Uterine artery embolization for fibroids is associated with an increased risk of miscarriage

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Objective: To investigate how uterine artery embolization (UAE) might alter the risk profile for pregnancies complicated by fibroids.
Design: Systematic literature review and meta-analysis of existing studies.
Setting: Academic reproductive medicine unit.
Patient(s): Women with fibroids.
Intervention(s): A systematic literature review, raw data extraction, and data analysis.
Main Outcome Measure(s): Rates of miscarriage, preterm delivery, malpresentation, intrauterine growth restriction (IUGR), cesarean delivery, and postpartum hemorrhage (PPH).
Result(s): Two hundred twenty-seven completed pregnancies after UAE were identified. Miscarriage rates were higher in UAE pregnancies (35.2%) compared with fibroid-containing pregnancies matched for age and fibroid location (16.5%) (odds ratio [OR] 2.8; 95% confidence interval [CI] 2.0–3.8). The UAE pregnancies were more likely to be delivered by cesarean section (66% vs. 48.5%; OR 2.1; 95% CI 1.4–2.9) and to experience PPH (13.9% vs. 2.5%; OR 6.4; 95% CI 3.5–11.7). Rates of preterm delivery (14% vs. 16%; OR 0.9; 95% CI 0.5–1.5), IUGR (7.3% vs. 11.7%; OR 0.6; 95% CI 0.3–1.3), and malpresentation (10.4% vs. 13%; OR 0.8; 95% CI 0.4–1.5) were similar in UAE pregnancies and in control pregnancies with fibroids.
Conclusion(s): The risk of miscarriage seems to be increased after UAE. In contrast, apart from an increased risk of abdominal delivery and PPH, critical adverse obstetric sequelae of IUGR and prematurity appear no more likely after UAE. (Fertil Steril® 2009;■:■–■. ©2009 by American Society for Reproductive Medicine.)

Key Words: Uterine artery embolization, UAE, miscarriage, pregnancy, fibroids, myomectomy

Uterine artery embolization (UAE) is fast gaining in popularity as an organ-preserving approach for treating symptomatic uterine fibroids. There is compelling evidence that UAE is a safe and effective alternative to hysterectomy for alleviating fibroid-associated bleeding problems and pressure symptoms (1–3). Data on pregnancies after UAE continue to accrue and demonstrate that women can and do conceive and have uncomplicated deliveries of healthy offspring. However, largely based on earlier reports suggesting increased risks of adverse pregnancy outcomes after UAE (4, 5), the American College of Obstetricians and Gynecologists recommended that UAE should be considered investigational or relatively contraindicated in women wishing to retain fertility (6).

One of these reports was the most recent comprehensive review on pregnancies after UAE for fibroids undertaken about 5 years ago (5). In addition to reviewing pregnancies after UAE, another objective of this study was to compare pregnancy outcomes in women who had either had UAE or laparoscopic myomectomy for the treatment of their fibroids. These investigators obtained all the data available at the time in the world literature regarding pregnancy outcome after UAE, representing a total of 51 completed pregnancies. The laparoscopic myomectomy group was derived from three of the largest published series of pregnancy after laparoscopic myomectomy, constituting a total of 139 pregnancies. When compared with pregnancies after laparoscopic myomectomy, they found that obstetric outcomes in pregnancies after UAE were at significantly higher risk for preterm delivery (odds ratio [OR] 6.2; 95% confidence interval [CI] 1.4–27.7) and malpresentation (OR 4.3; 95% CI 1.0–20.5). Based on this, these investigators concluded that pregnancies after UAE are at increased risk compared with pregnancies after laparoscopic myomectomy, strengthening the viewpoint that UAE impacts negatively on pregnancy success.

Implicit in the recommendation of the American College of Obstetricians and Gynecologists is the notion that UAE induces effects that confer additional deterrents to successful pregnancy outcome in women with fibroids. However, previous studies do not allow this conclusion to be drawn as none compared pregnancy outcomes in women with fibroids with those who had had UAE for treatment of fibroids. Instead, existing studies indicate that for women with symptomatic fibroids who are candidates for surgery, surgical intervention is associated with fewer pregnancy complications than UAE (5, 7, 8). But what of women who may elect to pursue UAE either by desire to avoid surgery or because their fibroids are too technically challenging for a surgical approach?

