GYNECOLOGY

Clinical investigation of fertility after uterine artery embolization

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BACKGROUND: Uterine artery embolization is an effective and safe technique for the treatment of uterine fibroids, but its use remains controversial for women who wish to procreate.

OBJECTIVE: This study aimed to study the clinical, anatomic, and obstetrical results of uterine artery embolization in patients of childbearing age not eligible for myomectomy.

STUDY DESIGN: This was a retrospective cohort study of 398 female patients under the age of 43 years who were treated by uterine artery embolization between 2003 and 2017 for symptomatic fibroids and/or adenomyosis. Uterine artery embolization was performed according to a standardized procedure (fertility-sparing uterine artery embolization technique), with ovarian protection in the event of dangerous utero-ovarian anastomosis. Magnetic resonance imaging and pelvic ultrasounds were performed before and after uterine artery embolization.

RESULTS: The overall clinical success rate (ie, resolution of pre-embolization symptoms such as heavy menstrual bleeding, iron-deficiency anemia, pelvic pressure) was 91.2%, and there were no major complications. One year after uterine artery embolization, we observed a mean 73% reduction in myoma volume. A total of 108 patients (49.3%) presented with dangerous utero-ovarian anastomosis and 33 (14.5%) benefited from ovarian protection. In our group, there were 148 pregnancies and 109 live births; 74 children were born at term; 23 were born preterm, on average at 35.12±2.78 weeks. Including preterm births, the mean birthweight and birth length of the children were within normal limits. Restoration of uterine anatomy and ovarian protection were identified as the main predictive factors for obstetrical success. Restoration was also a major predictive factor for clinical success and was associated with a lower rate of miscarriage.

CONCLUSION: This study provided detailed clinical and obstetrical outcomes for 398 female patients who underwent uterine artery embolization for fibroid treatment; it contributes to the identification of anatomic and technical factors that could have an impact on fertility after uterine artery embolization. Further controlled clinical trials are needed to confirm our findings and reevaluate this procedure's indications and limitations for women with a desire to procreate.

Key words: adenomyosis, fertility, interventional radiology, leiomyomas, sterility, uterine artery embolization, uterine fibroids

Introduction

Uterine fibroids and adenomyosis are frequent, benign, and often symptomatic conditions in women of childbearing age that can affect fertility, pregnancy, and childbirth.[1–5] Currently, myomectomy is the leading treatment for women wishing to procreate, and its indications were recently published by the American Society for Reproductive Medicine[1] and other learned societies.[2–4]

Despite the fact that uterine artery embolization (UAE) is seen as a safe and effective alternative treatment for appropriately selected women who wish to retain their uterus,[2] the effects of UAE on pregnancy remain understudied.[2] Presently, UAE remains highly controversial for women wishing to procreate, in particular owing to a presumably high rate of miscarriage[6–12] and high risks of placental abnormalities and postpartum hemorrhage (PPH).[7,9,12,13]

Several publications have shown the ability to have normal pregnancies after uterine embolization, but these dealt with modest cohorts over short periods.[8–10,14] Recently, Pisco et al[15] reported a series of 150 births with a 50.7% fertility rate and a 12.6% miscarriage rate using a partial embolization technique. Torre et al[16] published a prospective study on ovarian reserve and pregnancies after embolization with encouraging results, but here again, it only focused on a small number of patients. Therefore, American,[2,17] French,[3] and Canadian[4] learned societies do not recommend UAE for women with a desire to procreate.

This study provides a detailed analysis of fertility outcomes based on a single-center, retrospective cohort of 398 women under 43 years of age who underwent UAE for fibroids that were not eligible for myomectomy between 2003 and 2017.

Materials and Methods

Patients

All patients presented with one or more symptomatic fibroids and were referred to O.S.C. by their gynecologist. Before their referral, the feasibility of conventional myomectomy was assessed by the gynecologists according to the French guidelines[3] for the therapeutic management of uterine fibroid tumors. UAE indications were the occurrence of a single fibroid measuring more than 5 cm (volume, >40 cm^3) and/or the occurrence of several fibroids and/or adenomyosis. Any suspicion of a malignant or inflammatory or infectious disease was a contraindication for UAE.

The inclusion criteria for the study were an age of 43 years or under and UAE between January 2003 and December 2017. Adenomyosis and desire for fertility retention were not exclusion criteria. Patients lost to follow-up were not used in the analysis: consequently, of the 676 patients assessed for eligibility, a total of 398 were included in the study.

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AJOG at a Glance

Why was this study conducted?

This study aimed to evaluate clinical, anatomic, and obstetrical outcomes of uterine artery embolization (UAE) in patients of childbearing age not eligible for myomectomy.

Key findings

Among the 398 subjects who underwent UAE, there were 148 pregnancies and 109 live births. Complete necrosis of the treated lesions with restoration of uterine anatomy and ovarian protection were identified as the main predictive factors for obstetrical success.

What does this add to what is known?

UAE is known to be an effective and safe technique for the treatment of uterine fibroids, but its use remains controversial for women who wish to procreate. This study adds to the growing body of literature investigating the effects of UAE on fertility and could thus contribute to the reevaluation of this procedure's indications and limitations for women with a desire to procreate.

All of these patients had records including duplicates of the images from the embolization procedure with vascular anatomy and details concerning the technique used. These patients' records were supplemented by interviews with the gynecologist or general practitioner and by a direct telephone questionnaire with the patient. The following variables were collected:

- Preembolization: age, parity, symptoms (heavy menstrual bleeding, iron-deficiency anemia, pelvic pressure), gynecologic history (endometriosis, tubal disease, ovarian disease, sterility), history of early pregnancy failure (unsuccessful in vitro fertilization [IVF], miscarriage), wish to procreate, and comorbidities.
- Postembolization: symptoms, recurrence, secondary myomectomy and/or hysterectomy and/or embolization, and pregnancy occurrence. In the event of a patient becoming pregnant after UAE, we also recorded the obstetrical outcome (live birth, miscarriage, abortion), the length of pregnancy, the mode of delivery, and the child's characteristics (weight, height, normality). Clinical success was defined as resolution of the symptoms described above.

This study was conducted in concordance with the French legislation on biomedical research (Jarde law, n° 2012-300 du March 5, 2012, modified by ordinance n° 2016-800 du June 16, 2016). It was validated by the National Center for Informatic Liberties. Our declaration is recorded and accessible under the following reference: REF2219088. All data were anonymized. All patients signed an informed consent form before undergoing UAE. Verbal consent for the study was obtained from all patients who could be contacted by phone.

Preembolization magnetic resonance imaging

A pretherapeutic pelvic magnetic resonance imaging (MRI) scan with intravenous contrast was systematically performed to be able to more accurately determine the location and number of the fibroids and the volume of the dominant fibroid. The MRI scan also studied their impact on the uterine cavity and screened for associated adenomyosis. On this basis, the location of each fibroid was classified into one of the following categories: 1 submucosal fibroid (the International Federation of Gynecology and Obstetrics [FIGO] 0, 1, 2, or 3), 1 transmural fibroid (FIGO, 4 or 2−5), 1 subserosal fibroid (FIGO 6),[18] 2 myomas, polymyomatous uterus, adenomyosis+fibroids, or pure adenomyosis. MRI diffusion sequences provided a histopathologic approach to rule out uterine sarcoma and cervical or ovarian malignancy. After this examination, the interventional radiologist and gynecologist discussed each embolization.

Postembolization imaging

A pelvic MRI scan was systematically scheduled 3 months after UAE to confirm the complete necrosis of the treated lesions; this was followed by a consultation with a letter for the referring gynecologist. Anatomic progression was then monitored by ultrasound every 3 months for 1 year after UAE. The uterine cavity was considered "normal" if there were no leiomyomas distorting the cavity and if the endometrium was regular with a normal thickness for the stage of the menstrual cycle. Depending on the result and the morphologic progression, in particular migration to the cavity, a second MRI scan could be performed after 6 to 9 months.

