Pregnancy after uterine artery embolization for fibroids

Sukhbir S. Singh MD FRCSC **Risa Bordman** MD CCFP FCFP **Nicholas Leyland** MD MHCM FRCSC

Pron G, Mocarski E, Bennett J, Vilos G, Common A, Vanderburgh L; for the Ontario UFE Collaborative Group. Pregnancy after uterine artery embolization for leiomyomata: the Ontario multicentre trial. *Obstet Gynecol* 2005;105(1):67-76.

Research question

What are the outcomes for women who become pregnant after uterine artery embolization (UAE) for symptomatic fibroids?

Type of article and design

Case series

Relevance to family physicians

Uterine fibroids (also known as leiomyomas or myomas) are common, with a prevalence of 30% among women of reproductive age.[1] While most women are asymptomatic and require no treatment, some are troubled by abnormal bleeding, pelvic pressure, infertility, or pain. Medications such as tranexamic acid and low-dose oral contraceptive pills might help with menorrhagia. Gonadotropin-releasing hormone agonists, danazol, and possibly the progestin intrauterine system might reduce the size of fibroids as well.[1]

Until recently, management of symptomatic fibroids refractory to medical treatment required surgical intervention. Options included myomectomy (excision), myolysis (destruction of fibroids or their blood supply by an energy source), and hysterectomy.

Uterine artery embolization, which was first described in 1995,[2] is a radiologic procedure where angiography is used to catheterize both uterine arteries. Tiny particles (usually polyvinyl alcohol) are injected into the arteries in order to decrease perfusion to uterine fibroids. This technique has been found to result in an 80% to 90% improvement in menorrhagia and a 50% to 60% reduction in size of fibroids.[2,3]

As with any invasive procedure, UAE carries some risk.[4] The rate of serious morbidity associated with UAE is about 5% and the mortality rate is 0.1 to 0.2/1000. Postembolization syndrome (pain, general malaise, nausea, vomiting, low-grade fever, and leukocytosis) occurs in up to 40% of women but usually resolves within 48 hours. Other risks include infection (1% to 2%), ovarian dysfunction (<10%), pain (5% to 10% at >2 weeks), transient (15%) or permanent (3%) amenorrhea, hysterectomy (1% to 2%), and inadvertent embolization of a malignancy. Risk can be minimized through careful patient selection and consultation with gynecologists and interventional radiologists.

To date, myomectomy has been considered the only surgical option for women desiring future fertility.[1] Although UAE is now an acceptable alternative for managing symptomatic uterine fibroids, its effect on future pregnancy and fertility remains unclear.

Overview of study and outcomes

During a 2-year period, 555 women underwent UAE for symptomatic uterine fibroids in 8 Ontario hospitals as part of the Ontario Uterine Fibroid Embolization Trial.[3] Among these 555 women, 164 (30%) desired future fertility.

Average age of enrolled patients was 43 years; 50% were nulliparous. Women desiring future fertility were not excluded but were informed of the uncertain effects of UAE on future pregnancies. Exclusion criteria were active pelvic inflammatory disease, undiagnosed pelvic mass, endometrial carcinoma, pregnancy, and renal insufficiency. There were no limitations on fibroid size or location or on patient age.

Patients were prospectively followed with interviews and ultrasound scans. Response rate was 92% at 1 year and 84% at 2 years. To address the question of pregnancy outcome, patients were asked whether they had been trying to conceive and whether they had been successful. Women who reported pregnancies were then asked to consent to further follow up and release of the appropriate information.

Results

After 2 years, 21 women reported 24 pregnancies (3 women became pregnant twice). Average age at UAE was 34 years (range 31 to 42 years). Before UAE, 14 of these patients had experienced 1 or more miscarriages, and 3 had had prior myomectomies. All 21 women reporting pregnancies had documented intramural or subserosal fibroids, 7 had a single fibroid (size ranged from 4.7 to 10.8 cm), and 14 had multiple fibroids. After UAE, overall fibroid volume was reduced by 46% (standard deviation 22%), and all women had resumed menses 2 months later. Average time from UAE to conception was 15 months (range 2 to 42 months).

Twenty-three of the pregnancies were conceived spontaneously; 1 was assisted through in vitro

fertilization. The pregnancies resulted in 18 live births (4 preterm), 4 spontaneous abortions, and 2 elective terminations. Average age at delivery was 36 years. Among the 24 pregnancies, 21 were managed by obstetricians and 3 by family physicians.

Fourteen women underwent trials of labour. Nine of these had vaginal deliveries, and 5 required cesarean section (3 for nonreassuring fetal heart rate tracings, 1 for failure to progress, and 1 for failed induction of labour). Four women had elective cesarean deliveries due to prior myomectomy (1), repeat cesarean delivery (1), and placenta previa with bleeding (2). Three pregnancies (17% of live births) were complicated by abnormal placentation. Two of these had complete placenta previa (1 had a partial accreta), and the third was found to have placenta membranacea that required a cesarean hysterectomy due to extensive bleeding.

Of the 18 live-born infants, 5 (3 of whom were preterm) had low birth weights and 1 had a very low birth weight (1055 g). Twelve were appropriate weight for gestational age. Results are summarized in the box below.

Summary of results

- 164 women desired future pregnancy (30% of original group)
- 24 pregnancies occurred in 21 women
- 18 live births, 4 spontaneous abortions, and 2 elective terminations resulted
- 3 pregnancies (17% of live births) had abnormal placentation
- 6 babies (33%) were born with low or very low birth weights (some were born preterm)
- 4 deliveries (22%) were preterm

Analysis of methodology

The original trial was not designed with fertility or pregnancy outcomes in mind, and, as a result, no detailed reproductive histories were taken or investigations done. Since women were specifically advised about the uncertainty around the effect of the procedure on future pregnancies, this warning could have introduced selection bias. Interpretation of the data was made difficult by the following confounding variables: advanced maternal age (increased risk of gestational hypertension, miscarriage, etc); prior medical and reproductive issues; and the effect of remaining fibroids on pregnancy outcomes.