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What evidence is there that can be drawn upon to satisfactorily counsel this group regarding the potential risks or benefits that might be anticipated should they conceive after UAE?

To explore pregnancy outcomes after UAE, we conducted an exhaustive review of the world literature. The aim of this study was twofold: first to provide an up-to-date account of UAE pregnancies and second, to compare pooled data from the UAE pregnancies so identified with age-matched pregnancies in which fibroids were known to be present. In contrast to previous data that compared UAE with other treatment modalities (5, 7, 8) the design of our study sought to explore how embolization or its sequelae might influence key reproductive end points including miscarriage, preterm delivery, intrauterine growth restriction (IUGR), malpresentation, cesarean delivery, and postpartum haemorrhage (PPH).

MATERIALS AND METHODS

Search Strategy

Relevant studies were identified by a literature search of MEDLINE, EMBASE, Cochrane, OVID, and PubMed using the search terms "uterine artery embolisation," "UAE," and "pregnancy." Reference lists of retrieved articles were then hand-searched for further studies.

Institutional Review Board (IRB) approval was not sought as this was deemed unnecessary given that all data were extracted from previously published studies.

Inclusion Criteria and Analysis of Pregnancy Outcomes

Studies were included if they reported on completed pregnancies after a series of UAE cases conducted for symptomatic fibroids. Pregnancies occurring after UAE for nonfibroid pathology were excluded. Individual case reports were excluded on the basis of a potential for inherent bias in reporting pregnancy outcomes. For instance, on the basis of these criteria, a small series of six pregnancies after UAE was excluded as it involved four cases that were undertaken for adenomyosis-related complaints leaving only two that were undertaken purely for leiomyomata (9).

Our analyses were based on one early pregnancy complication, miscarriage, and five late (or obstetric) complications including preterm delivery (delivery at <37 completed weeks gestation), malpresentation, IUGR (<5th birthweight centile), cesarean section delivery, and PPH. Miscarriage rates were calculated by dividing the total number of miscarriages by the total number of completed pregnancies excluding ectopic pregnancies and voluntary terminations. The rates of obstetric complications were derived by dividing the total number of each event by the total number of completed singleton pregnancies excluding miscarriages, ectopic pregnancies, and elective terminations.

The Studies

Previously, the most recent review of the literature identified 51 eligible pregnancies after UAE for symptomatic fibroids (5). Our search identified an additional 176 completed pregnancies meeting our eligibility criteria from 7 reports that have since been published (7, 8, 10–14). In total therefore, we report on the outcomes of 227 completed pregnancies arising after UAE, the outcomes of which are summarized in Table 1.

Among the seven reports, there are five observational studies (10–14), one prospective cohort-controlled study comparing UAE and laparoscopic uterine artery occlusion (7), and one randomized controlled study of UAE versus myomectomy (8). Pregnancy numbers ranged from 9 in the smallest series (11) to 62 in the largest (14). Data on patient age were available for all UAE studies identified.

Three studies provided complete data for all parameters analyzed (5, 7, 13). The review by Goldberg et al. (5) was comprised of 51 pregnancies, the majority of which were derived from two prior reports (15, 16), in addition to additional unpublished cases that were obtained by direct contact with the investigators of these two reports. Pron et al. (13) reported on pregnancy outcomes obtained during the Ontario Multicenter Study, which evaluated 555 women undergoing UAE for symptomatic fibroids (17). In this population, after excluding 2 elective terminations, there were 22 relevant pregnancies identified by telephone interview during their 5-year follow-up period. Holub et al. (7) conducted a prospective cohort-controlled study, undertaken in the Czech Republic, designed to compare pregnancy outcomes after UAE and after combined laparoscopic uterine artery occlusion and laparoscopic myomectomy. Among 39 women successfully treated with UAE, there were a total of 28 pregnancies of which 4 were excluded (1 ongoing, 1 ectopic, and 2 terminations).