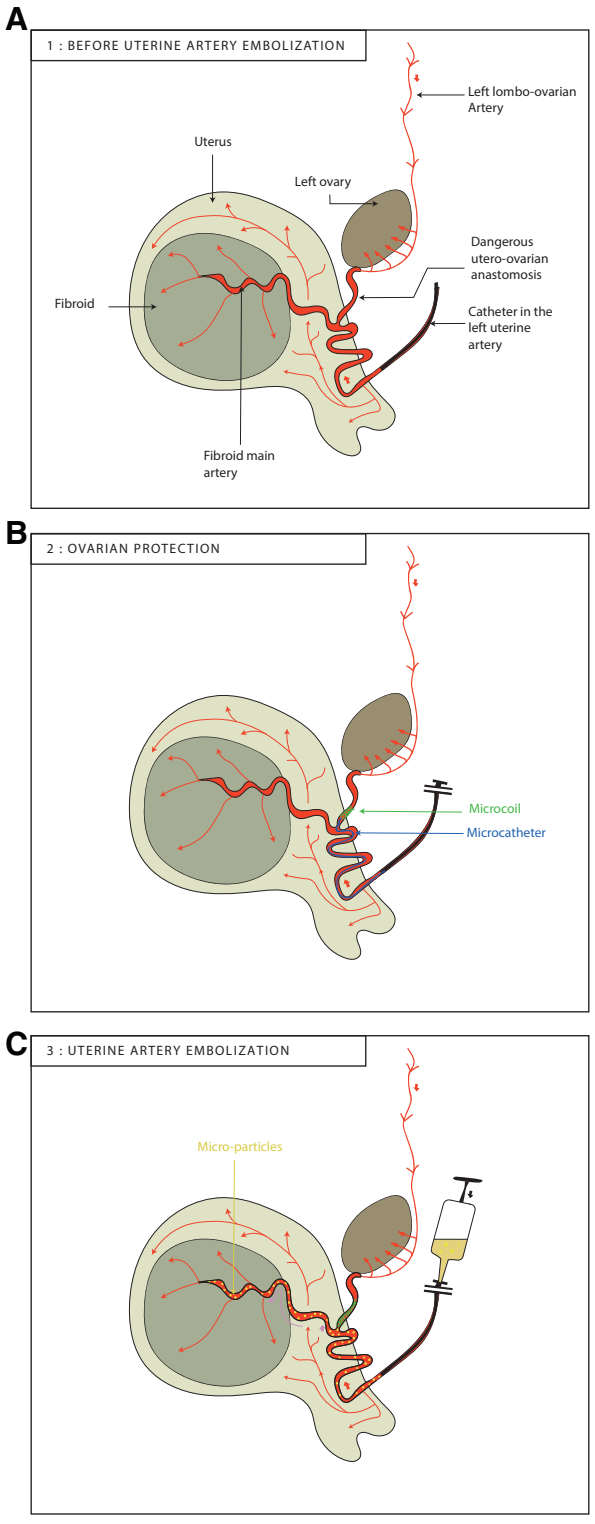
The following variables were collected by ultrasound 1 year after UAE: fibroid expulsion, volume in the event of a residual fibroid and uterine restoration (ad integrum restoration, partial restoration, nonrestoration) (classification details are given in Supplemental Data 1).

Procedure

Patients were informed of the risks and benefits associated with UAE and were provided with updated data on UAE's effects on fertility. They were also informed that they could abstain from therapy.[2,5] All procedures were performed by O.S.C, in 2 private clinics (Clinique du Parc, Castelnau-le-Lez, and Clinique du Millénaire, Montpellier, France) and at Béziers Hospital, affiliated with Montpellier University Hospital.

The "fertility-sparing UAE technique," described by Pelage et al,[19,20] was applied. If necessary, it was supplemented by ovarian protection to prevent inappropriate embolization of the ovaries and redirect the flow of particles to the uterine lesions to be treated[21] (Figures 1 and 2). In well-sedated patients, the right femoral artery was

FIGURE 1
Graphic representation of the ovarian protection procedure



punctured (4F), then enabling successive superselective catheterization of the uterine arteries. In the absence of utero-ovarian anastomosis (UOA) or if the UOA was smaller than the main artery of the fibroid, 500 to 700 and then 700 to 900 μm microparticles were injected by free flow into each artery (EmboSphere; Merit Medical Systems Inc, South Jordan, UT). In the presence of an accessible dangerous UOA (of the same size as the fibroid's main artery or larger), a microcoil was positioned in advance to protect the ovary (Tornado or Hilal; Cook Medical Inc, Bloomington, IN). If this dangerous UOA was inaccessible because the route was too long and sinuous, we directly used larger particles (700−900 μm, 900−1200 μm) (Embosphere) with the presumably higher risk of failure. UAE was complete when there was full devascularization of the fibroids and the uterine arteries remained permeable. We did not give any prophylactic antibiotics. The patient remained hospitalized for 1 day. After the procedure, the fibroids and/or adenomyosis were supposed to be fully necrotic, decrease in volume, and be fully

The fibroid is vascularized by branches of the uterine arteries. The ovary is vascularized by the lomboovarian artery. In some patients, a dangerous anastomosis exists between those arteries, exposing the ovary to an accidental embolization by the flow of particles used for the UAE if not protected beforehand. **A,** After puncturing the femoral artery, a catheter is inserted into the left uterine artery. **B,** In the presence of an accessible dangerous UOA, a microcoil is positioned in the anastomosis using a microcatheter. The ovary is still vascularized by the lomboovarian artery. **C,** Microparticles are injected by free flow into the artery to selectively embolize the fibroid. The microcoil placed in the UOA stops the flow of particles from reaching the ovary, thereby preventing its accidental embolization. This figure represents the procedure of (**B**) ovarian protection and (**C**) embolization of the left uterine artery.

UAE, uterine artery embolization; *UOA*, utero-ovarian anastomosis.

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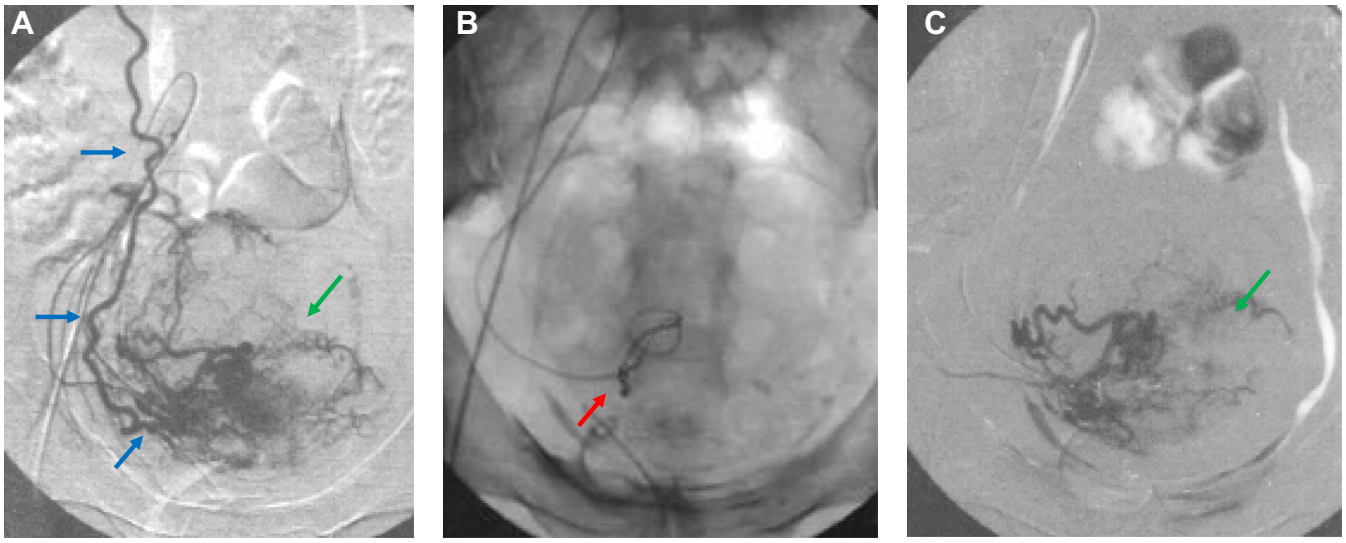
FIGURE 2
Angiographic images of the ovarian protection procedure



Before fibroid embolization, a microcoil was positioned to protect the right ovary and redirect the blood flow to the myoma. **A,** The myoma's vascularization (*green arrow*) and a right type 3 uterine artery anastomosis (*blue arrow*). **B,** The microcoil positioning (*red arrow*) during the ovarian protection procedure. **C,** The fibroid after ovarian protection and before selective embolization of the fibroid.

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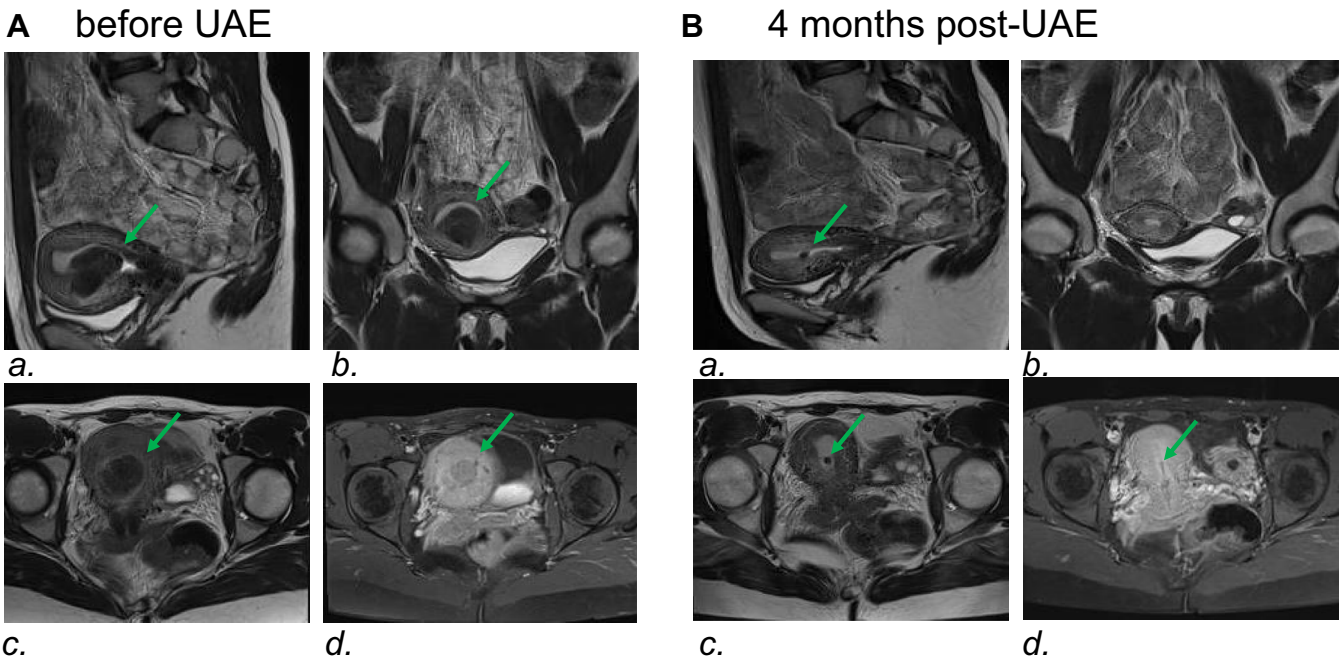
FIGURE 3
MRI before and after fibroid expulsion



A, The uterine fibroid (*green arrow*) before (**a**) embolization in sagittal, (**b**) coronal, and (**c** and **d**) axial planes. **A,** (**a**–**c**) T2 weighted and (**d**) T1 gadolinium-enhanced fat-saturated MRI sequence. **B,** The residual uterine fibroid 4 months after UAE. Sequences and planes are similar to panel **A**.