The small number of reported pregnancies and the way in which these reports were gathered likely led to reporting bias. In the original study, 164 women said they were interested in future fertility, but only 35 reported trying to conceive 1 to 2 years later. It would be very important to find out why 129 women were not at least attempting to conceive, because it might have been due to infertility or adverse outcomes preventing pregnancy. Also, information was not collected on the 14 women who were trying to conceive but had not been successful.

Application to clinical practice

It is not always possible or ethical to develop randomized controlled trials to answer all our clinical questions. For most new procedures, case series are useful to establish incidence of complications and initial success rates. Although the Ontario Uterine Fibroid Embolization Trial was not designed to address reproductive outcomes, it does offer some initial insights into this important question. The trial demonstrated that it is possible to conceive and carry a pregnancy successfully to term after UAE. It also demonstrated the risk of abnormal placentation, low or very low birth weights, and preterm deliveries following the procedure. The occurrence of 3 abnormal placentas (17%) is especially notable because this is well above the baseline incidence of 0.3%. The confounding variables and selection bias make generalization from the results limited at best.

The small number of patients and the relatively high number of pregnancy complications is of concern and reinforces the importance of avoiding UAE for symptomatic fibroids in patients interested in conceiving in the future. If pregnancy does occur after UAE, patients can have a successful birth and delivery, but careful obstetric monitoring, and in particular placental assessment, is advised.

BOTTOM LINE

- Desired future pregnancy remains a relative contraindication to UAE for symptomatic fibroids.
- Successful pregnancy outcomes after UAE have been reported, but all pregnancies after UAE require close monitoring for complications.
- Obstetric risks after UAE for fibroids include prematurity, intrauterine growth restriction, abnormal placentation, and increased likelihood of cesarean delivery.

POINTS SAILLANTS

- Une grossesse future souhaitée demeure une contre-indication relative de l'EAU pour des fibromes symptomatiques.
- On a rapporté des issues de grossesses sans problème à la suite d'une EAU, mais toutes les grossesses après une EAU exigent une surveillance étroite pour dépister toute complication.
- Au nombre des risques obstétriques après une EAU pour des fibromes figurent la prématurité, la restriction de la croissance intra-utérine, les anomalies du placenta et la probabilité accrue d'un accouchement par césarienne.

Results of this Canadian study are similar to those of a recent UK study that reported 56 pregnancies after UAE and also found increased rates of preterm delivery and postpartum hemorrhage.[5] A recent review by Golderg and Pereira[6] emphasized that myomectomy (hysteroscopic, laparoscopic, or by laparotomy) should be the recommended treatment rather than UAE for women considering future fertility.

More work is required in this area. Ideally, a prospective trial should be set up to compare myomectomy with UAE and to look specifically at subsequent pregnancy outcomes.

Dr Singh *is currently in Sydney, Australia, at the Centre for Advanced Reproductive Endosurgery completing a fellowship in advanced gynecologic endoscopy.* **Dr Bordman** *is a family doctor in Toronto, Ont, and Chair of toolkit development for the Benign Uterine Conditions Project at the Centre for Effective Practice in the Department of Family and Community Medicine at the University of Toronto.* **Dr Leyland** *is Medical Director of the Women's, Children's, and Family Health Program and Chief of Obstetrics and Gynecology at St Joseph's Health Centre in Toronto, Ont, an Associate Professor of Obstetrics and Gynecology at the University of Toronto, and Co-Chair of the Benign Uterine Conditions Project.*

References

1. Lefebvre G, Vilos G, Allaire C, Jeffrey J. The management of uterine leiomyoma. SOGC Clinical Practice Guidelines, no. 128. May 2003. *J Obstet Gynaecol Can* 2003;25(5):396-418.
2. Lefebvre G, Vilos G, Asch M. Uterine fibroid embolization. SOGC Clinical Practice Guidelines, no. 150. October 2004. *J Obstet Gynaecol Can* 2004;26(10):899-911.
3. Pron G, Cohen M, Soucie J, Garvin G, Vanderburgh L, Bell S; for the Ontario Uterine Fibroid Embolization Collaboration Group. The Ontario Uterine Fibroid Embolization Trial. Part 1. Baseline patient characteristics, fibroid burden, and impact on life. *Fertil Steril* 2003;79(1):112-9.
4. Singh S, Vilos G, McLachlin M, Kozak R, Rebel M. Improving quality of care for patients undergoing arterial embolization for uterine fibroids: case report and review. *J Obstet Gynaecol Can* 2005;27(8):775-80.
5. Walker WJ, McDowell SJ. Pregnancy after uterine artery embolization for leiomyomata: a series of 56 completed pregnancies. *Am J Obstet Gynecol* 2006;195:1266-71.
6. Goldberg J, Pereira L. Pregnancy outcomes following treatment of fibroids: uterine fibroid embolization versus laparoscopic myomectomy. *Curr Opin Obstet Gynecol* 2006;18(4):402-6.

* * *

Critical Appraisal reviews important articles in the literature relevant to family physicians. Reviews are by family physicians, not experts on the topics. They assess not only the strength of the studies but the "bottom line" clinical importance for family practice. We invite you to comment on the reviews, suggest articles for review, or become a reviewer. Contact Coordinator **Michael Evans** by e-mail **michael.evans@utoronto.ca** or by fax 416 603-5821.