The HOPEFUL study (Hysterectomy Or Percutaneous Embolisation For Uterine Leiomyomata) was a multicenter retrospective cohort study involving 18 United Kingdom NHS hospital trusts aimed at comparing UAE with hysterectomy during the medium term (18). Dutton et al. (10) reported on the main results of the HOPEFUL study regarding safety and efficacy of UAE compared with hysterectomy and also reported on pregnancy outcomes after UAE that were gathered by patient questionnaire. During an average follow-up of 4.6 years among 649 women receiving UAE from 1996–2002, there were 34 relevant pregnancies after excluding 2 ectopic pregnancies and 1 termination. Outcome data were available for miscarriage rates and mode of delivery (Table 1).

Subsequent to the commencement of a prospective observational study on UAE in December 1996 (19), Walker and co-workers established a database of UAE pregnancies in 2003 at which time a screening questionnaire identified 26 completed pregnancies (20). Subsequent to this, pregnancies were identified on a prospective basis using a combination of annual questionnaire survey and self-reporting. These investigators have since reported on 56 UAE pregnancies arising out of this cohort (21), with the most recent tally reaching

TABLE 1

Pregnancy complications after UAE.

Study	No.	Miscarriage (%)	Preterm (%)	CS (%)	Malpresentation (%)	IUGR (%)	PPH (%)
Goldberg et al., 2004	51	12/51 (23.5)	5/32 (15.6)	22/35 (62.9)	4/35 (11.4)	1/22 (4.5)	2/35 (5.7)
Pron et al., 2005	22	4/22 (18.2)	4/18 (22.2)	9/18 (50)	1/18 (5.6)	4/18 (22.2)	3/18 (16.7)
Walker & McDowell, 2006[a]	50	-	-	-	3/33 (9.1)	1/33 (3.3)	6/33 (18.2)
Walker & Bratby, 2007[a]	62	20/62 (34)	5/42 (11.9)	27/40 (67.5)	NR	NR	NR
Holub et al., 2007	24	14/24 (58.3)	2/10 (20)	8/10 (80)	2/10 (20)	1/10 (10)	2/10 (20)
Dutton et al., 2007	34	15/34 (44.1)	NR	15/19 (78.9)	NR	NR	NR
Mara et al., 2008	14	9/14 (64.3)	0/5 (0)	3/5 (60)	NR	0/5 (0)	1/5 (20)
Kim et al., 2008	9	3/9 (33.3)	0/6 (0)	5/6 (83.3)	NR	NR	NR
Pabon et al., 2008	11	3/11 (27.3)	1/8 (12.5)	4/8 (50)	NR	0/8 (0)	NR
Cumulative data	227	80/227 (35.2)	17/121 (14)	93/141 (66)	10/96 (10.4)	7/96 (7.3)	14/101 (13.9)

UAE = uterine artery embolization; No. = total number of pregnancies excluding ectopic pregnancies, elective terminations, and ongoing pregnancies; NR = not recorded; CS = cesarean sections; IUGR = intrauterine growth restriction; PPH = postpartum hemorrhage.

[a] This series of post-UAE pregnancies from Walker and others is continually being updated. The 2007 article contains the latest figures for miscarriage, preterm delivery, and CS, whereas the preceding article (2006) contains data for malpresentation, IUGR, and PPH.

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67 pregnancies among 108 women trying to conceive (14), representing the largest individual series of UAE pregnancies published to date. The 2007 study (14) provides the most recent figures for miscarriage, preterm delivery, and cesarean delivery, whereas data on malpresentation, IUGR, and PPH were only available in the 2006 article (21), hence the inclusion of both articles in Table 1.

