

Clinical experience and fertility outcome after uterine artery occlusion and embolization

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Abstract We evaluated the effects of uterine artery occlusion and embolization on clinical results and pregnancy outcome using information provided by the literature published in the MEDLINE biomedicine database. Uterine artery occlusion has the potential to compromise fibroid growth and its symptoms. There were only a few complications and adverse events associated with laparoscopic uterine artery occlusion (LUAO) and fibroid embolization. LUAO and uterine artery embolization (UAE) procedures are both minimally invasive operating procedures that preserve the uterus and ovarian blood supply and allow achievement of pregnancy in women with symptomatic fibroids. Women who became pregnant after uterine artery occlusion and embolization had increased risk of abortion, pre-term birth, malpresentation, and/or caesarean delivery.

Keywords Uterine artery occlusion · Laparoscopy · Embolization · Fibroid · Pregnancy

Introduction

Hysterectomy is the most common treatment for symptomatic fibroids. The demand for alternative treatments has increased since the end of last century, both by patients and by surgeons looking for less invasive procedures.

Laparoscopic myomectomy (LM) has become such an alternative procedure. Surgical myomectomy has been considered a treatment of choice for women with uterine leiomyomata who desire a safe pregnancy or wish to maintain their fertility. Laparoscopic myomectomy, rather than abdominal myomectomy, is naturally favoured by patients because it is less invasive and requires a shorter recovery time [1]. Myomectomy is less desirable for women who wish to avoid the possibility of conversion to hysterectomy and who desire a safe pregnancy without a risk of uterine rupture [2–4].

Uterine artery occlusion (UAO) is an increasingly popular alternative to hysterectomy and myomectomy as a treatment for uterine fibroid tumour or postpartum bleeding. Uterine artery embolization (UAE) and laparoscopic uterine artery occlusion (LUAO) are the most known forms of UAO. Information on its effects on fertility and infertility is limited. The purpose of this review was to evaluate the effects of uterine artery occlusion on pregnancy and delivery using information provided by the literature published in the MEDLINE biomedicine database.

Uterine artery embolization: current status

Historical

Trans-catheter uterine artery embolization was originally used in obstetrics in 1979 to control persistent massive postpartum haemorrhage after failure of surgical ligation of the hypogastric arteries. The same procedure was introduced by Ravina et al., in 1994, as a primary treatment for uterine fibroids [5].

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Preoperative patient assessment

Both the physician and patient should understand that UAE is a relatively new procedure and is associated with potential side effects and complications. Recommended preoperative evaluation tests are the following: physical/pelvic examination, imaging: sonography, CT scan, MRI ± hysteroscopy, laboratory tests (electrolytes, complete blood count, coagulation and renal function tests) and Papanicolaou smear within the past year. Contraindications to UAE are specified in Table 1 [6].

Technical overview of uterine artery embolization

The goal of UAE is to deliver particulate material—typically polyvinyl alcohol (PVA) particles, PVA microspheres, and/or gelatin-coated tris-acryl polymer microspheres—into both uterine arteries to produce ischaemic changes to myomas without causing permanent damage to the uterus [7]. Using conscious sedation, local or intravenous analgesia, or epidural analgesia, the surgeon inserts a 5F catheter into the right femoral artery. When both uterine arteries have been identified by subtraction angiography, arteriography is performed to confirm that no vascular anomalies are present. Once the desired artery is located, a variety of embolic agents is injected until the flow becomes sluggish [6].

Clinical outcomes of uterine artery embolization

An ideal conservative treatment of fibroids would eliminate symptoms, markedly reduce the size of fibroids, limit recurrence of future fibroids, and preserve fertility. In 2000, Hurst and associates published collective results of UAE as a treatment for symptomatic myomas [8]. Through a MEDLINE literature review, the authors identified seven major reports, which included a of 694 women. At variable follow-up intervals of 2 months to 12 months, abnormal uterine bleeding and uterine volume had decreased by 20% to 88% and 35% to 69%, respectively. In 2003, Pron et al.

reported a Canadian multicentre clinical trial on 555 women. UAE was accomplished bilaterally in 538 (97%) women, unilaterally in 14 (2.5%) and was unsuccessful in three (0.5%) women. Follow-up ultrasound at 3 months showed a mean uterine and dominant fibroid volume reduction of 35% and 42%, respectively [9].

