UTERINE ARTERY EMBOLIZATION (A SERIES)

Selective uterine artery embolization in the management of uterine myomas

Errico Zupi, M.D.,^a Marco Pocek, M.D.,^b Mario Dauri, M.D.,^c Daniela Marconi, M.D.,^a Marco Sbracia, M.D.,^d Emilio Piccione, M.D.,^a and Giovanni Simonetti, M.D.^b

Ospedale Sant Eugenio, Rome, Italy

Objective: To evaluate the effectiveness of uterine artery embolization in women with uterine myomas in terms of the clinical results for the relief of related symptoms.

Design: A pilot study on 26 women affected by uterine single myoma.

Setting: Tertiary level care in an university hospital.

Patient(s): Twenty-six patients, aged 32 to 54 years, suffering of menorrhagia, pelvic pain, and abdominal mass for single myoma, intramural localization.

Intervention(s): Selective uterine artery embolization performed under peridural anesthesia.

Main Outcome Measure(s): We measured the x-ray dose to which patients were exposed. Color power Doppler ultrasound examinations were performed during the follow-up evaluations at 1 to 6 months and 1 year after the procedure.

Result(s): Uterine artery embolization was successfully performed in 100% of cases. The mean fluoroscopy time was of 20 minutes during the procedure. The mean dose of x-ray absorbed by the ovary was estimated at 18.7 cGy and the mean dose of x-ray absorbed by the skin was 126.7 cGy. A reduction of myoma volume of 55% was found at 6 months' ultrasound examination and 75% at the 1-year examination.

Conclusion(s): Patients are well satisfied and have short recovery times with this procedure. Uterine artery embolization may be a valid alternative to traditional surgery. (Fertil Steril[®] 2003;79:107–11. ©2003 by American Society for Reproductive Medicine.)

Key Words: Uterine artery embolization, uterine myomas, menometrorrhagia, reproduction

Received January 24. 2002; revised and accepted May 14, 2002. Reprint requests: Marco Sbracia, M.D., Center for Endocrinology and Reproductive Medicine, Via Carlo Porta 10, 00153, Rome, Italy (FAX: 39-06-5880096; E-mail: marcandrea@hotmail.com). ^a Departments of Obstetrics and Gynecology, Tor Vergata University, Ospedale Sant Eugenio. ^b Departments of Radiology, Tor Vergata University, Ospedale Sant Eugenio. ^c Anesthesiology, Ospedale

Sant Eugenio. ^d Center for Endocrinology and Reproductive Medicine, Rome, Italy.

0015-0282/03/\$30.00 PII S0015-0282(02)04399-6 Uterine fibromyoma is a frequent clinical condition gynecologists must manage. These benign lesions may result in uterovaginal bleeding, menorrhagia with severe anemia, urinary disturbances and abdominal pressure, and pelvic pain (1). They may be the cause of infertility; often physicians remove the myoma or the uterus to resolve the symptoms (2).

Hysterectomy is the most common surgical procedure after dilatation and curettage; in the United States more than 500,000 hysterectomies are performed every year; uterine myoma is the most common benign indication for the procedure (3). Several alternative procedures have been suggested to reduce the number of invasive hysterectomies, such as minilaparotomy (4), laparoscopic hysterectomy or myomectomy (5), hysteroscopic myomectomy (6), and endometrial ablation (7).

Several medical treatments have been used to reduce the dimension of the myoma, including antiestrogen drugs such as GnRH analogs (8); however, after the discontinuation of treatment myomas start to grow again (9). Recently, selective embolization of the uterine artery has been suggested as an alternative method to treat uterine myomas and avoid their surgical removal (10).

Selective uterine embolization was first used in obstetrics and gynecology in 1979 to treat postpartum bleeding. In that case, hysterectomy and hypogastric artery ligature had failed to stop bleeding, but the selective embolization of a vaginal branch of the pudend artery was able to control the bleeding (11). Since that time, the selective embolization of the uterine artery has been used to stop postsurgical and ectopic pregnancy bleeding, and to treat arteriovenous fistulae (12); it is also used as a presurgical procedure to reduce the risk of bleeding in cases of placenta previa and accrete (13).

Ravina et al. (10) have suggested the use of this procedure to reduce the risk of bleeding in the case of extensive myomectomy. They reported that in some cases the procedure promoted such a massive myoma shrinkage that surgery was unnecessary. Although several studies have been conducted on this procedure, there are no conclusive data on its reliability or on the preservation of fertility (14), even though several pregnancies have been reported after the procedure (15).

In this pilot study we evaluated the effectiveness of the treatment for the relief of symptoms in a group of women of fertile age, and recorded the radiation dosage to which the patients were exposed, especially their ovaries.