Three additional studies were published earlier this year regarding pregnancy subsequent to UAE (8, 11, 12). Kim et al. (11) prospectively followed up 87 patients treated with UAE during a 3-year period, 41 of whom had uterovarian anastomoses. Fifteen pregnancies were recorded among 19 women attempting to conceive of which 5 resulted in terminations and 1 was an ectopic. Data were available for miscarriage rates, preterm delivery, and cesarean sections. Mara et al. (8) is the only randomized controlled trial published to date involving UAE in women harboring reproductive ambitions. There were 58 cases in the UAE arm versus 63 in the myomectomy arm (42 laparoscopic and 21 open). There were a total of 17 pregnancies in the UAE group among 26 women attempting conception during a mean follow-up of 24 months. After excluding 1 ectopic pregnancy, 1 termination, and 1 pregnancy that was still ongoing, 14 pregnancies were eligible for our analysis for which data could be extracted for all complications with the exception of malpresentation. Finally, the most recent series is a prospective observational study of pregnancies after UAE that was undertaken in 100 women between January 2002 and June 2006 (12). All 11 pregnancies met our eligibility criteria from which figures could be extracted for miscarriage rates, prematurity, mode of delivery, and IUGR.

Information regarding fibroid subtype were available for five of the eight studies included (7, 8, 12–14). In all studies where fibroid subtype was known, the overwhelming majority of cases were for intramural tumors. Patients with submucosal fibroids were excluded in three studies (7, 8, 13) and one study excluded subserosal fibroids (8). Two studies included a variety of fibroid locations, with intramural being the predominant subtype (12, 14).

For our control group, that is, pregnancies that were known to be complicated by the existence of fibroids, we selected studies that were identified in recent systematic reviews addressing the impact of fibroids on reproductive outcome (22–24). Given that individual fibroid subtypes have differing effects on miscarriage rates with submucosal and intramural categories being the most detrimental and subserosal less so (22–24), it was important to select a control group having comparable fibroid subtypes to those in women having UAE. On the basis of the five articles discussed in the preceding paragraph that identified intramural fibroids as the predominant category in UAE patients (7, 8, 12–14), we selected patients derived from 14 studies having intramural fibroids as the principal fibroid component (25–38) for comparative analysis of miscarriage outcomes. With regard to the control group for obstetric outcomes, we selected patients from 10 controlled studies that examined late pregnancy complications in women with fibroids (25, 28, 39–46).

Statistical Analysis

Statistical analysis was performed using Prism software (GraphPad Software, Inc.). Summary statistics for age are presented as means ± SD and for categorical variables are

shown as OR and 95% CI. Comparisons between continuous variables were performed using the Student's *t*-test, whereas categorical data were analyzed using 2×2 contingency tables in combination with Fisher's exact test. *P* values less than .05 (two-tailed) were considered to be statistically significant.

RESULTS

A total of 227 completed pregnancies after UAE were collected from the 8 included studies (5, 7, 8, 10–14). The mean age of the women at the time of conception after embolization was 35.4 ± 2.1 years. With regard to miscarriage rates, the control group was comprised of a total of 1,121 pregnancies having intramural fibroids derived from 14 studies (25–38). The mean age of the control group was 34.7 ± 1.4 years and was no different from that of the UAE group (*P*=.42; 95% CI -2.3–1.0).

For comparative analysis of obstetric outcomes, the control group was derived from a total of 4,454 pregnancies from 10 studies addressing pregnancies complicated by fibroids (25, 28, 39–46). Among these 4,454 pregnancies, not all were informative for all the main obstetric outcome measures assessed. The number of pregnancies available for analyzing each obstetric outcome is detailed in Table 2 and is as follows: 1,145 pregnancies for preterm delivery, 3,585 pregnancies for malpresentation, 961 pregnancies for IUGR, 4,322 pregnancies for cesarean delivery, and 3,535 pregnancies for PPH. The mean age of patients in the obstetric outcomes control group was 33.2 ± 1.2 years. When compared with this group, UAE patients demonstrated a nonsignificant trend toward being older (*P*=.1; 95% CI -4.7–0.40).

