

*COLLÈGE NATIONAL
DES GYNÉCOLOGUES ET OBSTÉTRICIENS FRANÇAIS
Président : Professeur J. Lansac*

Extrait des Mises à jour en Gynécologie et Obstétrique

—
**TOME XXXII
publié le 3.12.2008**



*TRENTE-DEUXIÈMES JOURNÉES NATIONALES
Paris, 2008*

Update on myomas treatments

O. ISTRE *
(Oslo, Norvège)

INTRODUCTION

Traditional operative treatments for symptomatic fibroids are laparotomy with hysterectomy or myomectomy, involving considerable morbidity [1, 2]. Myomectomy involves the shelling out of fibroids from the myometrium, and in the case of submucosal fibroids these can be removed surgically via hysteroscopic procedures [3]. Although morbidity is reduced with endoscopic surgery, this technique is not widely available and has limitations.

NEW TREATMENT OPTIONS

A number of minimally invasive treatments options are now available for the treatment of symptomatic fibroids. Surgical treatments

* Department of Obstetrics and Gynaecology - Ulleval University Hospital - 0407 Oslo Norway - E-mail: post@oistre.com

with endoscopic technique include hysterectomy, myomectomy and myolysis [4]. Multiple fibroids pose a significant problem for treatment. When myomectomy or myolysis is performed and all clinically identified fibroids are removed or « killed », in approximately half of the patients fibroids are seen at a later time [5].

Non-surgical treatments include medical therapy and treatments interfering with the blood supply to the uterus or the fibroids, uterine artery embolization performed by interventional radiologist or laparoscopic uterine artery occlusion by the gynaecologist. Even simpler treatment is the non-incision temporary uterine clamp, placed in the side fornices in the vagina directed with doppler ultrasound.

The continued therapy goal for symptomatic fibroids must take into consideration the needs and desires of the patients, i.e. length of hospital stay, time to return to work, adverse events and childbearing plans. Hysterectomy continues to be costly in billions of dollars spent annually, as well as in the more fundamental terms of morbidity and mortality when compared with the less invasive alternatives [6].

UTERUS CIRCULATION

Uterus has a very rich blood supply through two extrinsic arterial systems, the uterine and ovarian arteries. Intrinsic uterine arteries consist of ascending uterine, arcuate, radial, and peripheral arteries implicating free flow through the uterus. Fibroids receive their blood supply from the intrinsic arteries, primary from branches of arcuate arteries, and the vessels are located in the pseudocapsule around the fibroids. The ipsilateral uterine and ovarian arteries are connected by communicating branches. In addition to its primary (uterine artery) and secondary (ovarian artery) extrinsic blood supply, the uterus enjoys a vast network of lesser known arterial collaterals [7]. If the blood supply from the right or left uterine artery is occluded, blood from the left or right artery will supply the myometrium by communications through arcuate arteries. Finally, if both uterine arteries are occluded, blood flow to the myometrium will develop from the ovarian arteries through communicating arteries. In addition to the primary and secondary blood flow, the uterus has a vast network of collateral arterial communication from the aorta external iliac and femoral artery branch [8].

FIBROID LIFE CYCLE

Fibroid degeneration is the physiological way of terminating further growth of fibroids. Fibroids are particularly susceptible to degeneration because their rapid growths need increased blood supply. Fibroids have unsubstantiated connection to the uterine blood supply and as a consequence, they frequently outgrow their blood supply, and consequently two thirds of the fibroids show degeneration [9]. Larger fibroids are more frequently associated with degenerative changes compared to the smaller ones [10]. The different types of degenerative changes are hyaline or myxoid degeneration (75 %), calcification (10 %), cystic degeneration (10 %), fatty degeneration and red degeneration during pregnancy.

