) was initially performed to prevent or limit bleeding prior to myomectomy or for postpartum hemorrhage. Later, it was recognized as an effective treatment for uterine leiomyomas, typically with abnormal uterine bleeding.^{4,6–10} This is often referred to as uterine fibroid embolization (UFE). Work by Spies and others^{11,12} have advanced the technical aspects of the procedure and clinical evaluation and management of females undergoing embolization. UFE has increased in prevalence since it was first performed with estimates of annual worldwide procedures being about 25,000 in 2008.^{13,14} UFE has been

recognized as an effective treatment for fibroid-associated symptoms such as abnormal uterine bleeding and bulk symptoms resulting in pelvic pain and bladder and bowel symptoms.^{13,15–18} Compared to hysterectomy and myomectomy, length of hospital stay and major complications are lower with UFE, but there is a higher reintervention rate. Some studies report better symptom management with hysterectomy but future pregnancy is eliminated.^{19–25} Reports of uterine necrosis following UAE, while infrequent, do occur and are more common in patients with co-morbidities such as diabetes.²⁶

For many years, anecdotal evidence suggested UFE should be avoided in patients wishing to maintain fertility. This idea has been perpetuated by medical textbooks and practicing physicians and supported by individual case studies. While there are limitations to published studies in the literature, more studies are available for analysis. Ethical considerations and

Table 1. Fertility and obstetrical complications post-UFE

Study	^a Conception	Spontaneous abortion	Preterm delivery	Cesarean delivery
Pron et al (2005)	21/NR (UKN%) ^b 24	4/24 (16.7%)	4/18 (22.2%)	5/14 (35.7%)
^c Walker & Pelage, 2003	12/24 (50.0%) ^b 13	2/13 (15.4%)	1/9 (11.1%)	1/9 (11.1%)
^c Walker & McDowell (2006)	33/108 (30.6%) ^b 56	17/56 (30.4%)	6/33 (18.2%)	24/33 (72.7%)
^c Walker & Bratby (2007)	51/108 (47.2%) ^b 67	20/62 (32.3%)	5/42 (11.9%)	27/40 (67.5%)
Ravina et al (2000)	9/NR (UKN%) ^b 12	5/12 (41.7%)	3/7 (42.9%)	4/7 (57.1%)
Goldberg et al (2004)	53/NR (UKN%) ^b 53	12/51 (23.5%)	5/32 (15.6%)	22/35 (62.9%)
Walker & Pelage, 2003	10/ ^d 39 (25.6%) ^b 11	3/11 (27.3%)	1/8 (12.5%)	4/8 (50.0%)
Mara et al (2008)	13/26 (50.0%) ^b 17	9/14 (64.3%)	0/5 (0.0%)	3/5 (60.0%)
Holub et al (2008)	20/39 (51.2%) ^b 28	14/25 (56.0%)	2/10 (20.0%)	8/10 (80%)
Kim et al (2005)	5/6 (83.3%) ^b 8	0/8 (0.0%)	1/7 (14.3%)	2/7 (28.6%)
Walker & Pelage, 2003	14/ ^d 52 (26.9%) ^b 17	5/17 (29.4%)	NR	NR
Dutton et al (2007)	27/187 (14.4%) ^b 37	15/34 (44.1%)	NR	15/19 (78.9%)
General population	^{e, h} 75–95%	^e 15–25%	^f 12.6%	^f 31.9%

^aNumber of females who became pregnant/number of females desiring pregnancy, during follow-up period. This does not consider efforts made or neglected to the end of conception.

^bNumber of pregnancies reported during follow-up period.

^cThis was a continuing study with multiple reports.

^dThose desiring future fertility and under the age of 40 years.

^e*Evaluation and treatment of recurrent pregnancy loss: a committee opinion.* The American Society for Reproductive Medicine. 2012.

^f*Births: Final Data for 2016.* National Center for Health Statistics, Centers for Disease Control and Prevention. 2018.

^gTaylor, Alison. *ABC of subfertility, Extent of the problem.* British Medical Journal. 2003.

^hRates increase with follow-up length of time from 6 months to 2 years.

patient autonomy often restrict these studies to an observational scope.

There is little agreement regarding fertility status following uterine fibroid embolization.^{27–30} Approximations of fertility status post myomectomy are placed at 53.6–55.9%,³¹ but fertility rates post-UFE have not yet been effectively quantified. Published studies have limitations and biases while predictive values may be inaccurate. Our review attempts to analyze published reports (Table 1) and address qualitative perspectives.

PREGNANCY CONCERNS

Clinical concerns about post-UFE fertility involve the capability to conceive and maintain a pregnancy, premature menopause, radiation exposure risks, preterm delivery, postpartum hemorrhage, and spontaneous abortion rates.^{6,32}

Effect on conception, spontaneous abortion, preterm delivery, and cesarean delivery rates

Uneventful full-term pregnancies and healthy deliveries have been reported post-UFE with cautions of unknown complications and the necessity for further data.^{5,33–37} One of the largest studies reported was a multicenter Canadian trial by Pron et al.³³ They reviewed 555 patients treated for symptomatic fibroids and retrospectively analyzed fertility following treatment. A total of 24 pregnancies occurred in 21 females within 4 years following embolization; 23 spontaneously and 1 by *in vitro* fertilization. 18 live births (14 term, 4 preterm), 4 spontaneous abortions, and 2 elective abortions occurred in this subset. Of the term pregnancies, nine were delivered vaginally, and five by cesarean section. The mean maternal age at delivery was 36 years, highlighting advanced age as a confounding factor in this population. Of those patients, 31% were under 40 years of age and 16% of the participants were lost to follow-up after 2 years. Study limitations

included the uncertainty of desired pregnancy and contraception use.

