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Pregnancy after uterine artery embolization for leiomyomata: A series of 56 completed pregnancies

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KEY WORDS

Uterine artery embolization
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Objective: This study was undertaken to evaluate the incidence and outcome of pregnancies after uterine artery embolization (UAE) for symptomatic uterine fibroids.

Study design: A retrospective analysis of all pregnancies after UAE by a single interventional radiologist.

Results: Fifty-six completed pregnancies were identified in approximately 1200 women after UAE. One hundred eight patients were attempting to become pregnant and 33 of these became pregnant. Thirty-three (58.9%) of the 56 pregnancies had successful outcomes. Six (18.2%) of these were premature. Seventeen (30.4%) pregnancies miscarried. There were 3 terminations, 2 stillbirths, and 1 ectopic pregnancy. Of the 33 deliveries, 24 (72.7%) were delivered by cesarean section. There were 13 elective sections and the indication for 9 was fibroids. There were 6 cases of postpartum hemorrhage (18.2%).

Conclusion: Compared with the general obstetric population, there is a significant increase in delivery by cesarean section and an increase in preterm delivery, postpartum hemorrhage, miscarriage, and lower pregnancy rates. When taking into account the demographics of the study population, these results can be partly explained. There were no other obstetric risk identified.

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Uterine artery embolization (UAE) is a recognized treatment for symptomatic uterine fibroids, as described in numerous reports since 1995.¹⁻⁵ Information on its effects on fertility and infertility, however, is limited. Advice often given to women with uterine fibroids who desire to retain fertility is to avoid UAE. Pregnancy after UAE has been described in the literature in the form of case reports, and a review article,⁶ some

retrospective series⁷⁻⁹ and one retrospective cohort study comparing UAE with laparoscopic myomectomy.¹⁰

In December 1996, a prospective observational study was established to evaluate UAE in the management of symptomatic uterine fibroids.⁴ Most of the cases have been carried out at the Royal Surrey County Hospital with a minority performed privately at The London Clinic. All procedures were performed by a single interventional radiologist (W.W.). Pregnancy after UAE has been reported previously from this ongoing study, with a smaller population.¹¹ To our knowledge, 60 women have conceived after UAE. This article describes the outcomes of those pregnancies.

Study was performed at The Royal Surrey County Hospital, Guildford, UK.

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Material and methods

During the period December 1996 to May 2005 approximately 1200 women underwent bilateral UAE as described in our previous publication.⁴ Ethical committee approval was obtained before December 1996. All patients after embolization were sent a screening questionnaire. Information requested included: actively or previously attempted conception, not attempting conception, use of contraceptives, fertility problems before or after embolization, and other treatments offered by their primary gynecologist. If no reply was forthcoming, an additional questionnaire was sent out at 2 months, and if still no response, the patients were telephoned and the form filled out by a research assistant.

All these initial forms were either returned or discussed over the telephone if incomplete or unreturned. An additional questionnaire was sent to these women seeking information on pregnancy outcome, age at delivery, complications of antenatal, intrapartum and postpartum periods, mode of delivery, reason for assisted delivery, other surgical procedures, birth weight, and length of lochia. Of these, 3 forms remained incomplete from the miscarriage group. Sixty pregnancies were identified in 48 women. Four of these pregnancies were ongoing, therefore excluded from further evaluation. Several women had been pregnant twice, one 3 times, and one 4 times. The women were from multiple locations throughout the United Kingdom. In complicated cases, reference was made to the patients' medical records after their consent.

Results

From the approximately 1200 responses, 108 women had been seeking at some time to become pregnant, and 33 of these 108 women became pregnant at least once regardless of outcome. Eighteen women had unintentionally become pregnant; 30.5% of women wishing to become pregnant were successful regardless of outcome, and at least once after embolization. Of the 60 pregnancies, 19 had prior subfertility or infertility investigation, ranging from 18 months to 8 years. Twelve of these went on to have successful pregnancies. There was 1 successful in vitro fertilization (IVF) pregnancy. One other woman postembolization failed to become pregnant with IVF, but was successful later without IVF. Thirty-five pregnancies were first conceptions.

There were 33 (58.9%) successful live births in 27 women. Twenty-seven (81.8%) of the 56 pregnancies delivered at term (≥ 37 weeks' gestation), and 6 (18.2%) premature (< 37 weeks). There were 17 (30.4%) miscarriages, 3 (5.4%) terminations, 2 (3.6%) stillbirths, and 1 (1.8%) tubal ectopic.