IMPLICATION OF UTERINE ISCHEMIA

When the uterine circulation is interrupted, unperfused myometrium quickly becomes hypoxic, which will create pain. During ischemia, myometrial energy is derived anaerobically from the breakdown of glycogen through the glycolytic pathway [11]. After the uterine arteries are occluded, most blood stops flowing in myometrial arteries and veins, and the uterus becomes ischemic. It is postulated that myomas are killed by the same process that kills trophoblasts - transient uterine ischemia [12].

Over time, stagnant blood in these arteries and veins clots. Then, tiny collateral arteries in the broad ligament including communicating arteries from the ovarian arteries open, and cause clots within myometrium to lyse and the uterus to reperfuse. Fibroids, however, do not survive this period of ischemia [13]. This is a unique organ response to clot formation and ischemia. After the uterine arteries are bilaterally occluded, either by uterine artery embolization or by laparoscopic obstruction, women with fibroids experience symptomatic relief after some time.

PRACTICAL ASPECTS OF PROCEDURE: UTERINE ARTERY OCCLUSION

In 1964, Bateman reported the successful treatment of menorrhagia in four patients with fibroids and three with functional uterine bleeding [14]. This was the first published article that demonstrates that uterine artery occlusion by ligation, division or excision is an effective treatment for menorrhagia associated with fibroids and in patients without pathology.

Laparoscopic bipolar coagulation of uterine arteries and anastomotic sites of uterine arteries with ovarian arteries represents another modality of avoiding hysterectomy in some women [15, 16]. This procedure was first described in 2000 in three women with symptomatic fibroids who required conventional surgical treatment. Uterine size and dominant fibroid size were assessed by ultrasonography before and after surgery. Both uterine arteries, as well as anastomosis zone of uterine arteries with ovarian arteries, were occluded in all three women. Surgery was uneventful, and patients were hospitalized for only two days. All women experienced improvement in symptoms with no complications. Postoperative ultrasound showed progressive reduction in size of the dominant fibroid [17].

In our institution, we studied 46 premenopausal women, age 43 (34-51) years with symptomatic uterine fibroids, undergoing radiologic embolization ($n = 24$) or laparoscopic closure of the uterine arteries ($n = 22$) [18, 19]. The laparoscopic technique reduced picture blood assessment score after 6 months by 50 % in both groups. Uterus volume was also reduced by 35-40 % in both groups. Postoperative pain and use of pain relief differed significantly, as patients required more pain medication after embolization: ketobemidon 38 mg compared with 16 mg in the laparoscopic group ($P = 0,008$). In conclusion, we found that laparoscopic occlusion of uterine vessels is a promising new method for treating fibroid-related symptoms, with less postoperative pain than embolization and comparable effects on symptoms.

DESCRIPTION OF TECHNOLOGY: TEMPORARY ARTERY OCCLUSION

A new exciting device, utilizing the principle of interference with the blood circulation, has recently been developed (Vascular Control Systems, Inc., San Juan Capistrano, CA) (Flowstat) for the treatment of fibroids with non incision, only compression.

The system consists of a guiding cervical tenaculum, a transvaginal vascular clamp with integrated doppler ultrasound crystals, and a small, battery powered transceiver that generates audible doppler sound (Fig. 1). The clamp slides along the guiding tenaculum to the level of the lateral vaginal fornices at the 9:00 and the 3:00 cervical positions. When the crystals on the arms of the clamp contact the vaginal mucosa, they return audible signals from the right and left uterine arteries. When the clamp is further advanced along the guiding tenaculum, the clamp displaces the uterine arteries superior to their points of insertion into the uterus. When closed, the clamp occludes the uterine arteries bilaterally by squeezing them against the lateral borders of the uterus, and the clamp is remained in place for six hours (Fig. 1).

Fig. 1: The transvaginal vascular clamp with integrated Doppler ultrasound crystals and Doppler receiver. Pre-procedure = 82 cc. Post-procedure = 38 cc.