Walker and McDowell³² reported a series of 200 pregnancies following UFE over a 9-year period. In a cohort of 108 females attempting to conceive, 56 pregnancies were identified of which 33 (59%) were term and 6 were premature deliveries. In the remainder, there were 17 spontaneous abortions, 2 stillbirths, 1 ectopic pregnancy and 3 elective terminations. 24 of the 33 term pregnancies were delivered via cesarean section. Walker and Pelage⁵ reported 13 pregnancies post-UFE in 24 females. 10 of them were actively trying to conceive and 3 reported unexpected pregnancies. Of the 13 pregnancies, there were 9 successful deliveries (8 term and 1 at 27 weeks' gestation secondary to preeclampsia). The other four pregnancies ended in two spontaneous abortions, one ectopic pregnancy, and one elective termination. In the continuation of their study, Walker and Bratby³⁸ suggested that females with all subtypes of fibroids treated with UFE had the potential for future fertility.

Ravina et al³⁴ reported 12 cases of pregnancy in 9 females after UFE. The median maternal age was 40 years and time from UFE to pregnancy was 9 months. 5 of the 12 pregnancies ended in early spontaneous abortions and 7 had uneventful pregnancies: 3 delivered vaginally and 4 delivered via cesarean section. Three of the births were premature but this was determined to be unrelated to the UFE: one was complicated by severe AIDS and streptococcal septicemia, while the others were a twin pregnancy with late toxemia and gestational hypertension.

Another retrospective study comparing 53 pregnancies after UFE with 139 pregnancies after myomectomy (the study groups were not adjusted) found a higher rate of preterm delivery and malpresentation in the UFE cohort [odds ratio (OR), 6.2; 95% confidence interval (CI) (1.4–27.7), and OR, 4.3; 95% CI (1.0–20.5) respectively].³⁹

Pabón et al⁴⁰ prospectively studied a subset of 57 patients who desired to maintain fertility out of 100 patients who underwent UFE. They reported 11 pregnancies in 10 females resulting in 8 live births; 4 were spontaneous vaginal deliveries and 4 were cesarean deliveries. Three pregnancies ended in early miscarriages. Birth weights and placenta morphology were normal in the live births with one delivery before 37 weeks' gestation. It is unclear if the 57 females were actively attempting to become pregnant during the follow-up period which ended after 2 years for most the patients.

A randomized prospective trial comparing UFE with myomectomy and implications for future fertility was conducted by Mara et al.⁴¹ There was equipoise in post-procedural results with no significant difference between groups for the metrics of technical success rate, symptomatic effectiveness, post-procedural follicle stimulating hormone levels, reintervention rate, or complication rate. UFE, however, showed decreased length of hospital stay, lower serum inflammatory levels, shortened recovery period, shorter procedure times and less disability at greater than 2 weeks ($p < 0.0001$ for all parameters) (these data suggested that

UFE was the less invasive approach with improved recovery times). Perinatal outcomes including mean birth weight, mean completed gestational weeks, preterm delivery, cesarean section, post-partum hemorrhage, perinatal hypoxia, pre-eclampsia, and intrauterine growth restriction were similar in both groups. Study limitations were small sample size and unequal number in each group attempting to conceive (40 in myomectomy and 26 in UFE group). In addition, this study gave more insight into the effects of UFE on the fertility of younger females as the mean age of pregnant females after UFE was 32.8 years and that after myomectomy was 34.3 years. The rates of spontaneous abortion and pregnancy were 64 and 50%, respectively, after UFE (both higher compared to many other observational and retrospective studies), and 23 and 78%, respectively, after myomectomy. The differences in outcome for these two parameters were of statistical significance ($p < 0.05$). The relative risk of infertility after UFE compared to myomectomy in this study was 2.22 [95% CI (1.11–4.44)]. Holub et al⁴² also found an increased risk of spontaneous abortions in patients who had undergone UFE as compared to laparoscopic uterine artery occlusion (14/25 and 4/36 pregnancies respectively, $p < 0.001$).

A systematic review by Homer and Saridogan⁴³ found post-UFE pregnancies and fibroid-containing pregnancies experienced similar rates of preterm delivery, intrauterine fetal growth restriction, and malpresentation, while the post-UFE pregnancies were at increased risk for miscarriage [OR 2.8; 95% CI (2.0–3.8); $p < 0.001$], cesarean delivery [OR 2.1; 95% CI (1.4–2.9); $p < 0.0001$], and post-partum hemorrhage [OR 6.4; 95% CI (3.5–11.7); $p < 0.0001$]. In another retrospective multicenter study, Hirst et al⁴⁴ found fertility and miscarriage rates were similar between age-matched females who had undergone UFE and those who elected to receive no treatment at all.

