

Review Article

Fertility and pregnancy outcomes after uterine artery occlusion with or without myomectomy

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Abstract

Uterine artery occlusion (UAO) is one of the minimally invasive procedures used to treat uterine fibroids. It has demonstrated the potential to reduce fibroid growth and related symptoms with few complications and adverse effects. Meanwhile, it may preserve the uterus and ovarian blood supply to allow pregnancy in women with symptomatic fibroids. Similarly, myomectomy is an alternative to hysterectomy in the treatment of symptomatic fibroids, especially for patients who want to maintain fertility. However, only few articles have focused on fertility and pregnancy outcomes after the combined procedures of UAO and myomectomy. We reviewed the effects of UAO with or without myomectomy on fertility and pregnancy outcomes by searching the MEDLINE biomedicine database, using uterine artery occlusion, myomectomy and pregnancy as key words. In conclusion, conception and term pregnancy were possible after these procedures, but evidence on whether risks of abortion and preterm birth have been increasing simultaneously remains inconclusive. Therefore, good counseling on benefits and risks of pregnancy outcomes before performing these procedures is mandatory.

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Introduction

Uterine fibroids are the most common solid tumors occurring in the female pelvis. There is a growing demand for uterine preservation among women with symptomatic fibroids. There are several medical treatment modalities or surgical procedures that can fulfill this purpose such as abdominal myomectomy (AM) or vaginal myomectomy, medical therapy with gonadotropin-releasing hormone agonists, uterine artery embolization (UAE), uterine artery occlusion (UAO), myolysis, hysteroscopic myomectomy, endometrial ablation (EA), and magnetic resonance-guided focused ultrasound surgery.

Myomectomy is the conventional and most straightforward treatment for uterine fibroids. Nowadays, more women with symptomatic fibroids opt for laparoscopic myomectomy (LM) as they are encouraged by the availability of laparoscopic operations and health insurance coverage. The advantages of LM include smaller wound size, shorter recovery time, and higher resolution view of the anatomy. However, it remains a technically sophisticated procedure associated with higher incidence of surgical morbidity and blood transfusion. Appropriate preoperative planning on management strategy plus thorough discussion and counseling with patients and their family are necessary for LM, and the impact on fertility and pregnancy should be considered [1].

In 1999, Lee et al [2] reported on the feasibility of laparoscopic uterine artery ligation as the primary treatment of symptomatic uterine fibroids which resulted in obvious improvement. A growing number of surgeons managed uterine

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fibroids with combined UAO and myomectomy since 2000, following Liu's [3] advocacy on laparoscopic bipolar coagulation of uterine vessels. Many studies agreed that combined UAO and myomectomy had the advantages of decreased intraoperative blood loss and need for blood transfusion, increased symptomatic relief, and lowered recurrence rate, compared to myomectomy alone. In addition, successful term pregnancies had been reported after the procedures of uterine vessels occlusion. On the other hand, several research groups noted the increasing risks of spontaneous abortion, preterm delivery, malpresentation, cesarean section, and postpartum hemorrhage. Therefore, the issue of fertility and pregnancy outcomes following UAO with or without myomectomy needs more evidence for a better counseling.

Methods and procedures for UAO

There are a variety of procedures and methods for UAO depending on disease conditions and surgeons' technical preferences. The most popular procedure is to approach the retroperitoneal space by making a 3-cm vertical incision on the triangular area bounded by the round ligament, external iliac artery, and infundibulopelvic ligament. The uterine artery is separated from the ureter and the internal iliac artery by deviating the ureter medially, followed by the occlusion of the uterine artery. Many different methods of occlusion have also been advocated, such as bipolar coagulation, harmonic scalpel, ligation, vascular clipping, or clamping. In this report, we use the term "UAO" to represent all these procedures and methods. Among these, laparoscopic uterine artery occlusion (LUAO) is the most popular. However, there is a higher demand on skill proficiency for LUAO, and consequently, it should not be performed until familiarity with the anatomical site of origin of the uterine artery from the internal iliac artery and facility for the technique have been acquired [4].