For the analysis of miscarriage rates, given that maternal age and fibroid subtype are two influential determinants of early pregnancy loss, we sought to use two groups that were matched as much as possible for these two parameters. Referring to studies identified in recent reviews, the pooled miscarriage rate among 1,121 pregnancies with untreated intramural fibroids was 16.5% (25–38) (Table 3). In stark contrast, we found that the overall miscarriage rate for all 227 UAE pregnancies was 35.2%, more than double that for the control group (*P*<.0001; OR 2.8; 95% CI 2.0–3.8) (Table 3). When we compared the miscarriage rate for the 60 pregnancies in the three UAE studies in which submucosal fibroids were excluded (7, 8, 13), the difference was even more pronounced (45% in the UAE group vs. 16.5% in controls; *P*<.0001; OR 4.1; 95% CI 2.4–7.1) (Table 3).

Next we focused on obstetric outcome data (Table 2) for which we were able to compare groups that did not differ significantly in age. As the studies examining obstetric outcome did not characterize fibroids by subtype (25, 28, 39–46), it was unrealistic to expect to accurately match groups by fibroid location. We found that pregnancies after UAE were no more likely to suffer increased rates of preterm delivery (14% vs. 16%; *P*=.69), malpresentation (10.4% vs. 13%; *P*=.56), or IUGR (7.3% vs. 11.7%; *P*=.24) than pregnancies with fibroids (Table 2). In contrast, rates for cesarean section (66% vs. 48.5%; *P*<.0001) and PPH (13.9% vs. 2.5%; *P*<.0001) demonstrated highly significant increases in the UAE cohort (Table 2). Overall, therefore, treatment with UAE does not increase the risk for critical obstetric complications of preterm delivery and IUGR but is associated with marked increases in the rates of abdominal delivery and PPH.

DISCUSSION

Many women with symptomatic fibroids who wish to retain their fertility will be put forward for UAE if they are unsuitable candidates for surgery. For such women, the results of comparative studies conducted to date are of little relevance as all three have compared UAE with surgical interventions (5, 7, 8). Instead, it would be important for these women to know whether the process of embolization might introduce any additional reproductive risks over and above those associated with their original pathology or indeed whether their fertility prospects might be improved. This type of information is not readily forthcoming from existing studies as none compare UAE pregnancies with a control group of pregnancies having untreated fibroids.

With regard to early pregnancy complications, our analyses revealed that the risk of miscarriage is almost three times as high after UAE compared with cases in which fibroids are left untreated (Table 3). There are a number of fibroid characteristics that can independently influence the risk of miscarriage. One of the most important of these characteristics is

TABLE 2

Comparison of obstetric complications.

Complication	UAE (%)	Fibroids (%)	*P* value	OR	CI
Preterm delivery	17/121 (14)	183/1145 (16)	.69	0.9	0.5–1.5
Malpresentation	10/96 (10.4)	466/3,585 (13)	.56	0.8	0.4–1.5
IUGR	7/96 (7.3)	112/961 (11.7)	.24	0.6	0.3–1.3
Cesarean section	93/141 (66)	2,098/4,322 (48.5)	<.0001	2.1	1.4–2.9
Postpartum hemorrhage	14/101 (13.9)	87/3,535 (2.5)	<.0001	6.4	3.5–11.7

UAE = cumulative figures derived from Table 1; Fibroids = data for pregnancies complicated by fibroids; OR = odds ratio; CI = confidence interval.

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TABLE 3

Comparison of miscarriage rates.

	UAE (%)	Fibroids (%)	*P* value	OR	95% CI
Miscarriage[a]	80/227 (35.2)	185/1,12 1 (16.5)	<.0001	2.8	2.0–3.8
Miscarriage[b]	27/60 (45)	185/1,12 1 (16.5)	<.0001	4.1	2.4–7.1

UAE = uterine artery embolization; OR = odds ratio; CI = confidence interval.
[a] Includes all pregnancies in UAE patients.
[b] Restricted to pregnancies in UAE patients in whom submucosal fibroids were excluded.