Kim et al³⁷ studied six females who desired fertility and were making lifestyle choices amenable to conception, and found five (83%) became pregnant and one conceived a second time during the study period. In the total population followed, eight pregnancies occurred: six were planned, and two resulted from contraception failure. Among these pregnancies, one was terminated electively, five delivered vaginally and two by cesarean section. One case of premature rupture of membranes followed by preterm delivery of a small-for-gestational age neonate was reported.

Radiation exposure and premature menopause

Radiation exposure in UFE is a safety concern requiring disclosure during the consultation for uterine fibroid treatment. McLucas et al³⁵ found the average radiation exposure was 14 rad (radiation absorbed dose) among 50 patients undergoing UFE. Nikolic et al⁴⁵ estimated the average radiation doses absorbed to the ovaries and skin during UFE as 22.34 cGy (centigray) and 162.32 cGy respectively; concluding this exposure was unlikely to cause acute or long-term damage or to pose a risk to progeny of the exposed patient. Advances in techniques and radiation reduction methods are able to reduce the absorbed radiation dose.⁴⁶

Table 2. Gross pregnancy rate post-UFE

Study	Pabón et al, 2008	Mara et al (2008)	Holub et al (2008)	Kim et al (2005)	McLucas et al, 2001	Totals	Percentage
# of females becoming pregnant	10	13	20	5	14	62	38.3%
# of total included subjects	39	26	39	6	52	162	

UFE, uterine fibroid embolization.

Inclusion criteria: study included an age exclusion above 45 years (some included studies excluded at age 40 and above), subjects indicated a desire to either maintain fertility or become pregnant (most commonly through a questionnaire). There was no exclusion based on follow-up period or other factors affecting fertility.

McLucas et al⁶ reported 4 out of 163 patients developed premature menopause, with affected patients all over the age of 45 years. The Ontario trial³³ cited three cases of post-partum hemorrhage, due to placental abnormalities, among the 21 pregnancies. The likelihood of UFE causing amenorrhea appears to be largely age-dependent, with cases occurring under the age of 40 years being rare.¹⁵ In their study of 400 females, Walker and Pelage⁵ found that 26 patients (7%) experienced permanent amenorrhea following embolization, including 4 patients under the age of 45. Ovarian artery-to-uterine artery anastomoses have been classified into three different types and non-target embolization to one or both arteries is possible and implicated in ovarian failure or diminution of ovarian functional reserve following UFE.⁴⁷⁻⁵⁰ In cases where premature ovarian failure is a concern, occlusion of the uteroovarian collateral vessels prior to UFE could be protective.⁵¹ Ovarian artery collaterals are often diminutive and cannot be visualized at the time of UFE. Although premature ovarian failure may theoretically occur, it is likely a rare event, and current evidence is too sparse to draw any meaningful conclusions.³³

CONCLUSION

Uterine fibroid embolization has become an accepted non-invasive method for treatment of symptomatic leiomyomas in a wide range of patient ages, including reproductive age females. There are limitations in the reported literature on rates and outcomes of pregnancy in the subgroup of females of reproductive age desiring pregnancy who have undergone uterine artery embolization for any reason. Many patients included in the existing studies and case reports have variable factors that confound direct analysis or comparison that include, advancing maternal age, uterine wall compromise, previous spontaneous abortions, prior uterine surgeries, variable technique and skill of interventional radiologists, unknown desire to conceive and carry a fetus to term, and other unknown causes of infertility. Additionally, the most well-controlled studies encountered often

have small population sizes which make it difficult to gain meaningful clinical information from them.

It is clear, however, that pregnancy is attainable for females following UFE and many of these pregnancies proceed uneventfully to successful deliveries. The actual fertility rate following UFE remains uncertain,²⁷ but is approximated to 38.3% based on the published results available (Table 2). This number disregards factors such as patient age (this calculation includes females up to age 45), efforts to conceive, past surgical or medical history, and other pertinent considerations; it is reasonable to expect that a cohort of younger females trying to conceive would experience higher rates of fertility.

When compared to myomectomy for treatment of symptomatic uterine fibroids, UFE is superior in terms of symptom management and length of stay, however, may be associated with an increased risk of preterm delivery and spontaneous abortion. In comparing cesarean section rates between patients in each group, increased rates of cesarean delivery do not correlate with higher rates of complications. Conclusions on the expedience of UFE vs myomectomy for females wishing to maintain fertility are limited by small sample sizes, lack of randomization, and inability to control confounding variables. Another obstacle in comparing studies is the differences in follow-up periods that vary from 1 to 2 years to greater than a decade. Other treatment options, such as MRI-guided focused ultrasound surgery are increasing in availability and may be preferable in many situations.⁵² The decision to proceed with one treatment approach over the other should be made through in-depth discussion between the patient and physician, with the risks and limitations of each method being clearly outlined. Additional randomized, controlled research into fertility and pregnancy following UFE would be of great benefit.

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