IN-VITRO AND IN-VIVO STUDIES

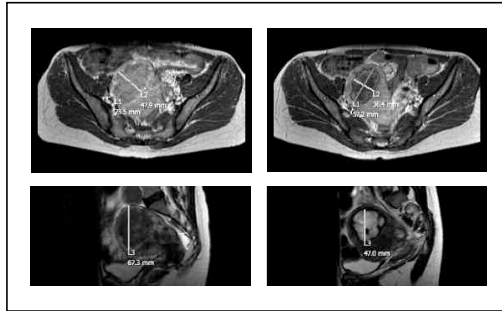
After uterine artery occlusion, pH falls and when clot lyses and reperfusion occurs, pH return to baseline. This has been investigated and monitored continuously before, during and 24 hours after laparoscopic occlusion of uterine arteries [20]. In patients with symptomatic fibroids, pH was measured with a catheter electrode embedded in the endometrium and in others in the myometrium. In 62 % of the patients pH dropped 0,4 to 0,8 units, while in 38 % the drop was greater, and the minimum was reached between 5 and 73 minutes. The return back to baseline was on average 5 hours. After the uterine artery is occluded, blood reaches the myometrium by secondary pathways and for most women, these vascular pathways are insufficient to maintain aerobic metabolism. Until clotting occurs, blood continues to flow and supply oxygen to the myometrium, although at a new and slower speed.

CLINICAL STUDIES

We presented the first publication with this new technique in 2004 where a 43-year-old woman with menorrhagia, dysmenorrhea and pelvic pain of several years duration with the uterus enlarged by fibroids to the size of a 16-week pregnancy was treated [21]. Her uterine arteries were noninvasive transvaginally identified and occluded for six hours with a clamp that was guided by audible doppler ultrasound. Following removal of the clamp, blood flow in the uterine arteries returned immediately. Three months following treatment, the uterine volume had decreased by 49 % and the dominant fibroid volume by 54 % (Fig. 2).

Thirty patients treated with this technique were presented in 2006. Two alternatives of analgesic was chosen (para cervical and epidural block was utilized in 17 and 13 patients respectively), menorrhagia was reduced in both groups, however in the para cervical group fibroid reduction was 12-24 % and in the epidural group 24-45 %. Two cases of hydronephrosis was observed and they were treated successfully with a stent [22]. The explanation of additional fibroid reduction in the epidural group could be related to a more stable tenaculum placement, lesser pain and consequently constant compression of the uterine artery during the treatment time.

Fig. 2: MRI showing Major Fibroid reduction 54 %



COMPLICATIONS

A disadvantage of the noninvasively transvaginal clamping technique is fibroid location close to the cervix, in which there is some difficulties to apply the clamp location correctly. In addition, possibility of clamping the urethers with subsequent hydronephrosis and possible damage of the renal function is of concern. Currently, a multicenter study is planned which will hopefully answer many of the questions of this technique before it can be fully applied into clinical practice and FDA approval.

Another possible application of the temporary artery uterine clamp is during and after myomectomy operations. Thereby, we can reduce peri- and postoperative bleeding. In addition, the clamping may act as adjuvant therapy of possible residual fibromas. However, few results exist so far, and further studies of this therapeutic approach are needed to prove its long term value.

USE AND INDICATION OF UTERINE ARTERY TECHNIQUES

The application of techniques like uterine artery occlusion is primarily for women who will avoid hysterectomy. Many women do not wish to undergo an operative procedure, as they may not accept the associated risks of the operation, and therefore prefer the less invasive

procedures. Both radiological and laparoscopic occlusion techniques are potential treatment options in the treatment of fibroids. However, insufficient long term follow up result do not exist at present. Furthermore, both techniques are associated with a high level of skill, and consequently they should be performed only in special centres with interest in this field. Anyhow, counselling of the patients is of utmost importance before they make their own treatment choice [23].

CONCLUSIONS

Fibroids present with different symptoms in different patients; i.e. infertility, bleeding problems, pressure and pain, single or multiple, different ages, which should be treated differently. In bleeding problems, an important issue is the location of the fibroid, and in cases with submucosal fibroids hysteroscopic resection is the method of choice. In cases with intramural, subserosal and even multiple fibroids, uterine artery therapy with embolization or laparoscopy seem to achieve good results on both bleeding problems and pressure symptoms. The temporary uterine clamp performed by general gynaecologist without incision may replace the more complicated procedures like embolization performed by radiologist and laparoscopic uterine artery closure performed by skilled endoscopist.

