

The role of preventive uterine artery occlusion during laparoscopic myomectomy: a review of the literature

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Abstract

Purpose Surgical myomectomy is currently regarded as the standard conservative treatment for patients who wish to preserve their fertility. However, it presents two main problems: the intra- and postoperative risk of bleeding and the risk of recurrence of leiomyomas. Preventive occlusion of uterine arteries was described during laparoscopic myomectomy as one of the procedures addressing these issues.

Methods We conducted a literature review to define the role of preventive uterine artery occlusion during laparoscopic myomectomy.

Results Nine non-randomized case–control studies and two randomized controlled trials were identified. The permanent and bilateral uterine artery occlusion technique is the most studied in the literature. The main purpose of facilitating the operative procedure by reducing blood loss has not been clearly demonstrated in randomized trials. Observational comparative studies found an improvement in the effectiveness of treatment, both on clinical symptoms and on the recurrence of leiomyomas. Finally, there are few data examining the effect of uterine artery occlusion on later fertility in female patients of childbearing age, which limits its current use.

Conclusion The preventive occlusion of uterine arteries is a safe surgical technique that can be performed during laparoscopic myomectomy. Further randomized studies are needed to better define the role of uterine artery occlusion in the surgical strategy, especially for women who want to preserve their fertility.

Keywords Myomectomy · Laparoscopy · Uterine artery · Occlusion · Fertility

Introduction

Uterine leiomyomas are the most common benign tumors of the female genital tract. Their prevalence increases with age, ranging from 20 to 40 % before the age of 35 and up to 70 % in the African American population after 50 years of age [1]. Despite these high percentages, most uterine leiomyomas are asymptomatic. Depending on their size and location, some leiomyomas can cause abnormal uterine bleeding and, less frequently, pelvic pain, compression of adjacent organs (leading to urinary and intestinal symptoms) and fertility problems (infertility, implantation failure, repeated abortions).

Hysterectomy, the standard surgical treatment of symptomatic leiomyomas, is the most effective treatment associated with a high rate of long-term satisfaction [2].

In the last decades, with the rise of the age at the first pregnancy, symptomatic leiomyomas are encountered with an increased frequency in women with a desire of future pregnancy. Several alternatives to hysterectomy have therefore been developed in women who wish to preserve their future fertility, including surgical myomectomy and radiological embolization of uterine arteries [3]. Surgical myomectomy is the standard treatment for women who want to become pregnant. Several surgical approaches are available depending on the location and size of leiomyomas: hysteroscopy, laparotomy, laparoscopy, robot-assisted laparoscopy and, more rarely, vaginal myomectomy. Hysteroscopic treatment is limited to isolated submucosal leiomyomas with a maximum size of 4 cm and a sufficient residual myometrial thickness [2]. This approach is usually

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technically feasible if the preoperative assessment has been thoroughly done. For the treatment of intramural and subserosal uterine leiomyomas, laparoscopy, with the benefits of a minimally invasive approach, has established itself over laparotomy [4]. It should be given priority except for leiomyomas measuring more than 9 cm or in the case of multiple leiomyomas (more than 3) [2]. Despite advances in minimally invasive surgery, conservative surgical treatment of leiomyomas still faces two major problems: the morbidity associated with surgery and the risk of recurrence of leiomyomas and/or symptoms.

As regards the morbidity related to surgery, myomectomy is associated with a high risk of intra- or postoperative bleeding, requiring a blood transfusion and/or hemostatic hysterectomy in some cases. This risk exists regardless of the surgical approach used. In some series relating the morbidity associated with abdominal myomectomy, the risk of blood transfusion is even higher than 20 % with a 2 % rate of hysterectomy [5]. Several techniques have been developed to reduce the risk of bleeding during myomectomy. They are based on two main principles:

- The removal of the blood flow from the uterine arteries: peri-cervical “tourniquet” technique, preoperative radiological embolization, preventive surgical occlusion of the uterine arteries;
- The use of uterotonic or vasoconstrictor agents: administration of oxytocin, misoprostol, sulprostone; intramyometrial injection of vasopressin or a mixture of bupivacaine and epinephrine.