MRI, magnetic resonance imaging; *UAE,* uterine artery embolization.

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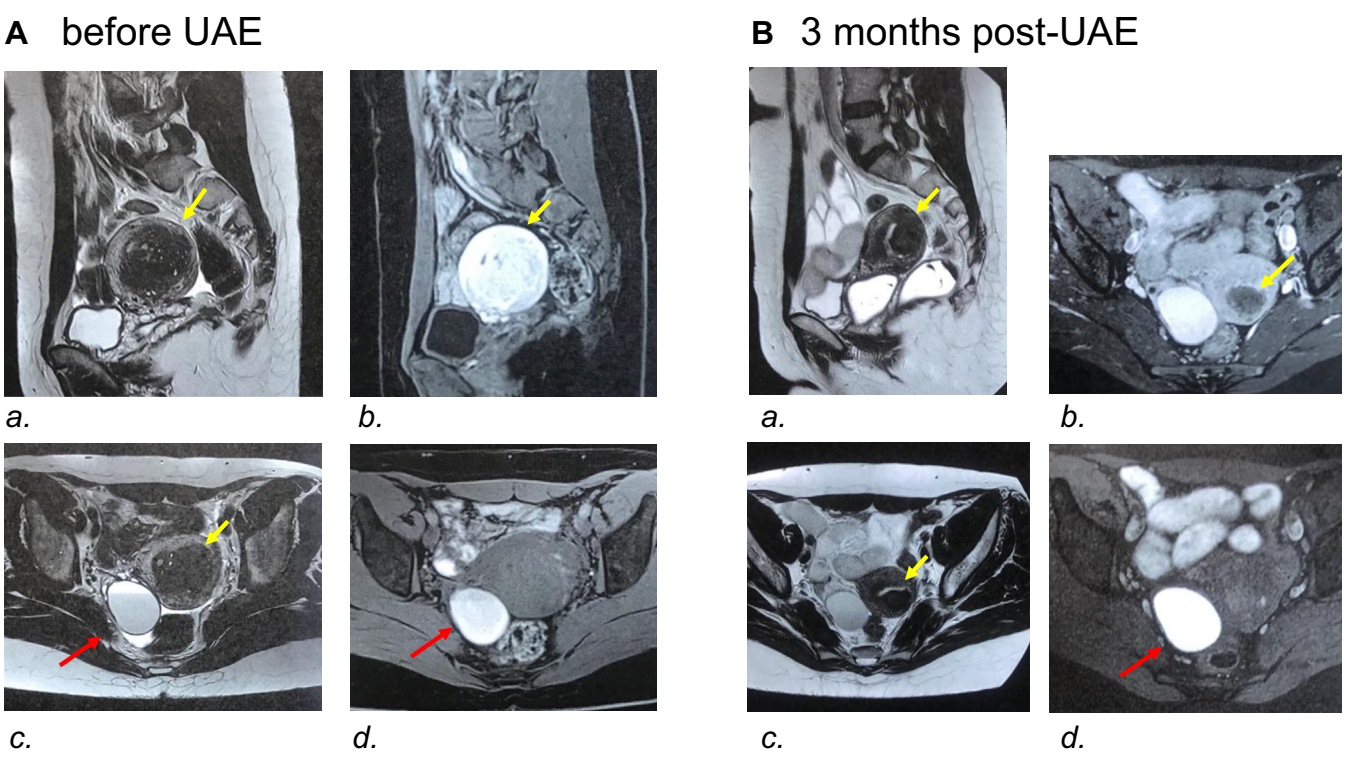
FIGURE 4
MRI before and after UAE in a patient with an adenomyoma



A, An adenomyoma (*yellow arrow*) and right ovarian endometrioma (*red arrow*) before UAE in (**a**) T2-weighted sagittal plane, (**b**) T1 gadolinium-enhanced fat-saturated sagittal plane, (**c**) axial T2-weighted plane, and (**d**) axial T1-weighted fat-saturated plane. **B,** The necrosis and reduction in size of the adenomyoma 3 months after UAE. Images are (**a**) T2-weighted sagittal plane, (**b**) T1 gadolinium-enhanced fat-saturated gadolinium axial plane, (**c**) axial T2-weighted plane, and (**d**) axial T1-weighted fat-saturated plane.

MRI, magnetic resonance imaging; *UAE*, uterine artery embolization.

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or partly eliminated during the menstrual cycle; they were expected to favorably heal within 6 to 12 months on average[17,22] (Figures 3 and 4).

Statistical analysis

All statistical analyses were performed using R software, version 3.6.3. If appropriate, the tests were conducted with a significance level set at 5% (ie, $P<.05$ as the rule for rejecting the null hypothesis).

The quantitative results are described as means and standard deviations; the qualitative results are expressed as percentages and numbers of cases.

Predictors of clinical success, obstetrical success, etc, were determined by logistic regression. The results are expressed as odds ratios (ORs) and their 95% confidence intervals obtained by profiling. In light of the low number of failures, we did not seek to build a multivariate model. However, for pregnancy outcomes, logistic regression adjusted for age during the first post-UAE pregnancy was performed. The levels of significance are provided in the tables, without correction for multiplicity; a corrected version based on the Bonferroni method to prevent the inflation of false positive rates that occurs with multiple statistical tests is specified in the text if necessary. The data were processed as complete cases.

Results

Patient characteristics before embolization (Tables 1 and 2)

The 398 women in our group had a mean age of 37.13±4.87 years and were all symptomatic at the time of the procedure. Of these patients, 161 had already mothered at least 1 child (43.4%), and a considerable share of the total group (n=158; 39.7%) had an active wish to procreate (Table 1). A full list of comorbidities can be found in Supplemental Data.

Before UAE, 347 of 363 patients (95.6%) had an abnormal uterine cavity owing to leiomyomas that distorted the cavity (ie, all locations except subserosal) or adenomyosis (Table 2).

Clinical and anatomic outcomes (Table 3)

Clinical success was observed in 363 patients (91.2%); 55 patients had recurrence of their symptoms (13.8%), on average of 6.63±2.77 months after UAE (Table 3).

TABLE 1
Patient characteristic of the myomas before uterine artery embolization

Characteristics		Patients monitored n=398	Patients with a wish to procreate n=158	Patients with at least 1 uninterrupted early pregnancy[a] n=102	Patients with at least 1 live birth n=89
General characteristics	Age at UAE (y)	37.13±4.87	34.89±4.87	34.26±4.41	33.88±4.35
	Parity (at least 1 child before UAE)	161 (43.4% of 371) 27 missing values	40 (26.85% of 149) 9 missing values	29 (29% of 100) 2 missing values	24 (27.27% of 88) 1 missing value
Symptoms	Heavy menstrual bleeding	318 (79.9)	128 (81.01)	87 (85.29)	76 (85.39)
	Iron-deficiency anemia	108 (27.14)	46 (29.11)	24 (23.53)	22 (24.72)
	Pelvic pressure	151 (37.94)	64 (40.51)	39 (38.24)	33 (37.08)
Gynecologic history	At least 1 . . .[b]	57 (14.32)	38 (24.05)	27 (26.47)	22 (24.72)
	Endometriosis	9 (2.26)	6 (3.80)	5 (4.90)	4 (4.49)
	Tubal disease	17 (4.27)	7 (4.43)	2 (1.96)	1 (1.12)
	Ovarian disease	17 (4.27)	14 (8.86)	10 (9.80)	9 (10.11)
	Sterility	22 (5.53)	19 (12.03)	16 (15.69)	14 (15.73)
Scarred uterus		48 (12.06)	25 (15.82)	20 (19.61)	18 (20.22)
History of early pregnancy failure	At least 1 . . .[b]	54 (13.57)	45 (28.48)	35 (34.31)	31 (34.83)
	Failed IVF	17 (4.27)	12 (7.60)	7 (6.86)	6 (6.74)
	Miscarriage	40 (10.05)	35 (22.15)	30 (29.41)	26 (29.21)
Comorbidities		45 (11.75% of 383) 15 missing values	17 (11.56% of 147) 11 missing values	11 (11.46% of 96) 6 missing values	9 (10.84% of 83) 6 missing values

[a] Patients who started at least 1 pregnancy that was not interrupted by abortion; [b] Refers to the number of patients that presented *at least 1* of the events from the category.