Risks of UAE, side effects and complications

Peri-operative risks and complications of UAE include bleeding and haematomas at the puncture site of the groin femoral artery, allergic or anaphylactic reactions to the iodinated contrast dye, incomplete uterine artery access, misembolization of non-target organs, and/or severe pain [6]. Major complications after UAE for uterine fibroids are estimated to occur in 1–5% of cases [10]. Serious infectious complications affect 1% to 2% of cases, and this problem is encountered more frequently with embolization of larger fibroids [11]. To date, three deaths attributable to sepsis have been reported in association with embolization of the uterine arteries [12–14]. Approximately one-third of all patients develops postembolization fever. Perhaps the most troubling aspect after embolization is that it may be difficult to distinguish between severe postembolization syndrome and a secondary infection [7]. Hysterectomy after UAE is necessary in approximately 1% of patients.

Fertility and pregnancy outcomes after uterine artery embolization

The first report of pregnancy after UAE occurred in 1995 [5]. There are not sufficient data to conclude that UAE is a safe option for women wishing to retain their fertility. Serious concerns have been raised about the potential effects of UAE on fertility and pregnancy outcomes [6]. A total of 107 pregnancies was reported after UAE for fibroids; delivery outcomes are provided for 69 of those pregnancies (Table 2).

In 2004, Goldberg et al. compiled data from 139 pregnancies after laparoscopic myomectomy and 53 pregnancies after fibroid embolization [15]. Of this total, 31 patients (58%) were from the collective experience of Ravina et al. in France. Authors reported that pregnancies after UAE were associated with significantly higher rates of pre-term labour (16%) and malpresentation (11%) than were pregnancies after laparoscopic myomectomy [odds ratio (OR) 6.2; 95% confidence interval (95% CI) 1.4–27.7 and OR 4.3; 95% CI 1.0–20.5, respectively]. Pron and colleagues (The Ontario Multicentre Trial) reported 24 pregnancies in 21 women from a population of 538 women treated with UAE for symptomatic fibroids [16]. The clinical outcomes did not differ from those reported in the general population. The authors concluded that women are

Table 1 Contraindications to UAE

Contraindicating factors	
1.	Current pregnancy
2.	Pelvic inflammatory disease or active pelvic infection
3.	Contrast medium allergy
4.	Uncorrected coagulopathy or vascular disorders
5.	Arteriovenous malformation
6.	Severe renal insufficiency
7.	Prior pelvic irradiation
8.	Ovarian, uterine, endometrial or cervical cancers or undiagnosed pelvic mass

Table 2 Pregnancy and delivery outcome after UAE

Reference	Number of UAE subjects	Number of pregnancies	Number of deliveries
Ravina et al. 2002 [52]	184	12	7
Goldberg et al. 2002 [15]	NS	2	2
Walker and Pelage 2002 [10]	400	13	9
Pron et al. 2005 [16]	555	24	18
Walker and McDowel 2006 [17]	1200	56	33

able to conceive after fibroid embolization and most of these pregnancies resulted in term deliveries of appropriately grown newborns. Walker and McDowell reported 56 completed pregnancies after UAE for leiomyomata [17]. Thirty-three (58.9%) of the 56 pregnancies had successful outcome. Six (18.2%) of these were premature. Seventeen (30.4%) pregnancies miscarried. There were three terminations, two stillbirths, and one ectopic pregnancy. Of the 33 deliveries, 24 (72.7%) were by caesarean section. There were 13 elective sections, and the indication for nine was a fibroid. There were six cases of postpartum haemorrhage (18.2%). Compared with the general obstetrics population, there was a significant increase in delivery by caesarean section and an increase in pre-term delivery, postpartum haemorrhage, miscarriage, and a lower pregnancy rate. When the demographic characteristics of the study population are taken into account, these results can be partly explained. There were no other obstetric risks identified. Mara et al. compared the effects of UAE and myomecomy on future fertility [18]. Their first results indicated that both methods were clinically successful in the majority of cases and were not connected with serious complications. On the other hand, premature menopause secondary to dissemination of embolization materials to the ovarian blood supply has been documented [7]. Additionally, decreased vascularity of the uterine endometrium and myometrium could affect embryo implantation. In fact, embolization particles have been identified after UAE in structures adjacent to the leiomyoma [19]. Ovarian function also may be compromised after UAE, and this is likely to reduce fertility.