A systematic Cochrane review published in 2011 found a significant reduction in intraoperative bleeding with the use of intravaginal misoprostol, vasopressin or an intramyometrial injection of the mixture epinephrine-bupivacaine, and peri-cervical tourniquet [6]. However, these conclusions are based solely on the results of one or two randomized trials for each of the analyzed techniques. Publications examining surgical vascular occlusion techniques were not included in this systematic review.

As regards the risk of recurrence after surgical myomectomy, Nezhat et al. [7] found a cumulative risk of recurrence of 51.4 % after 5 years in a series of 114 laparoscopic myomectomies. After abdominal myomectomy, the risk of second intervention after 10 years (myomectomy or hysterectomy) varies between 15 and 20 % [8–10]. Recurrences can be explained either by the appearance of new leiomyomas or a growth of leiomyomas left in place during myomectomy because of their small size or their deep location.

The preventive occlusion of uterine arteries is a surgical technique that can be performed during laparoscopic myomectomy. Its main objective is to facilitate the

operative procedure by reducing intraoperative blood loss and improving the quality of uterine suturing. Other expected long-term benefits are an improvement in the effectiveness of the treatment, both clinical symptoms and the recurrence of leiomyomas. There is, however, no data investigating the effect of the uterine arteries occlusion on the ovarian reserve of patients of childbearing age, which limits its current use. We, therefore, conducted a review of literature to define the exact role of preventive techniques of vascular occlusion during laparoscopic myomectomy.

Materials and methods

Operating techniques

Here we describe the different surgical procedures used for occlusion of the uterine arteries by laparoscopy [11].

The installation phase is identical to that of any laparoscopic myomectomy. A 10–12 mm trocar is inserted umbilically or supra-umbilically according to the uterine volume to benefit from a full panoramic view of the pelvis. It is necessary to work at a distance from the leiomyoma. Exploration of the pelvis makes it possible to examine the accessibility of the fibroid, the mobility of the uterus and consistency with the mapping of leiomyomas made preoperatively. Three accessory trocars—two 5 mm trocars and one 10 mm trocar are then placed.

The preventive occlusion of uterine arteries is carried out by either an “upper approach” at the pelvic triangle or by a more direct “posterior approach” at the posterior and lower part of the broad ligament. The preferred technique is the posterior approach because access to the uterine artery is more direct and least invasive. The operator can choose the upper approach intra-operatively according to local conditions (site and size of leiomyoma, uterine mobility, adhesions).

In the case of the posterior approach, the pelvic parietal peritoneum is incised over 15 mm under the ovarian fossa opposite the uterine artery, whose path runs parallel to the path of the ureter located just below. The ureter, therefore, has to be previously identified by transparency by its crawling movement so that the peritoneal incision is carried out parallel to its path 10 mm above it. Occlusion of the artery is performed by inserting 10 mm vascular clip across the 10 mm accessory trocar. The technique can be facilitated by temporarily fixing the ovary of the abdominal wall ipsilaterally.

In the case of the upper approach, the uterine artery is accessed through a peritoneal incision behind the round ligament that extends to the infundibulo-pelvic ligament. The umbilical artery is identified and then followed forward and backward as far as the identification of the uterine

artery at its origin. The ureter appears medial to the dissection and must be identified before any occlusive procedure.

By analogy with pelvic lymphadenectomy, there are no data supporting the need to close the peritoneum.

If a transient occlusion is decided by the operator, the clips can be easily removed at the end of procedure or “Bulldog” type clamps can be used instead of the clips.

Methods

This literature review includes all publications studying preventive uterine artery occlusion techniques by laparoscopy during myomectomy. The identification of studies comparing “myomectomy with preventive uterine artery occlusion” and “myomectomy only” groups is based on the search engines PubMed, Cochrane Library and EMBASE using the keywords: myomas, uterine artery, laparoscopy, myomectomy, uterine artery occlusion, uterine artery clipping, uterine artery ligation, uterine artery blockage. Scientific articles referenced until May 2014 were taken into account.

Results

Nine non-randomized case–control studies [12–19] and two randomized controlled trials [20, 21] were identified. The technique used was temporary preventive occlusion for 3 of the 11 studies analyzed [17, 19, 21].

Current data do not demonstrate any ureteral injury or specific vascular injury related to uterine artery occlusion, even if these are theoretically possible. In a prospective series including 114 procedures, Holub et al. describe a case of postoperative irritation of the obturator nerve successfully treated with non-steroidal anti-inflammatory drugs and electrostimulation. One case of failure of the vascular occlusion technique related to the presence of dense pelvic adhesions is also described [22]. In randomized trials, the mean operative time for dissection, identification and occlusion of the uterine arteries was 15 min [20, 21].