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TABLE 2
Anatomic characteristics of the myomas before uterine artery embolization

Characteristics		Patients monitored n=398	Patients with a wish to procreate n=158	Patients with at least 1 uninterrupted early pregnancy n=102	Patients with at least 1 live birth n=89
Anatomic situation	1 submucosal myoma	69 (19.01% of 363)	15 (9.934% of 151)	2 (2% of 100)	2 (2.299% of 87)
	1 transmural myoma	67 (18.46)	31 (20.53)	22 (22)	21 (24.14)
	1 subserosal myoma	16 (4.408)	7 (4.636)	5 (5)	5 (5.747)
	Polymyomatous uterus	68 (18.73)	36 (23.84)	27 (27)	22 (25.29)
	2 myomas	78 (21.49)	39 (25.83)	28 (28)	25 (28.74)
	Adenomyosis+fibroid	44 (12.12)	16 (10.6)	14 (14)	11 (12.64)
	Pure Adenomyosis	21 (5.785)	7 (4.636)	2 (2)	1 (1.149)
	Missing data	35 missing values	7 missing values	2 missing values	2 missing values
Number of uterine fibroids		4.496±4.517 152 missing values	5.035±5.048 40 missing values	4.627±4.322 18 missing values	4±3.613 16 missing values
Size of dominant uterine fibroid (cm^3)		149.6±212.7 41 missing values	132.8±168.6 10 missing values	133.9±188.5 3 missing values	134.4±193.3 3 missing values
Abnormal uterine cavity[a]		347 (95.59% of 363) 35 missing values	144 (95.36% of 151) 7 missing values	95 (95% of 100) 2 missing values	82 (94.25% of 87) 2 missing values
Utero-ovarian anastomosis	Absent	33 (15.07% of 219) 179 missing values	15 (13.16% of 114) 44 missing values	10 (12.82% of 78) 24 missing values	10 (14.08% of 71) 18 missing values
	Harmless[b]	78 (35.62)	46 (40.35)	28 (35.9)	26 (36.62)
	Dangerous[c]	108 (49.32)	53 (46.49)	40 (51.28)	35 (49.3)
Ovarian protection		33 (14.54% of 227) 171 missing values	22 (18.18% of 121) 37 missing values	21 (25% of 84) 18 missing values	18 (23.68% of 76) 13 missing values

Values are expressed as mean±standard deviation for quantitative variables (continuous or discrete) and as number of women (percentage) for qualitative variables ("Yes" response for binary variables, unless otherwise indicated).

IVF, in vitro fertilization; *UAE*, uterine artery embolization; *UOA*, utero-ovarian anastomosis.

[a] A uterine cavity is qualified as abnormal either in the presence of leiomyomas that distort the cavity (ie, all locations but subserosal) or adenomyosis; [b] UOA that is smaller than the main artery of the fibroid; [c] UOA that is of the same size as the fibroid's main artery or larger.

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TABLE 3
Clinical and anatomic outcomes

Outcomes		Patients monitored n=398	Patients with a wish to procreate n=158	Patients with at least 1 uninterrupted early pregnancy n=102	Patients with at least 1 live birth n=89
Clinical success		363 (91.21)	139 (87.97)	92 (90.2)	83 (93.26)
Anatomic outcome	Size of the residual fibroid (cm^3)	39.7±67.41 193 missing values 16 values NA	40.3±80.18 48 missing values 5 values NA	36.61±78.91 11 missing values 2 values NA	37.15±82.74 9 missing values 1 value NA
	Absolute reduction of fibroid size (cm^3)	−95.82±99.13 195 missing values 17 values NA	−82.39±86.21 50 missing values 6 values NA	−78.13±87.58 13 missing values 2 values NA	−79.38±84.26 11 missing values 1 valeur NA
	Relative reduction of fibroid size (%)	−72.86±25.77 195 missing values 17 values NA	−71.83±27.76 50 missing values 6 values NA	−72.78±28.66 13 missing values 2 values NA	−74.57±22.47 11 missing values 1 value NA
	Fibroid Expulsion	32 (8.04)	16 (10.13)	15 (14.71)	15 (16.85)
	Recurrence	55 (13.82)	18 (11.39)	11 (10.78)	8 (8.99)
	Time to recurrence (y)[a]	6.63±2.77 14 missing values	7.118±3.37 1 missing value	8±3.65 1 missing value	8.5±3.96
	Secondary myomectomy	23 (5.78)	15 (9.49)	15 (14.71)	13 (14.61)
	Hysterectomy	26 (6.53)	8 (5.06)	3 (2.941)	2 (2.25)
	Second embolization	30 (7.54)	14 (8.86)	7 (6.86)	4 (4.49)
Restoration	No	22 (11.83% of 186)	10 (9.01% of 111)	4 (4.17% of 96)	0 (0% of 86)
	Partial	122 (65.59)	74 (66.67)	65 (67.71)	61 (70.93)
	Ad integrum	42 (22.58)	27 (24.32)	27 (28.12)	25 (29.07)
	Missing data	199 missing values	44 missing values	6 missing values	3 missing values
Age of menopause[b]		49±5.00 5 missing values	50±4.29 2 missing values	50.33±5.96 2 missing values	48.8±5.17 1 missing value

Values are expressed as mean±standard deviation for quantitative variables (continuous or discrete) and as number (percentage) for qualitative variables (unless otherwise indicated).

NA, not applicable.

[a] Missing values are reported for patients with a known event of recurrence but no data on time to recurrence; [b] Missing values are reported for patients with a known occurrence of menopause but no data on the age at menopause.

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TABLE 4
Potential predictors of clinical success

Variable		Clinical success rate	Odds ratio	*P* value
Age at embolization (y)			0.95 (0.87; 1.02)	.1717
Fibroid location	1—submucosal	0.94	Reference	.1579
	1—transmural	0.93	0.76 (0.18; 3.01)	
	1—subserosal	1	2,618,000 (6.20e-16; 1.02e+130)	
	Polymyomatous	0.90	0.54 (0.13; 1.87)	
	Two myomas	0.94	0.90 (0.21; 3.53)	
	ADN+fibroid	0.86	0.39 (0.10; 1.45)	
	Pure ADN	0.76	0.20 (0.04; 0.82)	
Adenomyosis	No	0.93	Reference	.0414
	Yes	0.86	0.47 (0.23; 0.97)	
Number of fibroids			0.89 (0.82; 0.96)	.0037
Preprocedure fibroid size (cm^3)			0.99 (0.998; 1.001)	.2950
Restoration	No	0.55	Reference	<.0001
	Partial	0.93	10.46 (3.59; 31.72)	
	Ad integrum	1	2.62e+08 (2.52e-36; NA)	
Ovarian protection	No	0.92	Reference	1.0000
	Yes	0.94	1.39 (0.37; 9.09)	

The clinical success rate corresponded to the number of women who were asymptomatic after UAE among all treated women. Success rates have only been calculated for qualitative predictors and are expressed as absolute values (between 0 and 1). The odds ratios have been obtained by conventional logistic regression. Their 95% confidence intervals have been obtained by profiling. The levels of significance are those of the nested model test with asymptotic approximation of the χ^2 distribution for quantitative variables and those of Fisher exact test for qualitative variables; they have not been corrected for multiplicity. For 6 tests, the threshold to be used is $P<.008$ (Bonferroni method). Green indicates that the test is significant at the threshold of $\alpha=0.05$ after correcting for multiplicity, orange that the test is significant at the threshold of $\alpha=0.05$ before correcting for multiplicity, and yellow that the test is significant at the threshold of $\alpha=0.10$.

ADN, adenomyosis; *NA*, not available; *UAE*, uterine artery embolization.

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We did not find any necrosis or atrophy of the myometrium or endometrium on the control MRIs. One year after UAE, the mean size of the residual fibroid was 39.7 cm^3 for the total group, corresponding to a mean reduction of 96 cm^3 (and to a relative reduction of 73%). Expulsion occurred in 32 cases. Clinically, this corresponds to repeated contractions of the uterus with bleeding. It is not an emergency or a complication. In these patients, expulsion took place between 2 weeks and 10 months after UAE. Expulsion involved primarily transmural (n=8, 27%) and submucosal (n=7, 23%) fibroids with a mean initial volume of 108 cm^3. Secondary myomectomy was performed primarily in patients with a polymyomatous uterus (n=6, 29%), 2 myomas (n=6, 29%), or a transmural fibroid (n=5, 17%), with a large mean initial volume of 383 cm^3.

In patients having reached menopause in 2017, the mean age at occurrence was 49±5 years. We only had a single case of early clinical menopause in a 38-year-old patient, who was nonetheless able to have a child using assisted reproductive technology with oocyte donation.

Predictive factors for clinical success (Table 4)

Anatomic restoration of the uterine cavity and a low number of fibroids were identified as predictive factors for clinical success. Restoration was associated with clinical success ($P<.0001$), with a clinical success rate of 0.55 without restoration, 0.93 with partial restoration, and 1 with total restoration. Adenomyosis was associated with a lower clinical success rate before but not after correction for multiplicity (0.86 with vs 0.93 without adenomyosis).

Complications

There were no major complications related to the procedure; in particular, no emergency transfusions or hysterectomies were performed. Notably, 2 infections after embolization (one case of endometritis and one of salpingitis) occurred in 2 patients with an intrauterine device that could not be [T4] removed; they were medically and surgically treated.