In infertility patients, the single fibroid should be removed, while when multiple fibroids are present medical or circulation therapy may be the only option for uterus saving therapy.

Abstract

Women postpone their first delivery and the gynaecologist will have to take care of fibroids in a conservative manner. The past decade has witnessed highly sophisticated diagnostic and therapeutic technology development for fibroids.

Non-surgical treatments interfering with the blood supply to the uterus or the fibroids include uterine artery embolization performed by interventional radiologist or laparoscopic uterine artery occlusion/compression by the gynaecologist. Uterine arteries were non-invasive transvaginally identified and occluded for six hours with a clamp that was guided by audible doppler ultrasound.

Results. *In our institution, we studied 46 premenopausal women, with symptomatic uterine fibroids, undergoing radiologic embolization (n = 24) or laparoscopic closure of the uterine arteries (n = 22). The laparoscopic technique reduced picture blood assessment score after six months by 50 % in both groups. Uterus volume was reduced by 35-40 % in both groups. We found that laparoscopic occlusion of uterine vessels is a promising new method for treating fibroid-related symptoms, with less postoperative pain than embolization and comparable results. During temporary artery occlusion the uterine volume had decreased by 49 % and the dominant fibroid volume by 54 %. Currently multicentre investigation are including 300 patients with symptomatic fibroids are performed in Europe and USA.*

Complications. *The acute degenerative procedure can be very painful and infection can occur. Hysterectomy may again be required in the case of haemorrhage or severe tissue necrosis. Delivering fibroids or sections of fibroids may be a natural process after uterine artery embolization, therefore it is essential to warn women about the possible risk of infectious symptoms like heavy discharge, fever, consequently close follow-up is essential. A long-term side-effect could be premature ovarian failure secondary to interference with the ovarian blood supply.*

Conclusions. *Fibroids present with different symptoms in different patients. In bleeding problems, an important issue is the location of the fibroid, and in cases with submucosal fibroids hysteroscopic resection is the method of choice. In cases with intramural, subserosal and even multiple fibroids, uterine artery therapy with embolization or laparoscopy seem to achieve good results on both bleeding problems and pressure symptoms. The temporary uterine clamp performed by general gynaecologist without incision may replace the more complicated procedures like embolization performed by radiologist and laparoscopic uterine artery closure performed by skilled endoscopist. In infertility patients, the single fibroid should be removed, while when multiple fibroids are present medical or circulation therapy may be the only option for uterus saving therapy.*