Although the number of pregnancies after UAE is low, it seems that embolization may not be associated with adverse pregnancy outcomes.

The Society of Obstetricians and Gynecologists of Canada Clinical Practice Guidelines states: “UAE as a treatment for fibroids in patients wishing to preserve their fertility should be undertaken with full disclosure to the

patient about limitations of such a procedure and the lack of existing data regarding future fertility and pregnancy outcomes” [20].

Laparoscopic uterine artery occlusion: current status

Historical

In 1999, Lee and colleagues reported on the feasibility of laparoscopic uterine ligation in 62 women for primary treatment of symptomatic uterine fibroids [21]. The average reduction of dominant fibroid volume was 54%. The preliminary evidence suggested that laparoscopic occlusion of uterine arteries in women with symptomatic fibroids was feasible and safe.

Preoperative patient assessment

Physician and patients should also understand that LUAO is a new surgical procedure and is associated with potential side effects and complications related to the surgical nature of the procedure. Common contraindications for laparoscopy should be respected. Laparoscopic identification and occlusion of the uterine arteries require an excellent knowledge of retroperitoneal anatomy, expertise and skills (Fig 1). The use of laparoscopy in infertile women may help to detect tubal or ovarian disease. Also, the combining of the uterine artery occlusion procedure and myomectomy may be useful for the treatment of small fibroids, which have not been primarily removed. The operating technique for LUAO has been described in more detail elsewhere

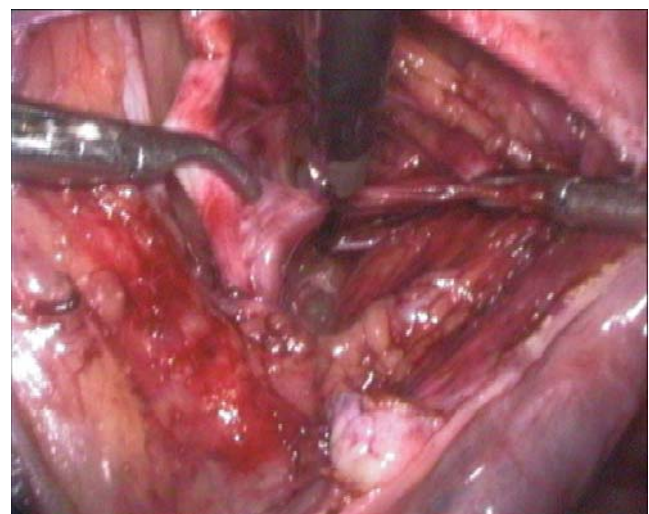


Fig. 1 Retroperitoneal pelvic topography. The grasper working on the left side separates the obturator nerve and obturator artery. Medially is displayed the umbilical ligament and coagulated left uterine artery before transection. Paravesical and pararectal spaces are developed

[22–25]. An overview of the surgical techniques of uterine artery occlusion is shown in Table 3.

Technical overview of laparoscopic uterine artery occlusion

The goal of the laparoscopic procedure is to occlude uterine arteries and ensure ischaemic change to myomas without causing permanent damage to the uterus. This occlusive procedure is performed under general anaesthesia. The surgeon enters the retroperitoneal space above the psoas muscle, lateral to the posterior broad ligament, and applies a ligature or vascular clip and/or coagulates the uterine artery using electrosurgery or a harmonic scalpel (Fig. 2, 3). Rather than occluding uterine arteries laterally, some surgeons have opted to occlude the uterine artery transvaginally or medially through the posterior leaf of broad ligament close to the place where the uterine artery crosses the ureter [25–27].

Clinical outcomes for LUAO

Liu et al. reported that laparoscopic bipolar coagulation of uterine vessels (LBCUV) was technically feasible in 97.7% of women with symptomatic fibroids [22]. Using measurements derived from ultrasound evaluations, they demonstrated that uterine and dominant fibroid volume was reduced by an average of 46% and 76%, respectively. Holub et al. reported short-term results of laparoscopic uterine artery dissection using UltraCision (ultrasonically activated shears) in 17 women with symptomatic fibroids [23, 24]. At 3 months and 6 months follow-up, respectively, the average reduction in uterine volume was 23.6% and 36.8%, and the average reduction in dominant fibroid was 28.6% and 56.8%; 94.1% of women had an improvement in menorrhagia or dysmenorrhoea, and 91.6% had an improvement in bulk-related symptoms or pelvic pain 6 months after treatment. In 2002, Lichtinger and associates reported on LUAO in a small group of women, six by ligature and two by vascular clips, with symptomatic leiomyomas [26]. Improvement of symptoms was reported by all patients. To date, publications on laparoscopic uterine occlusion have been case series showing technical feasibility,