Many of the patients had treatment for fibroids before and/or after embolization. Preembolization, 2

Table I Pregnancy complications

Complication	No. (% Rate)	Rate from literature (General obstetric population)
Miscarriage	17 (30.4%)	10%-15% ²¹
Morning sickness	20 (60.6%)	50%-70% ²²
First-trimester bleeding	8 (24.2%)	25% ²³
Second-trimester bleeding	5 (15.2%)	NA
Third-trimester bleeding	4 (12.1%)	17.6% ²⁴
Placenta previa	1 (3.0%)	0.4% ²⁵
Proteinuric hypertension	2 (6.1%)	8%-18% ²⁶
Premature rupture of membranes	3 (9.1%)	2%-3.5% ²⁷
IUGR	1 (3.0%)	5%
Preterm delivery	6 (18.2%)	5%-10% ²⁸
Postpartum hemorrhage	6 (18.2%)	5.4%-13% ^{19,29}

had previous open myomectomy, 2 had hysteroscopic resections, and 3 had laser ablation. Two had undergone "combined" procedures. This consisted of UAE before myomectomy in the same day and which aimed to virtually eliminate blood loss and kill any fibroids that would be difficult to remove surgically. Postembolization, 5 required hysteroscopic resection and 1 required a laparoscopic myomectomy. Of the 27 women with successful pregnancies, 14 had been previously offered hysterectomy as the only treatment option.

The mean age at cessation of all pregnancies was 37.44 (SD 3.90). The mean for the miscarriage group was 38.75 (SD 4.43), and for the successful pregnancies 36.30 (SD 3.34).

Of the miscarriages, 13 were early, or first trimester. One was second trimester (19 weeks), and for 3 cases the gestation at miscarriage was unavailable. In the first trimester miscarriages, 5 had a spontaneous miscarriage and 7 underwent evacuation for retained products of conception (ERPC). One required a second ERPC after developing infection for retained products of conception and a second required syntocinon for abnormal blood loss. The second trimester miscarriage was a 19-week missed miscarriage, which was revealed on ultrasound scan after a cessation in fetal movements. No cause was found for the miscarriage and post mortem examination was normal. This patient required a curettage for excessive vaginal bleeding after delivery.

There were 3 terminations, 2 for social reasons, and 1 at 25 weeks' gestation for trisomy 21. The 1 case of ectopic pregnancy was managed by salpingectomy at 6 weeks.

There were 2 stillbirths. The first was at 33 weeks' gestation, and was found to have a true knot in the cord. The second was at 37 weeks' gestation in a woman who had had a previous successful pregnancy after embolization, delivered by a cesarean. During this subsequent pregnancy she had severe abdominal pain develop at 35

Table II Preterm deliveries

Gestation (wks)	Weight (kg)	Indication for delivery	Complications/treatment	Mode of delivery
34	1.86	SROM, activated protein C resistance	Jaundice, antibodies	Cesarean
27	0.99	HELLP	Ventilation, PDA. No ongoing problems	Cesarean
32	2.18	Parvovirus/SROM/Chorioamnionitis	Hepatosplenomegaly, infection, antibiotics	Cesarean
31	1.51	SROM	Oxygen, no ongoing problems	Vaginal
33	1.65	PET	Oxygen, feeding tubes	Cesarean
36	1.96	Abruption	Resuscitation, oxygen	Cesarean

SROM, Spontaneous rupture of membrane; PET, preeclamptic toxemia.

weeks, but was not seen by an obstetrician until 37 weeks. At emergency cesarean she was found to have a ruptured uterus through her previous cesarean scar.

Twenty (60.6%) of the successful pregnancies had morning sickness. Eight (24.2%) of the 33 successful pregnancies had first-trimester bleeding, and 5 (15.2%) had second-trimester bleeding. There were 4 cases of third-trimester bleeding. Of these, 2 had major bleeds; one required admission from 29 weeks, and the other had an emergency cesarean for placental abruption.

One woman was found to have a placenta previa. Another 5 had low-lying placentas. These migrated upward before 20 weeks' gestation.