Effects, complications, and recurrence rate of UAO

UAO blocks the blood supply to the fibroids. To avoid permanent damage to the uterus, the uterus had been reperused at different times [5]. In 2003, Park et al [6] evaluated the efficacy of LUAO and UAE for uterine fibroids treatment. The uterine volume slightly reduced in 3 months and continued to reduce up to 6 months after LUAO. Furthermore, the mechanisms of volume reduction were speculated by using specimens obtained from biopsy taken from the procedure. They concluded that slow and gradual cellular ischemia and reoxygenation occurred in 6 months after LUAO, which induced gradual and persistent volume reduction via apoptosis.

After LUAO, the uterine and dominant fibroid volume was reduced with an average of 46% and 76%, respectively. Approximate 90% patients reported relief or resolution of symptoms [7]. The mean operation time was 35.2 minutes, and the mean blood loss was 15 mL. The rate of major complications (life-threatening events or organ injury) was 3.5%; these include: unplanned removal, injury, or repair of organ during operative procedure, or unplanned return to operating

room for surgery during the same admission, or unplanned readmission within 14 days or admission after return visit to the emergency department for the same problem. And the rate of minor complications—such as fever, active bleeding, obturator nerve irritation, or fibroid necrosis—was 4.4%. The 2-year recurrence rate was 9% (cumulative recurrence rate was 11.7%, with a median follow-up of 23.6 months), as reported by Holub et al [8]; this rate was even lower to that reported for LM alone [9–12].

Fertility and pregnancy outcomes after UAO

Outcomes and possible risks

As a general consideration, UAO is not suggested for women who plan to have more children. Presumably, the blood flow to myometrium and endometrium as well as the uterine and placental perfusion would be compromised. The effects became more prominent with time, whereas the rates of abortion, preterm delivery, and small for gestational age increased with time. In 2003, Chen et al [13] recruited 142 symptomatic fibroid patients who were younger than 40 years of age and underwent LUAO by bipolar coagulation. The pregnancy and term pregnancy rates were 41.6% (15 of 36) and 5.6% (2 of 36), respectively. Because a relatively high rate of early miscarriage (7 of 17, 41.2%) had been observed, the authors concluded that this procedure should be recommended only for women who plan no further childbearing.

Holub et al [14] recruited 337 patients who were treated with either LUAO or UAE in one prospective cohort study. There were 38 patients and 40 pregnancies after LUAO and results showed 26 live births with 4 spontaneous abortions, 4 preterm deliveries, and 1 ectopic pregnancy during 1–3 years after the treatment. The average age of these women was 34.1 ± 5.58 years. The pregnancy rate and spontaneous abortion rate after LUAO were 46.9% and 10.5%, respectively. Meanwhile, increased risks of cesarean section and preterm deliveries after LUAO (73.1% and 15.3%, respectively) in comparison with the general population were noted. In the general population, spontaneous abortion was known to increase with maternal age, ranging from 18% in the late 30s to 34% in the early 40s [15]. Therefore, the 10.5% spontaneous abortion rate in the LUAO group did not appear to be higher than that in the general population. However, a relatively high rate of early miscarriage (41.2%) after LUAO was observed in the cited study [13].

Benefits and possible mechanism

In contrast to previous results, more than 180 term deliveries had been reported after UAO or UAE, without small for gestational age or fetal distress [14]. And the possible mechanism of LUAO in patients with more uncomplicated pregnancy was supported by several studies (discussed below).

Burbank [16] postulated that vessels in the myometrium and fibroids clotted after childbirth. Clot in the myometrium soon lysed, and the myometrium was reperused. In contrast, clot in the fibroids did not lyse and the fibroids necrosed. Childbirth appeared to necrose fibroids via the mechanism of

transient uterine ischemia. The coagulation–lysis cycle following UAO was, therefore, a physiological event of the uterus during childbirth. This inferred that UAO would not interfere with the outcome of further pregnancy.