Obstetrical outcomes (Tables 5 and 6)

In our group, there were 148 pregnancies, 11 of which started via IVF (Table 4). They led to 109 live births (73.7% of all pregnancies), 26 miscarriages (17.6%), and 12 abortions (8.1%). The interval between UAE and the first pregnancy was 24.82±24 months on average (Table 5). A

TABLE 5
Pregnancies after uterine embolization

Obstetrical outcomes	Patients monitored n=398	Patients with a wish to procreate n=158	Patients with at least 1 uninterrupted early pregnancy n=102	Patients with at least 1 live birth n=89
Number of early pregnancies	148 (37.19)	134 (84.81)	139 (136.3)	123 (138.2)
Number of live births	109 (73.65) 1 missing value	106 (79.1) 1 missing value	109 (78.42) 1 missing value	109 (88.62)
Number of miscarriages	26 (17.57) 1 missing value	22 (16.42) 1 missing value	26 (18.71) 1 missing value	14 (11.38)
Number of abortions	12 (8.11)	5 (3.731)	3 (2.16)	0 (0)
Number of IVFs	11 (7.43)	11 (8.21)	11 (7.91)	9 (7.32)
Age at the time of first pregnancy (y)	36.24±4.33 33 missing values	36.07±4.29 23 missing values	36.24±4.33 24 missing values	36.24±4.33 11 missing values
Age at the time of second pregnancy (y)	36.47±3.944 96 missing values	36.47±3.944 83 missing values	36.47±3.94 87 missing values	36.47±3.94 74 missing values
UAE—first pregnancy interval (mo)	24.82±24 39 missing values	24.57±24.06 29 missing values	24.82±24 30 missing values	24.82±24 17 missing values
UAE—second pregnancy interval (mo)	46.2±17.02 17 missing values	46.2±17.02 16 missing values	46.2±17.02 17 missing values	46.2±17.02 14 missing values
Number of obstetrical complications	16 (10.81) 22 missing values	16 (11.94) 12 missing values	16 (11.51) 13 missing values	16 (13.01)

Values are expressed as the total number of events except for the intervals which are given as arithmetic mean±standard deviation. Missing values are reported for women who reported at least 1 uninterrupted early pregnancy (2 for the age at the time of second pregnancy and interval between UAE and second pregnancy).

UAE, uterine artery embolization.

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TABLE 6
Live birth characteristics

Characteristics	Patients with at least 1 live birth n=89
Number of live births	109 (88.62)
Number of births by cesarean delivery	51 (46.79% to 51/109)
Number of births at term	74 (75.51% to 74/98)
Number of preterm births	23 (23.47% to 23/98)
Prematurity (in wk of amenorrhea)[a]	35.12±2.78 2 missing values
Height of first child (cm)[b]	49.55±2.64 14 missing values
Weight of first child (g)[b]	3209±574.9
Height of second child (cm)[c]	50.07±2.31 4 missing values
Weight of second child (g)[c]	3339±718.8

Values are expressed as the total number of events (percentage of the number of live births) except for the intervals, heights, and weights which are given as arithmetic mean±standard deviation.

[a] Missing values are reported for women who declared at least 1 premature birth; [b] Missing values are reported for all women who declared at least 1 live birth; [c] Missing values are reported for all women who declared at least 2 live births.

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description of the pregnancies after UAE, stratified by age, is available in Supplemental Tables 1–4.

A total of 16 patients presented with obstetrical complications. Obstetrical complications included 2 cases of gestational diabetes, 1 case of gestational hypertension, 4 threats of preterm birth, 1 extrauterine pregnancy, 1 craniofacial malformation requiring therapeutic abortion at 19 weeks' amenorrhea, 1 placenta previa requiring a cesarean delivery at 36 weeks' amenorrhea, 1 fibroid previa, 1 hard-to-detach placenta, and 2 in utero deaths during twin pregnancies—one at 5 and a half months from twin-to-twin transfusion syndrome and the other from infection with loss of a 680 g child. The 2 remaining children were born alive (2545 and 790 g at 26 weeks' amenorrhea, respectively).

A total of 74 children (75% of the 98 for whom we have detailed information) were born at term; 23 were born

TABLE 7
Potential predictors of pregnancy occurrence

Variable		Pregnancy rate	Univariate analysis		Analysis adjusted for age at embolization (y)	
			Odds ratio	*P* value	Odds ratio	*P* value
Age at embolization (y)			0.88 (0.82; 0.95)	.0005		
Fibroid location	1—submucosal	0.2	Reference	.0047	Reference	.0086
	1—transmural	0.68	8.4 (2.12; 43.42)		6.32 (1.52; 33.75)	
	1—subserosal	0.71	10 (1.43; 101.8)		8.81 (1.16; 95.69)	
	Polymyomatous	0.72	10.4 (2.67; 53.28)		9.77 (2.40; 51.95)	
	Two myomas	0.69	9 (2.36; 45.14)		8.29 (2.10; 42.82)	
	ADN+fibroid	0.75	12 (2.45; 77.68)		15.52 (2.99; 107)	
	Pure ADN	0.29	1.6 (0.17; 12.92)		1.74 (0.17; 14.82)	
Adenomyosis	No	0.64	Reference	.3008	Reference	.7956
	Yes	0.53	0.64 (0.29; 1.44)		0.8936 (0.38; 2.12)	
Ovarian protection	No	0.61	Reference	.0010	Reference	.0005
	Yes	0.95	13.65 (2.68; 249.6)		13.62 (2.64; 250.5)	
Gynecologic history	No	0.59	Reference	.2500	Reference	.1554
	Yes	0.71	1.69 (0.79; 3.86)		1.79 (0.81; 4.17)	
History of pregnancy failure	No	0.56	Reference	.0111	Reference	.0055
	Yes	0.78	2.78 (1.29; 6.42)		3.06 (1.38; 7.31)	
Restoration	No	0.3	Reference	.0001	Reference	.0001
	Partial	0.85	13.36 (3.21; 69.85)		13.36 (3.12; 72.14)	
	Ad integrum	1	7.3e+8 (1.12e-47; NA)		7.3e+8 (2.06e-41; NA)	

This analysis was performed in the group of patients with a desire to procreate (n=158). Success rates have only been calculated for qualitative predictors and are expressed as absolute values (between 0 and 1). The pregnancy rate was defined as the number of women who started a pregnancy among the women with a desire to procreate. The odds ratios have been obtained by conventional logistic regression. Their 95% confidence intervals have been obtained by profiling. The levels of significance are those of the nested model test with asymptotic approximation of the χ^2 distribution for quantitative variables and those of Fisher exact test for qualitative variables with no correction for multiplicity. For 7 tests, the threshold to be used is $P<.00714$ (Bonferroni method). Green indicates that the test is significant at the threshold of $\alpha=0.05$ after correcting for multiplicity, red that the test is significant at the threshold of $\alpha=0.05$ before correcting for multiplicity, and yellow that the test is significant at the threshold of $\alpha=0.10$.

ADN, adenomyosis; *NA*, not available.

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preterm, on average at 35.12±2.78 weeks' amenorrhea. Overall, the average size and weight were 49.55±2.64 cm and 3209±574.9 g, respectively, for the first child and 50.07±2.31 cm and 3339±718.8 g, respectively, for the second child (Table 6). A description of these results stratified by age is available in Supplemental Tables 5–8.

Predictive factors for obstetrical outcomes (Tables 7 and 8)

Anatomic uterine restoration was a significant predictive factor for pregnancy occurrence with an OR of 13.4 for partial restoration and 7.3×10^8 for ad integrum restoration (vs without restoration; $P<.0001$). Ovarian protection was also significantly associated with pregnancy occurrence. Among the women with a desire to procreate, pregnancy occurred at a rate of 0.95 with ovarian protection vs 0.61 without ovarian protection (OR, 13.65; $P=.001$). These results remained statistically significant after adjusting for age at embolization ($P=.0001$ and $P=.0005$ for anatomic uterine restoration and ovarian protection respectively).

Approximately 95% of women who started a pregnancy had a residual fibroid size under 112 cc 1 year after UAE. This residual fibroid size was under 126.5 cc for 95% of women who gave birth to a live child.

A lack of anatomic restoration of a normal uterine cavity was significantly associated with the occurrence of miscarriage ($P<.01$), because the rate of miscarriage was 1 without restoration and 0.19 with partial restoration (presence of residue) and with total ad integrum restoration.