Uterine artery occlusion and results on symptoms

There are no prospective randomized studies comparing the improvement of symptoms in the case of myomectomy alone or combined with preventive occlusion of uterine arteries. However, all observational comparative series found a significant improvement in symptoms in the case of associated uterine artery occlusion.

Liu et al. [12] thus demonstrate a 99.1 % improvement in symptoms in the “occlusion + myomectomy” group

versus 81.5 % in the “myomectomy only” group ($p < 0.001$) for a minimum postoperative follow-up of 3 months.

Holub et al. [14] found a 100 % improvement in symptoms after 3 months in the “occlusion + myomectomy” group versus 85.7 % in the “myomectomy only” group ($p < 0.05$).

Finally, Alborzi et al. [16] confirm these data in a 24-month follow-up with an improvement in symptoms of 98.1 % in the “occlusion + myomectomy” group versus 83.1 % in the “myomectomy only” group ($p = 0.007$).

Uterine artery occlusion and leiomyoma recurrence

No prospective randomized study examines the risk of recurrence of leiomyomas and/or symptoms. Comparative non-randomized studies show significant heterogeneity in the definition of recurrence because they take into account the recurrence of symptoms, the ultrasonographic presence of leiomyomas or the need for another operative procedure. Similarly, the ultrasound definition of recurrence is not clearly defined, the size of the leiomyomas included in the studies varies between 5 and 20 mm. Some authors exclude patients with residual leiomyomas during postoperative ultrasound follow-up [17].

Table 1 summarizes recurrence rates found in the comparative series. All studies show a reduction in the rate of recurrence in the case of permanent occlusion of the uterine arteries. The rate of recurrence varies between 0 and 6.2 % for these women [12, 15, 16, 18]. In the case of transient occlusion of the uterine arteries, the rate of long-term recurrence in the seams is identical to that of myomectomy only [17, 19]. The transient occlusion of the uterine arteries does not appear to influence the rate of recurrence in the long term.

Uterine artery occlusion and blood loss

The evaluation of bleeding during myomectomy is the primary outcome in both currently published randomized studies [20, 21]. It can be done either directly by measuring the volume of blood loss during surgery or indirectly through changes in hemoglobin during hospitalization and the rate of blood transfusion.

Holub et al. [20] analyzed blood loss in a small sample by comparing the “occlusion + myomectomy” ($n = 16$) and “myomectomy only” ($n = 15$) groups. The results did not reach statistical significance for intraoperative bleeding, with an average blood loss estimated at 93.7 ml in the first group versus 134 ml in the second group ($p > 0.05$). However, postoperative bleeding, evaluated by drainage of the abdominal cavity, was significantly reduced in the “occlusion + myomectomy” group (46 versus 92.4 ml,

Table 1 Results of comparative studies on rates of recurrence for leiomyomas and/or symptoms

References	Mean follow-up (months)	Rate of recurrence (%)		<i>p</i>
		UAO + myomectomy	Myomectomy only	
Liu [12]	25.4	0	19.4	<0.001
Liu [15]	42.5	5.8	36.7	<0.001
Alborzi [16]	24	6.2	20.7	0.012
Liu [17] ^a	25	19.5	12.7	–
Bae [18]	11.1	2	13	0.04
Kwon [19] ^a	6	4.1	7.5	0.801

^a Transitory occlusion of uterine arteries

Table 2 Results of comparative studies on intraoperative blood loss and the number of blood transfusions

References	Blood transfusions (<i>n</i>)		Blood loss (ml ± sd)		<i>p</i>
	UAO + myomectomy	Myomectomy only	UAO + myomectomy	Myomectomy only	
Liu [12]	4	5	50 ± 26.9	250 ± 132.5	<0.001
Dubuisson [13]	1	0	–	–	–
Holub [14]	0	0	77.3 ± 81.2	147.4 ± 110.6	<0.001
Liu [15]	0	4	125 ± 72.6	550 ± 394.8	<0.001
Alborzi [16]	0	15	173.6 ± 91.5	402.9 ± 131.6	0.0001
Liu 2011 [17]	0	5	75	170	0.001
Bae [18]	0	0	72.3 ± 109	62.6 ± 77.3	ns
Kwon [19]	–	–	111.9 ± 78.9	203.4 ± 152.4	<0.001