There were 2 cases of proteinuric hypertension. The first was at 26 weeks' gestation. Treatment was commenced for the HELLP syndrome and the patient had an emergency cesarean section at 27 weeks. The second was at 29 weeks' gestation and required cesarean section at 33 weeks. There were 4 cases of pregnancy-induced hypertension, none of which required admission to hospital.

There were 3 cases of premature rupture of membranes. The first was at 32 weeks' gestation in a patient who had undergone 2 intrauterine fetal blood transfusions, and was subsequently found to have chorioamnionitis. The second was at 33 weeks' gestation in a patient who had a septate uterus and activated protein C resistance caused by factor V leiden coagulopathy. She had been treated with low molecular weight heparin. The third occurred at 31 weeks' gestation in a first conception. No cause was found and there were no associated factors identified.

There was 1 case of intrauterine growth retardation (IUGR) requiring a cesarean section at 33 weeks' gestation for impaired uterine artery blood flow. Data for all pregnancy complications are shown in Table I.

Six infants were born prematurely, 2 before 30 weeks' gestation. The average premature gestation was 32.17 (SD 3.06) weeks. These cases are described in Table II. The mean birth weight for term infants was 3.53 kg (SD 0.63). The mean maternal age at delivery for premature deliveries was 36.83 (SD 4.07).

Table III Cesarean sections

Gestation (wks)	Em LSCS/El LSCS	Indication
38	El	Placenta previa
37	El	Fibroids
37	El	Fibroids/previous cervical cone biopsy
39	El	Fibroids
39	El	Fibroids
38	El	Fibroids/previous cesarean
39	El	Fibroids
38	El	Fibroids/previous cesarean
39	El	Breech
39	El	Cephalopelvic disproportion
37	El	Fibroids
40	El	Previous cesarean
38	El	Fibroids
41	Em	Poor CTG secondary to true knot in cord
36	Em	Placental abruption
41	Em	FTP past 2 cm
42	Em	FTP past 3 cm
42	Em	Face presentation/obstructed labor
38	Em	Malpresentation/fibroids
33	Em	PET
27	Em	PET
38	Em	Fibroids
34	Em	Previous cesarean, SROM, uterine septum, activated protein C resistance
32	Em	Chorioamnionitis, SROM, parvovirus infection

Em, Emergency; LSCS, Lower segment cesarean section; El, elective; CTG, cardiotocography;

Nine (27.3%) of women with successful outcomes delivered vaginally and 24 (72.7%) by cesarean section. Five of the 6 premature deliveries were by cesarean, therefore of those deliveries at term (≥ 37 weeks), 19 (70.4%) of 27 were by cesarean section. Thirteen (54.2%)

of the cesarean sections were elective, and 11 (45.8%) were as an emergency. Fibroids were the indication for 9 of the 13 elective cesareans. The emergency cesareans had a variety of indications. Of the emergency cesarean sections, 5 attempted vaginal deliveries. One of the vaginal deliveries required ventouse for poor maternal effort. Indications for all cesarean sections are shown in Table III.

There were 5 cases of postpartum hemorrhage, 2 requiring blood transfusion. There were no cases of abnormal placentation other than the previa described previously.

The mean length of lochia was 4.63 weeks. Two women did not provide details and for 5 women lochia was not yet completed. There were 2 cases of presumed endometritis and 1 of postnatal depression.

Comment

Pregnancy after UAE is well documented. There are valid concerns regarding the effect of embolization on those women wishing to retain fertility, and on the pregnant uterus. The numbers of patients who have become pregnant remains relatively small, meaning information for medical staff to convey to prospective UAE candidates is limited or incomplete. A review in 2004 advised that until further data are available, laparoscopic myomectomy, open myomectomy, or hysteroscopic resection constitutes the standard of care in patients desiring future fertility.⁶ However, such cases may be difficult, particularly where there are numerous interstitial and/or submucous fibroids, and recurrence rates may be higher than 60%.¹² Fibroid embolization has the advantage over myomectomy in that it kills all the fibroids in 1 procedure, which then shrink or, in some cases, are passed vaginally. Our current series is the largest series to date of pregnancies after embolization for uterine fibroids. In this article we do not attempt to compare UAE with myomectomy, its object is to present the incidence of pregnancy, outcomes, and complication rates.