Bibliographie

- [1] Guarnaccia MM, Rein MS. Traditional surgical approaches to uterine fibroids: abdominal myomectomy and hysterectomy. *Clin Obstet Gynecol* 2001;44:385-400.
- [2] Dicker RC, Greenspan JR, Strauss LT et al. Complications of abdominal and vaginal hysterectomy among women of reproductive age in the United States. The Collaborative Review of Sterilization. *Am J Obstet Gynecol* 1982;144:841-8.
- [3] Fernandez H, Sefrioui O, Virelizier C, Gervaise A, Gomel V, Frydman R. Hysteroscopic resection of submucosal myomas in patients with infertility. *Hum Reprod* 2001;16:1489-92.
- [4] Dubuisson JB, Chapron C, Fauconnier A, Kreiker G. Laparoscopic myomectomy and myolysis. *Curr Opin Obstet Gynecol* 1997;9:233-8.
- [5] Nezhat FR, Roemisch M, Nezhat CH, Seidman DS, Nezhat CR. Recurrence rate after laparoscopic myomectomy. *J Am Assoc Gynecol Laparosc* 1998;5:237-40.
- [6] Goldfarb HA. Myoma coagulation (myolysis). *Obstet Gynecol Clin North Am* 2000;27:421-30.
- [7] Burbank F, Hutchins FL Jr. Uterine artery occlusion by embolization or surgery for the treatment of fibroids: a unifying hypothesis-transient uterine ischemia. *J Am Assoc Gynecol Laparosc* 2000;7:S1-S49.
- [8] Chait A, Moltz A, Nelson JH Jr. The collateral arterial circulation in the pelvis. An angiographic study. *Am J Roentgenol Radium Ther Nucl Med* 1968;102:392-400.
- [9] Huang SC, Yu CH, Huang RT, Hsu KF, Tsai YC, Chou CY. Intratumoral blood flow in uterine myoma correlated with a lower tumor size and volume, but not correlated with cell proliferation or angiogenesis. *Obstet Gynecol* 1996;87:1019-24.
- [10] Cramer SF, Horisznay J, Patel A, Sigrist S. The relation of fibrous degeneration to menopausal status in small uterine leiomyomas with evidence for postmenopausal origin of seedling myomas. *Mod Pathol* 1996;9:774-80.
- [11] Laudanski T. Energy metabolism of the myometrium in pregnancy and labor. *Zentralbl Gynakol* 1985;107:568-73.
- [12] Burbank F. Childbirth and myoma treatment by uterine artery occlusion: do they share a common biology? *J Am Assoc Gynecol Laparosc* 2004;11:138-52.
- [13] Lichtinger M, Burbank F, Hallson L, Herbert S, Uyeno J, Jones M. The time course of myometrial ischemia and reperfusion after laparoscopic uterine artery occlusion-theoretical implications. *J Am Assoc Gynecol Laparosc* 2003;10:554-63.
- [14] Bateman W. Treatment of intractable menorrhagia by bilateral uterine vessel interruption. *Am J Obstet Gynecol* 1964;89:825-7.
- [15] Liu WM. Laparoscopic bipolar coagulation of uterine vessels to treat symptomatic leiomyomas. *J Am Assoc Gynecol Laparosc* 2000;7:125-9.
- [16] Liu WM, Ng HT, Wu YC, Yen YK, Yuan CC. Laparoscopic bipolar coagulation of uterine vessels: a new method for treating symptomatic fibroids. *Fertil Steril* 2001;75:417-22.
- [17] Liu WM. Laparoscopic bipolar coagulation of uterine vessels to treat symptomatic leiomyomas. *J Am Assoc Gynecol Laparosc* 2000;7:125-9.
- [18] Hald K, Langebrekke A, Klow NE, Noreng HJ, Berge AB, Istre O. Laparoscopic occlusion of uterine vessels for the treatment of symptomatic fibroids: initial experience and comparison to uterine artery embolization. *Am J Obstet Gynecol* 2004;190:37-43.
- [19] Hald K, Klow NE, Qvigstad E, Istre O. Laparoscopic occlusion compared with embolization of uterine vessels: a randomized controlled trial. *Obstet Gynecol* 2007;109:20-7.
- [20] Lichtinger M, Burbank F, Hallson L, Herbert S, Uyeno J, Jones M. The time course of myometrial ischemia and reperfusion after laparoscopic uterine artery occlusion-theoretical implications. *J Am Assoc Gynecol Laparosc* 2003;10:554-63.
- [21] Istre O, Hald K, Qvigstad E. Multiple myomas treated with a temporary, noninvasive, Doppler-directed, transvaginal uterine artery clamp. *J Am Assoc Gynecol Laparosc* 2004; 11:273-6.
- [22] Vilos GA, Hollett-Caines J, Burbank F. Uterine artery occlusion: what is the evidence? *Clin Obstet Gynecol* 2006;49:798-810.
- [23] Hald K, Langebrekke A, Klow NE, Noreng HJ, Berge AB, Istre O. Laparoscopic occlusion of uterine vessels for the treatment of symptomatic fibroids: initial experience and comparison to uterine artery embolization. *Am J Obstet Gynecol* 2004;190:37-43.