No predictive factors were identified for cesarean delivery (Supplemental Table 9). Fibroid location was associated with delivery at term when adjusted for age at first pregnancy, before but not after correcting for multiplicity (Supplemental Table 10). Fibroid location was associated with low birthweight before but not after correcting for

TABLE 8
Potential predictors of miscarriage

Variable		Miscarriage rate	Univariate analysis	*P* value
Age at embolization (y)			1.07 (0.96; 1.20)	.1997
Age during first postembolization pregnancy (y)			0.99 (0.83; 1.18)	.9343
Fibroid location	1—submucosal	0	Reference	.7285
	1—transmural	0.18	9.45e+6 (1.88e-18; NA)	
	1—subserosal	0	1 (2.13e-31; 4.18e+29)	
	Polymyomatous	0.26	1.49 e+7 (9.09e-184; NA)	
	Two myomas	0.21	1.16e+7 (8.59e-184; NA)	
	ADN+fibroid	0.31	1.89e+7 (4.83e-183; NA)	
	Pure ADN	0.5	4.25e+7 (2.65e-61; NA)	
Adenomyosis	No	0.20	Reference	.2081
	Yes	0.35	2.15 (0.66; 6.54)	
Ovarian protection	No	0.18	Reference	.3389
	Yes	0.3	2.03 (0.61; 6.36)	
Gynecologic history	No	0.21	Reference	.5925
	Yes	0.27	1.36 (0.46; 3.72)	
History of pregnancy failure	No	0.21	Reference	.6252
	Yes	0.26	1.29 (0.48; 3.33)	
Restoration	No	1	Reference	.0029
	Partial	0.19	1.45e-08 (NA; 6.10e+51)	
	Ad integrum	0.19	1.45e-08 (NA; 4.43e+51)	

This analysis was performed in the group of patients with at least 1 uninterrupted early pregnancy (n=102). The miscarriage rate was defined as the number of miscarriages among the uninterrupted early pregnancies. Miscarriage rates have only been calculated for qualitative predictors and are expressed as absolute values (between 0 and 1). The odds ratios have been obtained by conventional logistic regression. Their 95% confidence intervals have been obtained by profiling. The levels of significance are those of the nested model test with asymptotic approximation of the χ^2 distribution for quantitative variables, and those of Fisher exact test for qualitative variables with no correction for multiplicity. For 8 tests, the threshold to be used is $P<.00625$ (Bonferroni method). Green indicates that the test is significant at the threshold of $\alpha=0.05$ after correcting for multiplicity, orange that the test is significant at the threshold of $\alpha=0.05$ before correcting for multiplicity, and yellow that the test is significant at the threshold of $\alpha=0.10$.

ADN, adenomyosis; *NA*, not available.

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multiplicity. This association did not persist after adjusting for age at first pregnancy (Supplemental Table 11).

Discussion

Principal findings

Our results suggest that UAE may restore a favorable uterine anatomy without intracavity distortion or residues, thereby enabling viable and trophic pregnancies. Ovarian protection further seems to have a strong beneficial effect on pregnancy occurrence. Finally, our results were also reassuring in terms of postembolization placental abnormality, PPH, and miscarriage rates, which seemed clinically acceptable.

Results

In our cohort, 102 of the 158 women (65%) with a desire to procreate started at least 1 pregnancy, resulting in 134 pregnancies and 106 live births. This was consistent with the data of 2 meta-analyses, estimating the pregnancy rate at 58.6% and 50% to 69%, respectively.[9,10]

The mean age at pregnancy of 36.2 years was comparable with or older than in other studies (35.9−37.6 years[8,9,15,23] and 32.8−35.1 years,[6,7,13,16] respectively) and far above average for a first child in the normal population in France (28.5 years, Institut National de la Statistique et des Etudes Economiques [INSEE]).

Our rate of miscarriage after UAE (17.57%) was similar to that of Pron et al[13] (16.7%) and much lower than the miscarriage rates frequently found in the literature[6−9,12] which are one of the main reasons why UAE is criticized. Torre et al[16] found a very low miscarriage rate (10%) presumably partly owing to the contraindication of adenomyosis and systematic performance of hysteroscopy with resection of synechiae after UAE to remove necrotic residues, enabling pregnancies to begin with a healthy uterine cavity.[24,25] This was consistent with our results showing an association between miscarriage occurrence

and insufficient restoration of the uterine cavity.

The rate of cesarean delivery was high in our study—like for Pron et al[13] (50%), Mara et al[6] (60%), Pisco et al[15] (61.3%), and Walker McDowell[8] (67.5%)—at 46.8% vs 21% in the normal population. This may partly have been caused by the fact that certain patients already had a previous scar or because the gynecologist considered embolization, in the same way as myomectomy,[13] as a risk factor for vaginal delivery and thus programmed the cesarean delivery in advance.

Our rate of placental abnormalities (1.7%) was the same as in Pisco et al's[15] study (1.3%); it was lower than in other studies (6.3%,[9] 12.5%[13]) and higher than in the normal population (0.4%[8]). Once again, the age of our group was a possible confounding factor, because the rate of placental abnormalities is higher after the age of 35 years (INSEE).

Moreover, 8 newborns (6.9%) born before at 35 weeks' amenorrhea weighed <2500 g. In these 6 patients, there were one or more explanatory causes (Supplemental Data 1).

The mean age at menopause in our group (49 years) was slightly lower than in the normal Western population (51 years[26]).

Overall, the fibroids of our patients were bulkier and more numerous than in studies on pregnancies after myomectomy.[6,11,13,14] A recent randomized trial[27] compared 2-year outcomes for UAE with myomectomy used to treat multiple voluminous fibroids. They showed no significant difference in the levels of ovarian reserve biomarkers between the groups; however, it has not yet been possible to study pregnancies.

The rate of recurrence in our group, evaluated at 13.8%, was consistent with the data from the literature. This rate was slightly above that for myomectomy[28, 29] (12.2%) and much lower than that after high-intensity focused ultrasound[28] (54%).

Clinical implications

To date, owing to a lack of comprehensive studies, learned societies do not recommend UAE for women wishing to procreate. This study adds to the growing body of literature investigating the effects of UAE on fertility. Further research—notably prospective cohorts and controlled randomized trials[27]—is needed to refine the indications of UAE as a possible therapeutic option based on anatomic and clinical parameters. Close collaboration with gynecologists as part of a multidisciplinary approach will be fundamental to ensure appropriate patient selection, treatment, and follow-up.

Research implications

Adenomyosis, a factor in hypofertility, surgically inaccessible, and often an exclusion criterion, was found in 18% of our treated patients. With a clinical success rate of 86% (Table 4) and an obstetrical success rate of 53% (Table 7), UAE could be a therapeutic option for those patients lacking alternatives. Future studies are needed to investigate the benefits and limitations of UAE for this specific group of patients.

Ovarian protection[22] was shown to have a strong beneficial effect on fertility in our cohort. However, to date, this technique has only been used by a limited number of practitioners. Future comparative studies are needed to confirm the role of ovarian protection in fertility preservation, broaden our understanding of its mechanisms and, should it prove beneficial, standardize its use.

Strengths and limitations

The strengths of this study lie in its extensive cohort of patients, long follow-up period, and exhaustive clinical, obstetrical, and anatomic data collection. Nevertheless, we are aware that our study presents several limitations. First of all, our cohort did not include a control group and fertility outcomes were not matched to controls based on age. A selection bias can be discussed, because only 57% of the women benefited from complete follow-up, that is, 398 of the 698 patients treated during this period. A comparison of pre-UAE characteristics between patients with and without follow-up is provided in Supplemental Data 1.

Conclusions

This study provides detailed clinical and obstetrical outcomes for 398 female patients who underwent UAE for fibroid treatment; it contributes to the identification of anatomic and technical factors that could have an impact on fertility after UAE. Further controlled clinical trials are needed to confirm our findings and reevaluate this procedure's indications and limitations for women with a desire to procreate. ■

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Supplemental Data 1

Postuterine artery embolization imaging classification of uterine anatomy restoration

Restoration of the uterine anatomy after uterine artery embolization (UAE) was classified as follows:

- Ad integrum restoration of the cavity if there was spontaneous expulsion or by secondary hysteroscopic myomectomy without involvement of the wall
- Partial restoration if there was a residual fibroid in the wall with no distortion of the cavity or if an abdominal or laparoscopic myomectomy procedure had supplemented the UAE
- Nonrestoration if the cavity remained compressed or blocked by a residual necrotic myoma or if the lesions had not been devascularized.

Comorbidities

Before UAE, there were 10 thrombotic disorders and coagulation defects, 6 cancers, 6 hepatodigestive disorders, 5 thyroid dysfunction disorders, 5 neuropsychiatric diseases, 3 HIV cases, 3 metabolic disorders, 3 kidney diseases, 3 heart diseases, 3 chronic rheumatic diseases, 2 cases of systemic lupus erythematosus, 2 cases of diabetes mellitus, and 2 cases of high blood pressure. Before embolization, 6 cases of in utero deaths between months 4 and 7 and 4 cases of severe prematurity (<32 weeks' amenorrhoea; 680−2370 g) had been reported after an important increase in myoma volume (7/10), red degeneration (2/3), or a placental abnormality (1/2), usually with cesarean delivery.

Low birthweight

A total of 8 children were born before 35 weeks' amenorrhoea and weighed <2500 g. In these 6 patients, there were one or more explanatory factors:

- Age >39 years (3)
- Twin pregnancies (3)
- Persistence of vascularized residual myomas or adenomyosis (3)
- Assisted reproductive technology (2)
- High blood pressure (2)
- Gestational diabetes (1)
- Systemic lupus erythematosus (1)
- Bulky residual uterus (1040 cc) (1)

Patient lost to follow-up characteristics

Compared with the patients lost to follow-up, patients with follow-up were 1 year younger on average (37.14 vs 38.28 years for patients lost to follow-up); were more likely to be nulliparous (57% vs 48%); had a history of more gynecologic complications (14% vs 7.7%), especially miscarriages (10.1% vs 3.3%); and were more likely to have a polymyomatous uterus (18.7% vs 13.2%).