One parameter of tissue perfusion is the pH of the tissue, which had been used for measuring ischemia in brain, myocardium, skeletal muscle, and fetus. Lichtinger et al [5] measured the myometrial pH continuously before, during, and 24 hours after LUAO. The pH reached its minimum at a median period of 36 minutes after occlusion, and returned to baseline after 2–8 hours of the occlusion. The uterus was free from ischemia within 6 hours in 80% of the patients.

Dubuisson et al [17] observed that during LUAO combined with LM, over the first few minutes following LUAO, the fibroid turned white before the uterus did. The uterus turned back to red color at the end of the operation, suggesting a fast revascularization. The uterus was collaterally vascularized by the cervicovaginal, ovarian, uterosacral, and round ligament arteries.

Fertility and pregnancy outcomes after combined UAO and myomectomy

Although the operation time and hospital stay were not shortened, procedures combining UAO and myomectomy had become more popular. It decreased intraoperative blood loss and blood transfusion needs due to transient ischemia of the fibroid and uterus. It also provided a higher rate of symptomatic improvement and a lower rate of recurrence compared to myomectomy alone because it could destroy the remained small, concealed “seeding” fibroids that might later become symptomatic [18]. In addition, the technique of preventive UAO limited the bleeding and avoided excessive coagulation and necrosis of the myometrium during myomectomy. This would reduce the risk of uterine rupture during pregnancy after myomectomy. Theoretically, the preventive UAO procedure was beneficial regarding the risk of uterine rupture after myomectomy [16].

Chang et al [19] prospectively measured the differences in uterine blood flow and perfusion of 105 symptomatic fibroid patients who underwent LM with or without LUAO. Power Doppler ultrasound was used to measure uterine artery resistance, pulsatility indices (RI and PI), and peak systolic velocity (PSV). Three-dimensional (3-D) power Doppler ultrasound was used to measure vascularization, flow, and vascularization flow indices (VI, FI, and VFI) of the uterus with VOCAL™ (Virtual Organ Computer-aided Analysis, Kretztechnik AG) software. The values of RI, PI, and PSV were comparable between the two groups preoperatively. These values were significantly lower in the LM with LUAO group 1 week after surgery and comparable again 3 months later. The myometrial VI and VFI decreased after surgery, and all 3-D power Doppler indices were similar in both groups throughout the study period. It had been concluded that concurrent of LUAO and LM reduced the intraoperative blood loss without permanently compromising uterine perfusion.

So far, there is still insufficient information to predict the percentage of women who are able to become pregnant after

uterine artery coagulation and myomectomy. It is very likely that the chances of pregnancy would depend on the extent of the fibroids and the quality of myometrial perfusion after the previous UAO [14]. Articles published on the MEDLINE biomedical database related to this topic included those discussed in the following subsections.

Laparotomic or laparoscopic UAO combined AM or LM

Liu et al [18] enrolled 342 patients aged 24–49 years who had uterine fibroids with symptoms warranting surgical treatment and wished to retain their uteri. Ligation of the uterine arteries was performed by either abdominal or laparoscopic approach before myomectomy. The operation time, intraoperative blood loss, postoperative improvement of symptoms, and recurrence rates were compared between the myomectomy alone and UAO combined with myomectomy groups. On average, an additional 13 minutes of operating time was required for the uterine occlusion procedure. Lower average blood loss (50 vs. 250 mL), more obvious menorrhagia resolution (100% vs. 84%), and lower recurrence rate (0% vs. 19.4%) were observed in the ligation combined with myomectomy group than in the myomectomy-only group ($p < 0.001$). In the myomectomy-only group, 58 of 98 (59.2%) patients attempting conception after surgery became pregnant, and 49 (50%) had live births. In the ligation combined with myomectomy group, 21 of 40 (52.5%) patients became pregnant and 15 (37.5%) had live births. The difference in live birth rates between the two groups was not statistically significant ($p = 0.182$). The results concluded that fertility capacity was not compromised by this new treatment approach—UAO combined with myomectomy. It might be because ligation was performed only on the uterine arteries before myomectomy, thus sparing the anastomotic circulations of the uterine arteries. Therefore, the impact on ovarian function was small for this procedure.