sd standard deviation, *ns* non-significant

$p < 0.05$). Similarly, the measurement of changes in hemoglobin on the third postoperative day is in favor of preventive uterine artery occlusion (0.6 versus 1.2 g/dl, $p < 0.005$). It is worth mentioning the low volume of leiomyomas removed during the procedure in this study: 4.4 cm for the “occlusion + myomectomy” group and 4.7 cm for the “myomectomy only” group. The benefit of systematic drainage of the abdominal cavity in this context was also not shown.

Vercellino’s multicenter, randomized trial-studied transient occlusion of the uterine arteries during laparoscopic myomectomy by comparing two groups of 80 and 86 patients [21]. Intraoperative blood loss was not directly evaluated in this study because this method of measurement was considered too approximate by the authors. The results show a significant difference of hemoglobin levels on the third postoperative day: a drop of 1.20 g/dl in the “occlusion + myomectomy” group versus 1.45 g/dl in the “myomectomy only” group ($p < 0.05$). Two cases of postoperative bleeding were identified in the “occlusion + myomectomy” group versus one in the “myomectomy only” group. There was no blood transfusion in either group. The authors outline the possible disadvantages of transient occlusion of uterine arteries that may mask bleeding during removal of vascular clamps or promote postoperative cervical hematoma.

Other non-randomized studies have demonstrated a significant reduction in blood loss in the “occlusion + myomectomy” group compared to the “myomectomy only” group (Table 2). The comparative “case-control” study by Bae et al. [18] was the only one not to find any significant difference between the two groups. In this study, it is noteworthy that patients in each group received an intramyometrial injection of vasopressin. For a comparable mean diameter of leiomyomas, the intraoperative bleeding volume appears very low compared to other studies.

Uterine artery occlusion and fertility

No randomized study has examined long-term fertility. Table 3 summarizes the different pregnancy rates in observational comparative studies.

Regarding the risk of spontaneous abortion, Liu et al. [15] found a rate of 3.8 % in the “occlusion + myomectomy” group versus 11.1 % in the “myomectomy only” group. In addition, the particularly low rate of spontaneous pregnancy observed in this series (22.2 % in the “occlusion + myomectomy” group and 19.2 % “myomectomy alone” group) can be explained by the characteristics of the selected population. Firstly, the average age is higher than in other studies (39.7 years) and, secondly, the selected

Table 3 Results of comparative studies on later pregnancy

References	Number of pregnancies (<i>n</i>)	Percentage of pregnancies (%)		Percentage of children born alive (%)	
		UAO + myomectomy	Myomectomy only	UAO + myomectomy	Myomectomy only
Liu [12]	79	52.5	59.2	37.5	50
Holub [14]	6	50	33.3	50	33.3
Liu [15]	9	19.2	22.2	11.5	11.2
Alborzi [16] ^a	12	35	35.7	28.5	30
Liu [17]	31	31.3	38.1	–	–

^a Percentage of pregnancies and living children reported from a sub-population of infertile women

patients have already undergone a myomectomy and therefore present a significant risk of adhesions.

Discussion

The principle of preventive uterine artery occlusion as surgical treatment of uterine leiomyomas was introduced by Liu [23]. It developed with the advent of laparoscopic myomectomy to reduce the morbidity associated with surgery, including the risks of bleeding and blood transfusion. Initially, the procedure was performed by laparoscopy without associated myomectomy, but the risk of recurrence appeared much lower in the case of associated myomectomy. Wang et al. [24] studied the long-term results for each of the two procedures in a cohort of 163 patients. They compared two groups who underwent uterine artery occlusion with or without associated myomectomy. The long-term results found 28.4 % recurrence of symptoms after 4 years in the absence of myomectomy versus 7.4 % with myomectomy ($p = 0.001$). The second intervention rate reached 13.7 % in the group without myomectomy versus 0 % in the group with myomectomy.