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fibroid subtype with recent meta-analyses consistently demonstrating that the risk of miscarriage is greatest for submucosal and intramural subtypes and negligible for the subserosal variety (22–24). We compared miscarriage rates in UAE patients with that in women having predominantly intramural fibroids on the basis that this was the predominant subtype in the five UAE studies in which information on fibroid location could be extracted (7, 8, 12–14). It remains possible, however, that the three UAE studies in which fibroid location was not stated (5, 10, 11) may have contained a disproportionate amount of submucosal fibroids, which, by virtue of greater uterine cavity distortion, could have underpinned the higher rates observed in the UAE group. Although we cannot conclusively disprove such an assertion, we believe that a number of factors lessen the likelihood of this being the case. First, fibroids that are predominantly submucosal are far more likely to have been treated through hysteroscopic resection (47) than to have been allocated to treatment by embolization. Second, when we subanalyzed the three UAE studies in which patients with submucosal fibroids were excluded from treatment (7, 8, 13), the miscarriage rates after UAE were not reduced but were in fact increased from 35%–45% (Table 3). Third, the miscarriage rates were comparable between the five studies with known fibroid location and the three studies where location was unknown (40.4% vs. 44.8%; *P*=.78). Overall, therefore, our results support the contention that UAE may increase the risk of miscarriage in women with fibroids.

With regard to other fibroid characteristics, such as size, number, and location (fundal, anterior wall, or posterior wall), it could be argued that heterogeneity between the two groups may have contributed to the differences in miscarriage rates that we observed. Regrettably, a meaningful comparison between the UAE and control groups in terms of these features was not possible either due to lack of sufficient data or because of differences in how data were reported. For instance, only two reports in the control group (34, 36) and none in the UAE group commented on fibroid location. Among the control group, the parameter used for reporting fibroid size in 11 of 14 studies was mean diameter (25, 27, 30–38), whereas in the UAE group, 3 studies provided only the diameter of the largest fibroid (5, 8, 13) and 4 studies measured fibroid volumes (7, 11, 12, 14). With regard to fibroid numbers, 8 of 14 control studies reported mean numbers (25, 27, 30–32, 34–36), whereas this information was forthcoming in only 1 of 8 UAE articles (13).

The available evidence does, however, tend to suggest that patients in the UAE group may have had a more severe fibroid burden than controls. In three UAE studies, the largest fibroids were in excess of 8 cm (5, 8, 14) and accounted for 14% of all fibroids in one report (8). In contrast, the evidence from control studies suggests that in the majority of instances, patients with fibroids larger than 8 cm were excluded. In addition, in two UAE studies a substantial proportion of patients possessed more than five fibroids (8, 14), whereas the mean fibroid number from the eight control studies in which this information could be gleaned was 1.8 (25, 27, 30–32, 34–36). Indeed, although Walker and McDowell (21) did not detail fibroid numbers, they commented that their UAE patients often possessed multiple complex fibroids of large size that precluded other treatment modalities. Ensuring that fibroid burden is comparable between treatment and control groups will therefore be an important goal of any future prospective studies in this area.

Other potential confounding factors are patient-specific characteristics, such as maternal age, body mass index (BMI), and parity, which may exert independent effects on pregnancy outcomes. Among these, maternal age is arguably the most influential with advancing female age strongly associated with increased risks for embryonic aneuploidy and consequently with an exponential increase in miscarriage rates (48). Notably, our results are not due to biases between the two groups in terms of maternal age. We could not, however, account for other factors as no more than half of the studies in each group reported on parity and only two studies in the control group (35, 38) and none in the UAE group recorded BMI.

An inherent weakness of this study highlighted in the foregoing discussion is that it combines results from multiple disparate studies and reports aggregate outcomes. For instance, the control group was derived primarily from infertility patients (12 of 14 studies) who were largely asymptomatic (26, 27, 29–38). In contrast, UAE patients were symptomatic and occasionally had undergone previous forms of fibroid treatment. This heterogeneity in population demographics would be expected to compromise to some extent the

reliability of results derived from our pooled data sets. We could not account for this heterogeneity in our statistical analysis.