LUAO combined with repeat AM in recurrent fibroids

In 2007, Liu et al [4] enrolled 82 women with symptomatic, “recurrent” fibroids who had warranted surgical treatment but still wanted to retain their uteri. LUAO was performed before minilaparotomic myomectomy. The blood loss, need for blood transfusion, postoperative febrile morbidity, recurrence rates of the uterine fibroids, and fertility rates were compared between the AM alone and LUAO combined with AM groups. Although an average of additional 16 minutes was required for the LUAO combined with myomectomy group, the average blood loss (125 vs. 550 mL) and recurrence rate (5.8% vs. 36.7%) were significantly lower compared to the myomectomy only group ($p < 0.001$). In the LUAO combined with myomectomy group, 5 (19.2%) women had 6 clinical pregnancies among 26 women without receiving assisted reproductive techniques, including 3 (11.5%) women delivering 4 healthy infants with a preterm but healthy infant, 1 (3.8%) spontaneous abortion, and 1 (3.8%) ectopic pregnancy. In the myomectomy only group, 4 (22.2%) had clinical pregnancies out of 18 women who wanted pregnancy, including 2 (11.1%) live births and 2 (11.1%) spontaneous abortions. The

Table 1
Fertility and pregnancy outcome after LUAO with or without combined myomectomy.

Study	Procedure	Pregnancy (n)	Pregnancy rate (%)	Live birth (%)	Preterm, n (%)	Abortion, n (%)
Chen et al 2001 [13]	LUAO	17	41.6 (15/36)	5.6 (2/36)	NR	7 (41.2%)
Holub et al 2007 [26]	LUAO	22	48.7 (20/41)	34.1 (14/41)	2 (14.2%)	3 (15%)
	UAE	17	51.8 (14/27)	29.6 (8/27)	1 (12.5%)	7 (43.7%)
Liu et al 2004 [18] (both LM or AM)	Myomectomy	58	59.2 (58/98)	50.0 (49/98)	NR	NR
	LUAO + myomectomy	21	52.5 (21/40)	37.5 (15/40)		
Liu et al 2007 [4]	LUAO + mini-AM	6	19.2 (5/26)	11.5 (3/26)	1 (3.8%)	1 (3.8%)
(for recurrent myoma)	Mini-AM	4	22.2 (4/18)	11.1 (2/18)	0	2 (11.0%)
Holub et al 2008 [14]	LUAO	40	46.9 (38/81)	32.1 (26/81)	4 (15.3%)	4 (10.5%)
	LUAO + LM ^a	14	51.8 (14/27)	44.4 (12/27)	NR	1 (7.1%)
	UAE	28	51.2 (20/39)	25.6 (10/39)	2 (20.0%)	14 (56%)
Alborzi et al [24]	LM	7	35.7 (7/20)	30.0 (6/20)	0	1 (14.3%)
(women with infertility)	LUAO + LM	5	35.0 (5/14)	28.5 (4/14)	0	1 (20.0%)

AM = abdominal myomectomy (laparotomy); LM = laparoscopic myomectomy; LUAO = laparoscopic uterine artery occlusion; mini-AM = minilaparotomy myomectomy; NR = not reported; UAE = uterine artery embolization.

^a Included in LUAO group.

difference of live-birth rates between the two groups was not statistically significant ($p = 1.026$).

Most studies reported successful pregnancy outcomes between 20% and 50% of patients after primary myomectomy [20–22]. Only a few studies reported natural pregnancy outcome following secondary myomectomy. The 19.2% and 22.2% pregnancy rates of two groups in Liu et al's study were comparable to that reported by Frederick et al [23] (15%) in 2002. The possible reasons for the poor fertility outcome in both secondary myomectomy series [4,23] compared with primary myomectomy ones were severe pelvic adhesion and technical difficulty of procedures. However, there were no differences between the two groups in this study and Dr Liu's [18] other aforementioned studies in pregnancy rates' comparison. It was concluded that fertility had not been compromised by the incorporation of laparoscopic UAO into the repeated myomectomy procedure.