and mostly short-term outcomes (less than 1 year) or small randomised studies [22–28]. Mid-term results (up to 3 years), with a median follow-up of 14.5 months, showed a high rate of technical feasibility (98.5%), a low complication rate of 7.3%, and an average surgical time of 30.8 min [29]. The average reduction of the dominant fibroid was 57.8% in patients who were followed up on for longer than 12 months, and symptom improvement was 93.2%. The two comparative studies evaluated the treatment efficacies of uterine artery embolization and laparoscopic uterine artery ligation [28, 30]. Park et al. suggested that LUAO results mainly in physiological cell death, i.e. apoptosis, whereas the corresponding result is cell necrosis for uterine artery embolization [28]. Istre et al. compared the clinical outcome 6 months after treatment with bilateral laparoscopic occlusion of uterine embolization versus fibroid embolization [30]. Both laparoscopic occlusion of uterine vessels and embolization of uterine leiomyoma improved clinical symptoms in the majority of patients. Participants who had undergone the laparoscopic procedure had less postoperative pain but heavier menstrual bleeding for 6 months after treatment. The authors concluded that a larger study and longer follow-up are necessary before a definite conclusion can be made regarding the most effective treatment.

Risks of LUAO, recurrence and complications

To date, there are few significant data regarding complications and fibroid recurrence after surgical occlusion or transection of the uterine artery. The incidence of complication following the procedure is not yet clear, because few published studies are of sufficient size and follow-up period to determine the frequency of complications and incidence of fibroid recurrence [22, 26, 28, 30]. Hald et al. reported the results of a study of a small group of 22 women undergoing LUAO who had been treated using a vascular clip at the level of the internal iliac artery [31]. Suspicion of an effect on the obturator nerve was raised in three patients. These patients complained of a disturbance of skin sensibility and reduction of adduction of the leg corresponding to innervations of the nerve. The

Table 3 Overview of surgical techniques of uterine artery occlusion

Author	Reference	Year	Technique	Approach to the uterine artery
1. Liu et al.	[22]	2001	Bipolar coagulation	Laparoscopy
2. Holub and Kliment	[23]	2002	Harmonic scalpel	Laparoscopy
3. Pelozi	[25]	2006	Ligation	Transvaginal
4. Lichtinger et al.	[26]	2002	Ligation	Laparoscopy
5. Park et al.	[28]	2003	Vascular clip	Laparoscopy
6. Vilas et al.	[27]	2005	Clamp	Transvaginal
7. Hald et al.	[31]	2004	Clips + bipolar coagulation	Laparoscopy

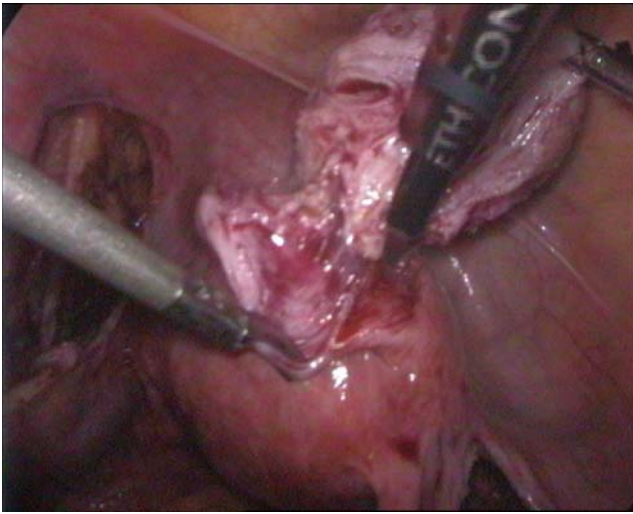


Fig. 2 Laparoscopic sub-serosal myomectomy. The ischaemic margins of the fibroid bed are white, after previous uterine artery occlusion