The population in this series is approximately double of that in the previous series.¹¹ The demographics of the population have remained similar, but with higher numbers of normal, uncomplicated pregnancies. It is important to emphasise that the population involved is not a cohort typical of the general obstetric population. The mean age for all pregnancies at cessation was extremely high at 37.44 years. There are known associations between fibroids, subfertility, pregnancy loss, and pregnancy complications.¹³ Advanced maternal age adversely affects ovarian function, causing a decline in the number of good quality oocytes, resulting in chromosomally abnormal conceptions that rarely develop further.

Of the women who became pregnant, 39.5% had some form of investigation for infertility before

embolization. Of 108 patients attempting to become pregnant, 33 were successful. Also, 58% of all pregnancies (including ongoing) were first conceptions, and these patients generally have higher rates of pregnancy-related complications. The information for this study was primarily obtained from patient questionnaire(s). Patients had pregnancy care from all over the United Kingdom, making it difficult to obtain medical records in all cases. Only in complicated cases were the medical records sought out. Optimally, all records should be perused. If there was confusion in the questionnaire, patients were telephoned by an obstetrically trained medical practitioner. Also, in the initial questionnaire, women were not asked if they had a history of subfertility, only if they had been attempting pregnancy or intending to attempt pregnancy. The reason for this was that most patients were advised other treatment regimens if desiring to keep their fertility. Only those who achieved pregnancy after embolization were sent a second questionnaire detailing any history of subfertility. From our study other comments relating to previous infertility, treatment and cause, cannot be made.

Overall, most pregnancy complications were within normal ranges for the general obstetric population. The rate of miscarriage was high at 30.4%. The Royal College of Obstetrics and Gynaecology gives a 10% to 15% risk of spontaneous miscarriage. Rates of miscarriage increase 2- to 3-fold over the age of 40 years.¹⁴ The mean age in the miscarriage group was 38.75 years, and the ages ranged from 30 to 50 years. Of our patients who miscarried, 7 were older than 40 years, and all but 2 were older than 35 years. The rates of miscarriage in our study are higher; however, this may be explained, or partly explained, by the increased maternal age.

The rates of first-trimester vaginal bleeding for successful pregnancies was also at the upper limit for the normal obstetric population; however, this has reduced since our previous series¹¹ from 40% to 24.2%. The continued moderately higher rate may again be due to the older age group in our study population with corresponding higher risk factors. It could also be due to differences in embolization technique, as in the initial 400 patients who were embolized with polyvinyl alcohol particles to the branch vessels of the uterine arteries and coils blocking or restricting flow in the main uterine arteries. Subsequent patients were embolized with particles only and without occlusion of the main uterine arteries. Thus, there may have been a possibility of ischemia to the normal uterus and this may have contributed to the slightly increased complication rate in the earlier cases. Also, increasing technical experience led to progressive improvement in the reliability and efficiency.

There were 6 (10.7%) cases of low-lying placenta; however, only 1 failed to migrate. Fibroids and abnormal uterine shape can be associated with placenta previa, therefore theoretically one might expect the rates of

placenta previa to be higher than the general obstetric population. The Ontario multicenter trial⁹ had 3 cases of placenta previa (14.3%), 2 of which had antepartum hemorrhage that required delivery. The relevance or our increased rate of placenta previa is debatable with only a single case identified.

Abnormal placentation can be a contributory factor to proteinuric hypertension and IUGR. The rate of proteinuric hypertension and IUGR in our series are below the general obstetric population. Of the 3 cases of premature rupture of membranes, 2 are likely to be associated with other factors (an intrauterine septum and intrauterine blood transfusions). Therefore, the adjusted rate is 3.0%. This is within the normal range.

The rate of premature delivery (18.2%) is higher than the rates for the general obstetric population (5%-10%).^{15,16} It has been documented that women older than 35 years have approximately double the risk of premature delivery.¹⁶ The mean maternal age for the preterm group was 36.8 years. The preterm delivery rate is similar to the Ontario trial⁹ 4 of 18 (22.2%) and the Goldberg study¹⁰ 5 of 32 (16%). The laparoscopic myomectomy group in the Goldberg study had a much lower rate of preterm delivery at 3%. Although the numbers are still small, it appears that rates of preterm delivery are higher than the general obstetric population. This may well be explained by increased maternal age.