SUPPLEMENTAL TABLE 1

Pregnancies after uterine artery embolization stratified on age of first pregnancy at ≤32 years

Obstetrical outcomes	Patients monitored n=14	Patients with a wish to procreate n=14	Patients with at least 1 uninterrupted early pregnancy n=14	Patients with at least 1 live birth n=14
Number of early pregnancies	21 (150)[a]	21 (150)[a]	21 (150)[a]	21 (150)[a]
Number of live births	20 (95.24)	20 (95.24)	20 (95.24)	20 (95.24)
Number of miscarriages	1 (4.76)	1 (4.76)	1 (4.76)	1 (4.76)
Number of abortions	0 (0)	0 (0)	0 (0)	0 (0)
Number of IVFs	0 (0)	0 (0)	0 (0)	0 (0)
Age at the time of first pregnancy (y)	30.29±1.82	30.29±1.82	30.29±1.82	30.29±1.82
Age at the time of second pregnancy (y)	34±2 8 missing values	34±2 8 missing values	34±2 8 missing values	34±2 8 missing values
UAE—first pregnancy interval (mo)	21.43±16.64	21.43±16.64	21.43±16.64	21.43±16.64
UAE—second pregnancy interval (mo)	55±13.42	55±13.42	55±13.42	55±13.42
Number of obstetrical complications	1 (4.76)	1 (4.76)	1 (4.76)	1 (4.76)

IVF, in vitro fertilization; *UAE*, uterine artery embolization.

[a] The percentage corresponds to the number of early pregnancies divided by the number of patients (of each category).

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SUPPLEMENTAL TABLE 2
Pregnancies after uterine artery embolization stratified on age of first pregnancy at 32 to 37 years

Obstetrical outcomes	Patients monitored n=35	Patients with a wish to procreate n=34	Patients with at least 1 uninterrupted early pregnancy n=34	Patients with at least 1 live birth n=34
Number of early pregnancies	47 (134.3)[a]	47 (138.2)[a]	47 (138.2)[a]	47 (138.2)[a]
Number of live births	43 (91.49)	43 (91.49)	43 (91.49)	43 (91.49)
Number of miscarriages	4 (8.51)	4 (8.51)	4 (8.51)	4 (8.51)
Number of abortions	0 (0)	0 (0)	0 (0)	0 (0)
Number of IVFs	3 (6.38)	3 (6.38)	3 (6.38)	3 (6.38)
Age at the time of first pregnancy (y)	34.82±1.60	34.82±1.604	34.82±1.60	34.82±1.604
Age at the time of second pregnancy (y)	35.83±1.72 28 missing values	35.83±1.72 28 missing values	35.83±1.72 28 missing values	35.83±1.72 28 missing values
UAE—first pregnancy interval (mo)	20.19±19.38 3 missing values	20.19±19.38 3 missing values	20.19±19.38 3 missing values	20.19±19.38 3 missing values
UAE—second pregnancy interval (mo)	36.17±13.53 6 missing values	36.17±13.53 6 missing values	36.17±13.53 6 missing values	36.17±13.53 6 missing values
Number of obstetrical complications	9 (19.15)	9 (19.15)	9 (19.15)	9 (19.15)

IVF, in vitro fertilization; *UAE*, uterine artery embolization.

[a] The percentage corresponds to the number of early pregnancies divided by the number of patients (of each category).

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SUPPLEMENTAL TABLE 3
Pregnancies after uterine artery embolization stratified on age of first pregnancy at 37 to 42 years

Obstetrical outcomes	Patients monitored n=24	Patients with a wish to procreate n=21	Patients with at least 1 uninterrupted early pregnancy n=23	Patients with at least 1 live birth n=23
Number of early pregnancies	30 (125)[a]	28 (133.3)[a]	30 (130.4)[a]	30 (130.4)[a]
Number of live births	26 (86.67)	24 (85.71)	26 (86.67)	26 (86.67)
Number of miscarriages	4 (13.33)	4 (14.29)	4 (13.33)	4 (13.33)
Number of abortions	0 (0)	0 (0)	0 (0)	0 (0)
Number of IVFs	2 (6.67)	2 (7.14)	2 (6.67)	2 (6.67)
Age at the time of first pregnancy (y)	39.48±1.12	39.52±1.12	39.48±1.12	39.48±1.12
Age at the time of second pregnancy (y)	40.5±0.71 21 missing values	40.5±0.71 19 missing values	40.5±0.71 21 missing values	40.5±0.71 21 missing values
UAE—first pregnancy interval (mo)	28.4±21.19 3 missing values	29.78±21.78 3 missing values	28.4±21.19 3 missing values	28.4±21.19 3 missing values
UAE—second pregnancy interval (mo)	48±33.94 4 missing values	48±33.94 4 missing values	48±33.94 4 missing values	48±33.94 4 missing values
Number of obstetrical complications	4 (13.33)	4 (14.29)	4 (13.33)	4 (13.33)

IVF, in vitro fertilization; *UAE*, uterine artery embolization.

[a] The percentage corresponds to the number of early pregnancies divided by the number of patients (of each category).

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SUPPLEMENTAL TABLE 4
Pregnancies after uterine artery embolization stratified on age of first pregnancy at >42 years

Obstetrical outcomes	Patients monitored n=7	Patients with a wish to procreate n=6	Patients with at least 1 uninterrupted early pregnancy n=7	Patients with at least 1 live birth n=7
Number of early pregnancies	8 (114.3)[a]	7 (116.7)[a]	8 (114.3)[a]	8 (114.3)[a]
Number of live births	8 (100)	7 (100)	8 (100)	8 (100)
Number of miscarriages	0 (0)	0 (0)	0 (0)	0 (0)
Number of abortions	0 (0)	0 (0)	0 (0)	0 (0)
Number of IVFs	3 (37.5)	3 (42.86)	3 (37.5)	3 (37.5)
Age at the time of first pregnancy (y)	44.43±1.40	44.5±1.52	44.43±1.40	44.43±1.40
Age at the time of second pregnancy (y)	47±NA 6 missing values	47±NA 5 missing values	47±NA 6 missing values	47±NA 6 missing values
UAE—first pregnancy interval (mo)	24.75±25.02 3 missing values	13±10.54 3 missing values	24.75±25.02 3 missing values	24.75±25.02 3 missing values
UAE—second pregnancy interval (mo)	50±NA	50±NA	50±NA	50±NA
Number of obstetrical complications	1 (12.5)	1 (14.29)	1 (12.5)	1 (12.5)

IVF, in vitro fertilization; *NA*, not available; *UAE*, uterine artery embolization.

[a] The percentage corresponds to the number of early pregnancies divided by the number of patients (of each category).

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SUPPLEMENTAL TABLE 5
Live birth characteristics after uterine artery embolization stratified on age of first pregnancy at ≤32 years

Characteristics	Patients with at least 1 live birth n=14
Number of live births	20 (95.24)
Number of births by cesarean delivery	10 (50% to 10/20)
Number of births at term	17 (89.47% to 17/19)
Number of preterm births	2 (10.53% to 2/19)
Prematurity (wk of amenorrhea)[a]	35±NA
Height of first child (cm)[b]	50.18±2.401 2 missing values
Weight of first child (g)[b]	3392±373.7
Height of second child (cm)[c]	50.5±1.58 1 missing value
Weight of second child (g)[c]	3450±450.5

NA, not available.

[a] Missing values are reported for women who declared at least 1 premature birth; [b] Missing values are reported for all women who declared at least 1 live birth; [c] Missing values are reported for all women who declared at least 2 live births.

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SUPPLEMENTAL TABLE 6

Live birth characteristics after uterine artery embolization stratified on age of first pregnancy at 32 to 37 years

Characteristics	Patients with at least 1 live birth n=34
Number of live births	43 (91.49)
Number of births by cesarean delivery	20 (46.51% to 20/43)
Number of births at term	27 (67.5% to 27/40)
Number of preterm births	13 (32.5% to 13/40)
Prematurity (wk of amenorrhea)[a]	35.78±0.44 1 missing value
Height of first child (cm)[b]	49.41±2.75 3 missing values
Weight of first child (g)[b]	3131±521.1
Height of second child (cm)[c]	48.93±2.24 1 missing value
Weight of second child (g)[c]	3269±515.5

[a] Missing values are reported for women who declared at least 1 premature birth; [b] Missing values are reported for all women who declared at least 1 live birth; [c] Missing values are reported for all women who declared at least 2 live births.

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SUPPLEMENTAL TABLE 7

Live birth characteristics after uterine artery embolization stratified on age of first pregnancy at 37 to 42 years

Characteristics	Patients with at least 1 live birth n=23
Number of live births	26 (86.67)
Number of births by cesarean delivery	11 (42.31% to 11/26)
Number of births at term	18 (72% to 18/25)
Number of preterm births	6 (24% to 6/25)
Prematurity (wk of amenorrhea)[a]	35±2 1 missing value
Height of first child (cm)[b]	49.83±2.66 7 missing values
Weight of first child (g)[b]	3297±625.5
Height of second child (cm)[c]	54±NA 2 missing values
Weight of second child (g)[c]	2867±1305

NA, not available.

[a] Missing values are reported for women who declared at least 1 premature birth; [b] Missing values are reported for all women who declared at least 1 live birth; [c] Missing values are reported for all women who declared at least 2 live births.

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SUPPLEMENTAL TABLE 8

Live birth characteristics after uterine artery embolization stratified on age of first pregnancy at >42 years

Characteristics	Patients with at least 1 live birth n=7
Number of live births	8 (100)
Number of births by cesarean delivery	7 (87.5% to 7/8)
Number of births at term	7 (87.5% to 7/8)
Number of preterm births	1 (12.5% to 1/8)
Prematurity (wk of amenorrhea)[a]	26±NA
Height of first child (cm)[b]	49±3.46
Weight of first child (g)[b]	2991±1037
Height of second child (cm)[c]	52±NA
Weight of second child (g)[c]	4650±NA

NA, not available.