symptoms disappeared before 3-months' control in one of the patients and before 6-months' control in the second. The third improved after 6-months' control, but she still complained of some muscle weakness and lack of sensibility. One patient had a pulmonary embolism postoperatively. One hysterectomy was necessary, due to the lack of effect of the laparoscopic procedure. Recently, two small studies with 21 and 14 women, respectively, reported very low complication rates with the laparoscopic occlusive procedure (i.e. fever, infection) during a short-term period of follow-up [32, 33]. Only one recent study documented leiomyoma recurrence to be 9.0% at a medium follow-up of 23.6 months, with a 7.1% complication rate, including leiomyoma necrosis and endometrial stromal sarcoma [34]. The overall results, in terms of clinical improvement, failure, recurrence, and complications, are shown in Tables 4



Fig. 3 The grasped umbilical ligament is shown on the left side, and medially, the grasped uterine artery and pressed ureter

and 5. In one case, port-site intra-abdominal bleeding was observed 6 h after surgery and was treated successfully with a repeat laparoscopy, Foley catheter, and transfusion. Antibiotic therapy was administered postoperatively in cases of pyrexia. Neuritis of the obturator nerve was observed postoperatively in one patient, and this subsided after anti-inflammatory and electrostimulative convalescence therapy. However, the general application of laparoscopic uterine artery occlusion is limited by three factors: first, the operating technique can be used only on fibroids below the umbilicus; secondly, laparoscopy carries its own inherent risk and complication; and thirdly, the identification of retroperitoneal structures, such as the hypogastric artery, ureter and obturator nerve, and occlusion of the uterine artery require surgical expertise and skills beyond the capability of the average gynaecologist.

Fertility and pregnancy outcomes after laparoscopic uterine artery occlusion

To date there have been few significant data published about pregnancy outcomes and deliveries after surgical occlusion or coagulation of the uterine artery. A systematic search of the biomedicine database MEDLINE from 1976 to 2006, using terms such as pregnancy, occlusion, coagulation and/or dissection uterine vessels and fibroid only, identified case reports, pilot study or cohort study from a few institutions [35–38]. The first case of a successful pregnancy following classic bilateral uterine artery ligation was reported by Mitchell et al. [35]. Chen et al. [36] described one pregnancy with the delivery of a normal foetus following LBCUV and proposed that the procedure might not affect subsequent reproductive function. One year later, the same authors evaluated the incidence and outcome of post-LBCUV pregnancies with controversial conclusions [37]. Chen et al. [37] reported that the pregnancy and term pregnancy rates in sexually active women without contraception were 41.6% and 5.6%, respectively. Because a relatively high rate (41.2%) of early miscarriages was observed, they recommended that this procedure be employed only for women who did not desire additional children. In contrast to the previous outcomes,

Table 4 Symptom improvement, clinical failure and recurrence (Holub Z et al.; [34]). Two cases of fibroid necrosis were excluded

Length of follow-up (months)	Significantly improved	Slightly improved	Failed	Recurred
3 and 6	21	1	2	0
12	29	1	1	6
24	24	1	0	4
36	2	1	0	0

Table 5 Summary of complications experienced by patients (Holub Z et al.; [34]).

Variable	Number
Major complications	4
Minor complications	5
Intraoperative complication	0
Early postoperative complication	6
Port-site injury bleeding	1
Fever	4
Obturator nerve irritation	1
Late postoperative complication	3
Uterine or fibroid necrosis	2
Submucous fibroid expulsion	1

Holub et al. [38] reported more hopeful pregnancy and delivery outcomes of a small group of ten women following LUAO. Recently, the same authors compared the pregnancy results in women with symptomatic fibroids who had been treated by laparoscopic uterine artery occlusion with the results in women who had been treated by uterine artery embolization [39]. Pregnancies after uterine embolization had a higher rate (43.7%) of spontaneous abortion than pregnancies after surgical artery occlusion (15%), ($P < 0.05$). There were no significant differences between the groups in the pre-term deliveries (14.2% LUAO group versus 12.5% UAE group). The pregnant women from both groups studied did not show signs of significant foetal distress or growth retardation.