In view of the results presented in this literature review, uterine artery occlusion associated with laparoscopic myomectomy appears to be an effective procedure because it improves results on symptoms and at the same time reduces the risk of recurrence. The occlusion of uterine arteries promotes involution by ischemia of deeper and smaller leiomyomas left in place and thereby reduces the risk of symptomatic recurrence [12]. The quality of the uterine suture is a key factor in determining the risk of uterine rupture during pregnancy and the indication for a cesarean section in a subsequent pregnancy. The absence of excessive bleeding in the myometrium probably improves uterine healing and reduces the risk of scarring necrosis.

The two randomized studies do not confirm the expected results regarding the reduction of risk of intraoperative and postoperative bleeding. Holub et al.'s [20] study did not reach the threshold for statistical significance for a

reduction in bleeding. Vercellino et al.'s [21] study only carries out an indirect analysis by measuring postoperative hemoglobin levels. Other non-randomized studies show significant heterogeneity in terms of treatment with differences associated with:

- The size of resected leiomyomas;
- Injection of vasoconstrictors or not;
- The occlusion technique itself (transient or permanent);
- Methods for evaluating blood loss.

It is difficult to know the real impact of uterine artery occlusion on clinical practice regarding the risk of bleeding. Alborzi et al. [16] Iranian study, however, shows a significantly higher rate of blood transfusion in the “myomectomy only” group reaching more than 17 versus 0 % in the “occlusion + myomectomy” group ($p < 0.00036$), which is a significant clinical impact.

By analogy with the radiological embolization of uterine arteries, there are still many uncertainties about the effect of uterine devascularization on later fertility. The impact on ovarian reserve and the effect of myometrial ischemia, even transitory, on implantation and placentation are indeed controversial. All the studies focusing on this are observational and have many selection biases.

The occlusion of uterine arteries is responsible for a decrease of about 40 % of the uterine vascularization [25]. The preservation of collaterals and vascular anastomoses during the selective occlusion of the uterine arteries would rapidly revascularize and supplement healthy uterine tissue, while leiomyomas would continue their involution by necrobiosis [26]. The comparative study of Doppler vascularization before and after occlusion of uterine arteries in 43 patients did not show significant differences in the resistance index of the uterine arteries and the homogeneity of the myometrial vasculature [13]. The same results were found at 3, 6 and 12 months postoperatively by Liu et al. [17].

Razavi et al. [27] identified three types of anastomoses by examining 76 patients eligible for radiological embolization of uterine leiomyomas using angiography:

- Type I (21.7 %, 33/152 arteries): the flow comes from the ovarian artery and travels to the uterus via the main uterine artery;
- Type II (3.9 %, 6/152 arteries): ovarian artery directly irrigates the leiomyoma;
- Type III (6.6 %, 10/152 arteries): the main part of the flow irrigating the ovary comes from the uterine artery.

Therefore, the risk of injuring the ovarian reserve during radiological embolization of uterine arteries depends essentially on the anastomotic vasculature of the ovary. In addition, to avoid occlusion of the anastomotic branches, it is currently recommended to use microspheres of over 500 microns in diameter during radiological embolization of uterine arteries [28]. This risk would be reduced with selective surgical occlusion of the uterine arteries.

In a prospective observational study involving 35 patients aged 36–45 years operated on for uterine leiomyomas, Wang et al. found a significant decrease in serum levels of anti-Müllerian hormone (AMH) in the second postoperative day after myomectomy only. AMH levels returned to baseline levels 3 months after surgery [29]. A more recent study complements these results by showing no significant changes in markers of ovarian reserve 6 months after myomectomy [30]. Myomectomy alone does not appear to influence the long-term ovarian reserve.

In a cohort study published in 2010, Qu et al. [31] compared the ovarian reserve (FSH, LH and inhibin B levels) in a “myomectomy with uterine artery occlusion” group and a “myomectomy only” group. At 1, 3 and 6 months postoperatively, the authors found no significant differences between the two groups. Preventive uterine artery occlusion during myomectomy does not appear to alter hormones of the pituitary-ovarian feedback loop compared with myomectomy alone, although these findings are based on the results of retrospective studies [31].

As regards later fertility, pregnancy can occur following permanent and transient uterine artery occlusion. Prospective data are, however, lacking to determine the real impact on ovarian reserve, the course of pregnancy, the mode of delivery and the risk of bleeding (placentation), which limits its current use. Although current data are reassuring, it is not recommended to use this technique routinely outside of clinical trials in patients who wish to become pregnant.

Conflict of interest The authors declare that they have no conflict of interest.

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