The rate of cesarean section was extremely high at 72.7%. The rate of elective cesarean is also high at 39.4%. The indication in 9 of the elective sections was either partly or solely caused by fibroids, whereas in the emergency group, only 1 had fibroids as the indication. This may demonstrate that of those who elect to attempt a normal vaginal delivery will not necessarily then need an emergency section with fibroids as the indication. Understandably, obstetricians take a conservative approach to managing labor in these patients because of limited information on pregnancy after UAE. However, the rate of cesarean sections in those going to term and planning a normal vaginal delivery remains well above normal rates at 42.9% (6/14). The overall rate of cesarean sections for England and Wales was 21.9% in 2001 and 2002. This demonstrates that this conservatism is not without reason. The Goldberg study¹⁰ found rates of cesarean high in both the UAE group (63%) and the laparoscopic myomectomy group (59%). The Ontario multicenter trial⁹ found cesarean rates of 50%.

The Goldberg study¹⁰ also found high rates of malpresentation in 4 of 35 cases (11%). Fibroids are linked with both malpresentation¹⁷ and preterm labor,¹⁸ probably by distorting the uterine cavity. Our study identified 2 of 33 (6.1%) malpresentations, and 1 face presentation, a rate that is not increased.

Postpartum hemorrhage was increased at 18.2%. Current evidence linking fibroids with postpartum hemorrhage is inconsistent.¹⁷ One large multicenter study has

concluded fibroids are an independent risk factor for increased postpartum blood loss.¹⁹ There was 1 case of abnormal placentation, a placenta previa. The Ontario trial⁹ identified 3 cases of abnormal placentation, all of which had postpartum hemorrhage and the Goldberg study found a low rate of postpartum hemorrhage at 6%. We have not been able to find evidence that adequately corrects for age and the presence of fibroids. Our study found an increased risk of postpartum hemorrhage that has not been replicated in other studies, but this may be explained by age and the presence of fibroids.

The overall pregnancy rate for women wishing to become pregnant is 30.5% (33/108). This is much lower than that reported for pregnancy rate after laparoscopic myomectomy. A review by Poncelet et al²⁰ in 2002 of myoma and infertility showed that within 24 months of surgery almost 60% of patients spontaneously conceived. It should be noted, however, that many of our patients would have been unsuitable for laparoscopic myomectomy, (ie, with 1 or 2 suitably positioned fibroids <8 cm), and most of our patients were only offered UAE if they had fibroids that were considered not amenable to laparoscopic or hysteroscopic resection. Many of our patients had difficult multiple complex fibroids and had been rejected by referring gynecologists for other procedures. Fourteen, in fact, had been offered hysterectomy.

The object of this study was not to compare myomectomy with the efficacy of myomectomy versus fibroid embolization. The latter would require a randomized controlled trial, in which patients were very accurately matched particularly with regard to the magnetic resonance imaging evaluation of the number and types and size of fibroids involved. The main purpose of this article is to present the outcome of pregnancies after embolization and their complication rates. The cases in which other fibroid treatment procedures were performed are therefore included, as these patients were still exposed to the "risk" of embolization of the uterine arteries.

From our results, it is evident women can conceive after UAE, and a successful pregnancy outcome is possible. Successful pregnancy outcome was finally achieved in some patients having previous failed myomectomies and in 14 patients only offered hysterectomy. Two patients with virtually untreatable fibroid disease achieved pregnancy after combined procedure(s). Rates of miscarriage, preterm delivery, and postpartum hemorrhage were higher than the general obstetric population; however, this population of patients is not typical and has additional risk factors. From our data, it appears that there is an increase in miscarriage, preterm deliveries, and postpartum hemorrhage, which may be explained by the increased age of the study population and the history of a fibroid uterus. There is a significantly increased rate of cesarean section compared with the national average. Taking the

demographics of the study population into account, we did not identify any other major obstetric risks.

We believe that our results have influenced the way in which patients with fibroids wanting to become pregnant should be counseled. For those patients with large and/or multiple submucous or interstitial fibroids where resection would be difficult and likely to recur and in those with failed previous fibroid surgery, UAE should be considered as an option for treatment with advice that a successful pregnancy outcome is possible after UAE. A randomized controlled trial of myomectomy versus UAE is required to optimally evaluate pregnancy rates but such a trial would be an enormously complex undertaking to accurately match patients in the 2 groups.

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Condensation: Pregnancy after uterine artery embolization for symptomatic fibroids has higher rates of cesarean section, miscarriage, preterm delivery, and postpartum hemorrhage but without other major obstetric risks.