Notwithstanding these potential limitations, the increase in miscarriage rate is impressive and suggests that the endometrial cavity incurs irreversible damage as a consequence of embolization. One possibility is that UAE-induced endometrial ischemia imparts a marked deleterious effect on potential implantation sites. In support of this, there have been case reports of endometrial atrophy after UAE (49) and even of uterine necrosis requiring hysterectomy (50). The UAE might alter the embryo–endometrium interface through other mechanisms. The UAE does not eliminate fibroids completely but instead induces a reduction in fibroid volume of ~50%–60% (2, 51) and could result in distortion of the endometrial cavity. Among 51 women who were followed up by hysteroscopy after UAE for intramural fibroids, there was intrauterine protrusion of the fibroid remnant in 37%, intrauterine or cervical adhesions in 14%, and a communication between the myoma and the endometrial cavity in 10%; in only 37% of cases was hysteroscopy completely normal (52). Any distortion of the endometrial cavity as a consequence of UAE in combination with relative endometrial ischemia are almost certain to escalate the risk of early pregnancy failure.

Reassuringly, for pregnancies that successfully negotiate the early stages, our data do not reveal any increased risk for preterm delivery, malpresentation, or IUGR when compared with women with untreated fibroids (Table 2). These results contrast sharply with earlier suggestions that UAE imparts higher risks for prematurity and malpresentation and suggests that failure to control for key confounding variables, such as maternal age, may have influenced the results (5). Based on our analysis, pregnancies do, however, remain at heightened risk for cesarean section and for PPH. A lower threshold for elective cesarean section is perhaps not surprising as practitioners may adopt a cautionary approach in women in whom the integrity of the myometrium is potentially compromised. It must also be remembered that UAE does not remove fibroids and the mere presence of such tumors could sway decision away from vaginal delivery. In one series of completed pregnancies after UAE, 72.7% (24/33) of live births were delivered by cesarean section of which 54.2% (13/24) were elective with fibroids being the indication in 69.2% (9/13) of these (21). In addition, the increased risk of malpresentation associated with pregnancies in women with fibroids does not appear to be reduced by UAE.

As with miscarriage analyses, we would urge some measure of caution when interpreting the obstetric comparisons. Studies from which the control fibroid population were derived were very often retrospective and susceptible to ascertainment bias as they frequently identified fibroids after patients developed complications such as pain or underwent cesarean delivery (22). This contrasts with the studies that formed the basis for the miscarriage controls, which often identified and characterized fibroids in asymptomatic patients undergoing IVF (22). That said, it is encouraging that there was no increased risk in important obstetric end points of prematurity and IUGR, although the UAE group exhibited a tendency toward more advanced female age. Our data are entirely consistent with the results of the two recent prospective studies that do not reveal any increased obstetric risks after UAE when compared with either myomectomy or laparoscopic uterine artery occlusion (7, 8). The increased risk of PPH that we observed in UAE pregnancies is likely to be a consequence of the increased rates of cesarean delivery. We cannot, however, rule out the possibility that some degree of myometrial compromise consequent on embolization-induced ischemia might contribute to a reduced capacity for efficient contractility after delivery and consequently to uterine atony.

In striking contrast to myomectomy for fibroids, which might confer benefits regarding fertility prospects (23), our data indicate that UAE is not only not beneficial, it may actually be hugely counterproductive to the safety of early pregnancy. The results presented herein support the current recommendation that UAE be considered a relative contraindication among women wishing to retain their fertility (6). Notably, however, based on our analyses, this vindication is not due to the perceived UAE-related obstetric risks on which the original recommendation was made (5), but instead relates to a substantial increased risk of early pregnancy loss. Interestingly, two small prospective studies comparing UAE and surgical intervention indicate significantly higher miscarriage rates after UAE but no difference in obstetric outcomes (7, 8), thereby supporting our assertion that early pregnancy may become particularly vulnerable after embolization. Ideally, to formally address the impact of embolization on pregnancy risk profiles, a prospective study that incorporates a UAE arm and a nontreatment arm would be required. In lieu of further evidence, a cautious approach in recommending UAE to women desirous of pregnancy remains justified.

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