LUAO combined with LM

Only few articles have addressed the fertility and pregnancy outcome after a combined treatment of LUAO and LM. Their conclusions are summarized below.

Alborzi et al [24] enrolled 152 women with symptomatic uterine fibroids which required surgical intervention with the intention of uteri preservation. Sixty-five women underwent LUAO combined with myomectomy, while 87 women underwent LM only. All patients completed the 24-month follow-up in this prospective, controlled clinical trial. This study comprised the largest number of patients, particularly infertile patients, for both LUAO combined with LM group and LM only group. Infertility was the chief complaint of 14 (21.5%) patients in the LUAO combined with LM group and 20 (23%) in the LM only group. Operating time, blood loss, blood transfusion, febrile morbidity, improvement of symptoms, recurrence rate, and pregnancy rate were compared. Results showed that the LUAO procedure not only achieved an effective hemostasis during myomectomy but also prevented

intraoperative blood transfusion, with good justification of the additional 17 minutes operating time. Although febrile morbidity and average length of postoperative hospital stay were similar in both groups, blood loss (112 vs. 402 mL, $p < 0.001$) and recurrence rate (6.2% vs. 20.75%, $p = 0.012$) were significantly lower and improvement of symptoms (98.1% vs. 83.1%, $p = 0.007$) was significantly higher in the LUAO combined with LM group than in the LM only group.

For infertile patients in this study, the pregnancy rate and live birth rate were 35% (5 of 14) and 28.5% (4 of 14) in the LUAO combined with LM group, and 35.7% (7 of 20) and 30% (6 of 20) in the LM only group. One patient aborted in each group, which was not statistically significant. It was postulated that only the uterine arteries were ligated; therefore, both the pregnancy rate and live-birth rate were statistically insignificant. Thus, LUAO combined with LM might be an effective alternative for symptomatic fibroid patients who wish to preserve their fertility.

Temporary UAO combined LM

Liu et al [25] developed a new approach for LUAO: laparoscopic transient uterine artery ligation (LTUAL). The procedure involves "temporarily" ligating the uterine artery by a slipknot with a surgical suture, before performing LM, followed by untying the slipknot. They found unchanged menstrual pattern and uterine artery resistance index before and after surgery. Meanwhile, there were no significant differences in fibroid recurrent rates and pregnancy rates between LM with LTUAL and LM without LTUAL groups. Overall, the results showed that LTUAL combined with LM was preferable in patients who wanted pregnancies.

Conclusion

In conclusion, UAO combined with myomectomy is a new conservative treatment for symptomatic fibroids. It is minimally invasive, effective, and reliable in reducing operative

morbidities such as intraoperative hemorrhage, volume of blood transfusion, and recurrence rate. Only few low-incidence adverse events such as febrile morbidity, hemorrhage, obturator nerve irritation, and fibroid necrosis were associated with this procedure [8]. However, advanced skills were required to perform LUAO; therefore, it should not be performed until the surgeon is familiar with the pelvic anatomy and has achieved technical proficiency [4]. The potential risk of severe complications including life-threatening events or organ injury should be cautiously managed [8].

The fertility and pregnancy outcome after UAO and myomectomy are summarized in Table 1 [4,13,14,18,24,26]. Fertility may not be compromised, and there are no significant maternal complications or fetal abnormality reported in the available literature. The rationale of choosing such a conservative treatment is the commitment to preserve fertility. However, main concerns are the risks of spontaneous abortion, preterm delivery, and cesarean section. Particular caution should be exercised during occlusion procedures since significantly higher spontaneous abortion rates had been demonstrated [13]. Patients should be well counseled regarding the benefits and risks of these procedures before undergoing surgery. As a whole, all these issues need to be further investigated in large prospective clinical trials.

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