[a] Missing values are reported for women who declared at least 1 premature birth; [b] Missing values are reported for all women who declared at least 1 live birth; [c] Missing values are reported for all women who declared at least 2 live births.

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SUPPLEMENTAL TABLE 9
Potential predictors of cesarean delivery

Variable		Cesarean delivery rate	Univariate analysis		Analysis adjusted for age during first post-UAE pregnancy (y)	
			Odds ratio	*P* value	Odds ratio	*P* value
Age at embolization (y)			0.93 (0.84; 1.03)	.1721		
Age during first postembolization pregnancy (y)			1.01 (0.91; 1.12)	.9054		
Fibroid location	1—submucosal	1	Reference	.7084	Reference	.2452
	1—transmural	0.4762	5.81e-08 (NA; 1.52e+108)		7.11e-08 (NA; 6.41e+107)	
	1—subserosal	0.6	9.58e-08 (NA; 1.19e+70)		6.44e-08 (NA; 3.14e+87)	
	Polymyomatous	0.55	7.67e-08 (NA; 2.02e+108)		8.58e-08 (NA; 6.34e+107)	
	2 myomas	0.4	4.26e-08 (NA; 1.24e+108)		3.05e-08 (NA; 2.33e+107)	
	ADN+fibroid	0.55	7.67e-08 (NA; 9.53e+107)		1.01e-07 (NA; 9.18e+106)	
	Pure ADN	0	4.08e-15 (0; 1.25e+43)		3.74e-15 (NA; 3.55e+153)	
Adenomyosis	No	0.49	Reference	.7740	Reference	.9106
	Yes	0.43	0.77 (0.23; 2.43)		0.93 (0.26; 3.30)	
Ovarian protection	No	0.53	Reference	.4189	Reference	.0507
	Yes	0.39	0.55 (0.18; 1.61)		0.30 (0.08; 1.00)	
Gynecologic history	No	0.45	Reference	.3264	Reference	.2278
	Yes	0.59	1.78 (0.68; 4.86)		1.95 (0.66; 6.12)	
History of pregnancy failure	No	0.48	Reference	1.0000	Reference	.5598
	Yes	0.48	1.00 (0.42; 2.41)		1.33 (0.51; 3.52)	
Restoration	Partial	0.44	Reference	.2369	Reference	.1641
	Ad integrum	0.6	1.89 (0.74; 4.99)		2.13 (0.77; 6.54)	

This analysis was performed in the group of patients with at least 1 live birth (n=89). The cesarean delivery rates have only been calculated for qualitative predictors and are expressed as absolute values (between 0 and 1). The cesarean delivery rate was defined as the number of cesarean deliveries among live births. The odds ratios have been obtained by conventional logistic regression. Their 95% confidence intervals have been obtained by profiling.

The levels of significance are those of the nested model test with asymptotic approximation of the χ^2 distribution for quantitative variables, and those of Fisher exact test for qualitative variables with no correction for multiplicity. For 8 tests, the threshold to be used is $P<.00625$ (Bonferroni method).

ADN, adenomyosis; *NA*, not available; *UAE*, uterine artery embolization.

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SUPPLEMENTAL TABLE 10
Potential predictors of delivery at term

Variable		Delivery at term rate	Univariate analysis		Analysis adjusted for age during first post-UAE pregnancy (y)	
			Odds ratio	*P* value	Odds Ratio	*P* value
Age at embolization (y)			0.97 (0.87; 1.08)	.5815		
Age during first postembolization pregnancy (y)			1.01 (0.90; 1.15)	.8152		
Time between embolization and first pregnancy			1.01 (0.98; 1.04)	.5767	1.01 (0.98; 1.04)	.7177
Fibroid location	1—submucosal	0	Reference	.0625	Reference	.0298
	1—transmural	0.8571	9.39e+7 (5.05e-108; NA)		1.39e+08 (1.64e-107; NA)	
	1—subserosal	0.4	1.04 e+7 (1.03e-85; NA)		5.18e+6 (3.564e-46; NA)	
	Polymyomatous	0.7727	5.32 e+7 (2.25e-108; NA)		9.05 e+7 (9.94e-108; NA)	
	Two myomas	0.68	3.33 e+7 (1.18e-108; NA)		4.62 e+7 (5.13e-108; NA)	
	ADN+fibroid	0.5455	1.88 e+7 (1.33e-108; NA)		3.85 e+7 (1.15e-107; NA)	
	Pure ADN	1	2.45e+14 (3.49e-67; NA)		2.64e+14 (4.03e-152; NA)	
Adenomyosis	No	0.72	Reference	.5399	Reference	.9788
	Yes	0.64	0.7 (0.22; 2.5)		1.02 (0.26; 5.04)	
Ovarian protection	No	0.69	Reference	.0000	Reference	.9539
	Yes	0.72	1.17 (0.38; 4.09)		0.96 (0.27; 4.01)	
Gynecologic history	No	0.69	Reference	.5910	Reference	.2498
	Yes	0.77	1.55 (0.53; 5.22)		2.18 (0.60; 10.53)	
History of pregnancy failure	No	0.72	Reference	.6352	Reference	.8051
	Yes	0.68	0.8 (0.31; 2.11)		1.15 (0.39; 3.68)	
Restoration	Partial	0.72	Reference	.7950	Reference	.8824
	Ad integrum	0.68	0.821 (0.30; 2.33)		0.914 (0.28; 3.15)	

This analysis was performed in the group of patients with at least 1 live birth (n=89). Delivery at term rates have only been calculated for qualitative predictors and are expressed as absolute values (between 0 and 1). The delivery a term rate was defined as the number of pregnancies that were delivered at term among live births. The odds ratios have been obtained by conventional logistic regression. Their 95% confidence intervals have been obtained by profiling. The levels of significance are those of the nested model test with asymptotic approximation of the χ^2 distribution for quantitative variables, and those of Fisher exact test for qualitative variables with no correction for multiplicity. For 9 tests, the threshold to be used is $P<.00556$ (Bonferroni method). Green indicates that the test is significant at the threshold of $\alpha=0.05$ after correcting for multiplicity, orange that the test is significant at the threshold of $\alpha=0.05$ before correcting for multiplicity, and yellow that the test is significant at the threshold of $\alpha=0.10$.

ADN, adenomyosis; *NA*, not available; *UAE*, uterine artery embolization.

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SUPPLEMENTAL TABLE 11
Potential predictors of low birthweight (<2 kg)

Variable		Low birthweight rate	Univariate analysis		Analysis adjusted for age during first post-UAE pregnancy (y)	
			Odds ratio	*P* value	Odds ratio	*P* value
Age at embolization (y)			1.25 (1.01; 1.62)	.0434	1.66 (0.96; 4.14)	.0818
Age during first postembolization pregnancy (y)			1.17 (0.95; 1.48)	.1499		
Time between embolization and first pregnancy			0.97 (0.85; 1.03)	.3854	0.97 (0.85; 1.03)	.3893
Fibroid location	1—submucosal	0.5	Reference	.0246	Reference	.0537
	1—transmural	0	1.17e-09 (NA; 6.83e+175)		5.77e-10 (NA; 8.55e+164)	
	1—subserosal	0	1.17e-09 (NA; ∞)		9.10e-10 (NA; ∞)	
	Polymyomatous	0.10	0.11 (0.0031; 3.33)		0.04 (0.00048; 1.82)	
	Two myomas	0	1.17e-09 (NA; 2.13e+156)		3.33e-10 (NA; 1.13e+155)	
	ADN+fibroid	0.22	0.29 (0.0081; 9.45)		0.07 (0.00085; 3.62)	
	Pure ADN	0	1.17e-09 (NA; ∞)		7.52e-10 (NA; ∞)	
Adenomyosis	No	0.04	Reference	.1469	Reference	.2278
	Yes	0.17	4.6 (0.56; 31.26)		3.54 (0.41; 25.05)	
Ovarian protection	No	0.07	Reference	.5660	Reference	.2100
	Yes	0	3.98e-08 (NA; 7.18e+124)		5.16e-08 (NA; 4.84e+135)	
Gynecologic history	No	0.06	Reference	1.0000	Reference	.5001
	Yes	0.05	0.74 (0.04; 5.36)		0.46 (0.02; 3.83)	
History of pregnancy failure	No	0.05	Reference	1.0000	Reference	.6694
	Yes	0.07	1.36 (0.17; 8.69)		1.52 (0.18; 10.15)	
Restoration	Partial	0.07	Reference	1.0000	Reference	.9937
	Ad integrum	0.04	0.61 (0.03; 4.44)		1.01 (0.05; 10.03)	

This analysis was carried out in the group of patients with at least 1 live birth (n=89). Low birthweight rates have only been calculated for qualitative predictors and are expressed as absolute values (between 0 and 1). The low birthweight rate was defined as the number of children born with a low birthweight (<2kg) among live births. The odds ratios have been obtained by conventional logistic regression. Their 95% confidence intervals have been obtained by profiling. The levels of significance are those of the nested model test with asymptotic approximation of the χ^2 distribution for quantitative variables, and those of Fisher exact test for qualitative variables with no correction for multiplicity. For 9 tests, the threshold to be used is $P<.00556$ (Bonferroni method). Green indicates that the test is significant at the threshold of $\alpha=0.05$ after correcting for multiplicity, orange that the test is significant at the threshold of $\alpha=0.05$ before correcting for multiplicity, and yellow that the test is significant at the threshold of $\alpha=0.10$.

ADN, adenomyosis; *NA*, not available; *UAE*, uterine artery embolization.

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