Fertility and myomas. Obstetrics outcomes after myomectomy: comparative data

Fibroids are found in 0.9–3.9% of pregnancies [40]. Their prevalence has been increasing as women proceed through the reproductive years. Prospective ultrasound studies of myomas throughout pregnancy have shown that there is an increased growth of less than 25%, mainly in the first

trimester [41]. It appears that fibroids play a role in infertility, and myomectomy has been shown to improve conception rates, especially when the lesions are submucosal [42, 43]. A similar relationship has been shown with miscarriages. The contribution of fibroids to infertility and reproductive failure is difficult to assess. It appears that fibroids, which distort the uterine cavity, may cause infertility and lead to recurrent miscarriages. Treatment is usually reserved for symptomatic fibroids or for infertile women. Conservative surgical options include hysteroscopic myomectomy, abdominal myomectomy, laparoscopic myomectomy and surgical occlusion of the uterine artery. Hysteroscopic myomectomy is an effective procedure for submucous leiomyomas. Abdominal and laparoscopic myomectomy may well be an excellent option for women who desire future childbearing or who wish to retain their uterus. Based on the limited available data, pregnancies after myomectomy and LUAO, compared with those pregnancies after UAE, may be at decreased risk for pre-term delivery and spontaneous abortion (Table 6).

Mechanism of action of uterine artery occlusion and pregnancy theoretical implication

Burbank [49] proposed that, after UAO by any means, both the uterine and myoma vessels occlude by clotting, resulting in organ ischaemia. After a few hours, the uterus initiates fibrinolysis, which results in its lysing its own clots, and reperfusion begins. Fibroids do not initiate fibrinolysis, which results in prolonged ischaemia and fibroid death. Clotted myomas do not reperfuse; they die. Childbirth appears to kill myomas through the mechanisms of transient uterine ischaemia. To test the above hypothesis, Lichtinger et al. [50] studied the time courses of myometrial ischaemia and reperfusion after LUAO in a small group of women with fibroids. The pH was measured with a catheter electrode embedded in the endometrium and myometrium. The pH

Table 6 Fertility and pregnancy outcomes after myomectomy and LUAO (LM laparoscopic myomectomy, AM abdominal myomectomy, MLPT mini-laparotomy)

Investigator (Ref)	Procedure	Pregnancy <i>n</i>	Delivery <i>n</i>	Pre-term <i>n</i> (%)	Abortion <i>n</i> (%)
Holub et al. [39]	LUAO	22	14	2 (14.2)	3 (15)
	UAE	17	8	1 (12.5)	7 (43.7)
Connolly et al. [44]	AM	25	19	-	6 (24.0)
Kumakiri et al. [45]	LM	47	32	1 (3.1)	11 (23.4)
Seracchioli et al. [46]	LM	158	106	2 (2) ^a	43 (27.2)
Palomba et al. [47]	LM	37	32	1 (3.1)	4 (10.8)
	MLPT	27	22	1 (4.5)	4 (14.8)
Goldberg et al. [48]	UAE	53	35	5 (24)	12 (24.0)
	LM	139	104	3 (3.0)	20 (15.0)

^a Under 36 weeks

reached its minimum by a median time of 36 min. The pH returned to base line after 2–8 hours of UAO. The uterus escaped ischaemia within 6 h of UAO in 80% of women.

On the basis of the above theory, we assume that uterine artery occlusion allows the preservation of the uterus and the achievement of pregnancy, and, also, following child-birth, it may help to treat fibroids through mechanisms of transient ischaemia.

Conclusion

Uterine artery occlusion has the potential to compromise fibroid growth and its symptoms. There were only a few complications and adverse events associated with LUAO and UAE procedures. Both laparoscopic uterine artery occlusion and fibroid embolization are minimally invasive operating procedures that preserve the uterus and ovarian blood supply and allow achievement of pregnancy in women with symptomatic fibroids. At this time, there is insufficient information to predict the percentage of women who will be able to become pregnant after uterine artery coagulation or embolization. It is very likely that the chance of pregnancy will depend on the extent of the fibroids and the quality of myometrial perfusion after previous uterine artery occlusion. Lichtinger et al. [50] and Burbank and Hutchinson [51] hypothesised a role of reperfusion and transient uterine ischaemia after UAO. Women who became pregnant after uterine artery occlusion had an increased risk for pre-term birth and for caesarean delivery. The issue involving clinical and pregnancy outcomes after uterine artery occlusion in UAE, laparoscopic bipolar or ultrasonic coagulation of the uterine artery needs to be studied prospectively in a large prospective study.

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