MATERIALS AND METHODS

All patients treated at the obstetrics/gynecology department of Tor Vergata University for uterine bleeding from April 1999 to February 2000 were evaluated for inclusion in the study. Inclusion criteria were single myoma or a large myoma (well-evident myoma separated from the close uterine tissue), intramural extension of myoma, high vascularization with terminal vascular branch, and fertile age. Exclusion criteria were uterine fibromatosis or adhenomiosis (large uterus with irregular margins and with a sonographic pattern of diffuse fibrosis), subserosus localization, or other gynecologic diseases such as salpingitis or endometriosis. The study was reviewed and approved by the institutional review board, and all patients signed a consent form.

A total of 26 women were selected to undergo uterine artery embolization. The mean age of the patients was 39.5 \pm 3.3 (range: 32 to 54 years; the single patient over 50 years old was still cycling). The dimension of the myomas were calculated during sonography with the formula of ovoid Length \times Width \times Depth \times 0.5236.

Patients underwent transabdominal and transvaginal sonography (ATL HDI 5000), using a low-frequency 700– 1,000 MHz pulse of repetitive frequency, and filter of 50Hz. Furthermore, the sonography was performed using endovenous sonographic contrast medium (Levovist SHV 508 A, Shering, Berlin, Germany) to enhance the signal of blood flow and color Doppler velocimetry (Seattle, WA).

Even though all patients showed myomas with high vascularization, we further classified the patients into three arbitrary groups, depending on their Doppler examination: [1] myoma with high vascularization (14), [2] myoma with moderate vascularization (8), and [3] myoma with mild vascularization (4). Patients also underwent NMR (Gyroscan NT1.5T Philips), with the administration of endovenous paramagnetic contrast medium (Gaddolino GdDTPA, Schering).

Antibiotic prophylaxis was administered to the patients for 3 days before the procedure and 3 days afterward. Peridural anesthesia was performed in all patients by positioning a catheter in L1-L2 for continuous administration of ropivacaine (75 mg) and clonidine (50 mg at 0.2%).

A thermoluminescent dosimeter for x-rays was positioned in the posterior fornix of the vagina and on the skin of the patients to record the amount of radiation absorbed by the women's abdomen. Angiographic examination was performed with a pulsed fluoroscopy (Digital Angiography Integris 5000 Philips, Rotterdam, The Netherlands).

We performed the embolization with a bilateral transfemoral access. Both hypogastric arteries were catheterized at the same time with a hydrophile guide (J 0.035 inch, Terumo, Europe NV, Belgium) into which a 5F catheter (Glidecath, Terumo) was guided.

The uterine artery canalization was performed with coaxial catheter 3F (Tagest Therapeutics, Berlin, Germany). Before embolism, an angiographic examination was performed with a low number of expositions, for a total acquisition of 10 images (1 image/second for the arteriography and 1 image/2 seconds in parenchymatographic fluoroscopy). Embolization was performed with polyvinyl alcohol (PVA), Contour 355–500 μ m (Tagest).

All patients were reevaluated with sonographic and Doppler velocimetry at 1, 3, and 6 months after the treatment. One year later the women were reevaluated with magnetic resonance imaging (MRI).

RESULTS

The patients underwent embolization for uterine myomas that had dimensions ranging between 40.3 mL and 863.5 mL with a mean 276.8 \pm 241.2. The indications for surgery are reported in Table 1.

The procedure was successfully completed in all patients, and in all patients we were able to selectively embolize the branch of uterine artery supplying the myoma (Fig 1A and B). After embolization, the volume of myomas was reduced significantly: $55.0 \pm 16.9\%$ after 6 months with a dimension ranging from 21.1 mL to 314.0 mL (mean 98.7 \pm 72.5 mL). One year later, they measured from 17.1 to 113.0 with a mean 46.6 \pm 29.3 mL, for a mean reduction of 75.0 \pm 13.3 (see Table 1).

The most relevant reduction was correlated with the myomas that were most strongly supplied by blood flow (P<0.01; see Table 1), as evidenced by Doppler velocimetry. These showed a more intense signal on MRI using the paramagnetic contrast medium Gaddolino. In most patients, a complete relief of symptoms was observed, and in only three cases there was no variation of symptoms, as reported in Table 1.

After the procedure 19 patients had a fever for 24 to 72 hours, and all patients experienced abdominal pain, which was treated with nonsteroidal anti-inflammatory drugs (NSAIDs). Fifteen patients had discomfort such as nausea

Clinical outcome after the treatment with embolization.

	Pretreatment	Six months after trea	tment O	ne year after treatment	
Uterine dimension (%)	276.8 ± 241.2	98.7 ± 72.5 (55.0 ± 16.9)		46.5 ± 29.3 (75.0 ± 13.3)	
Symptoms	No. of patients	Total regression	Mild reduction	No variation	
Menorrhagia	21	12	6	3	
Pain	9	7	1	1	
Urinary disturbances	12	8	3	1	
Abdominal weight	18	18	7	1	
Vascolarization	No. of patients		Posttreatmen	Posttreatment uterine reduction (%)	
High	14		8	85.26 ± 4.12	
Moderate	8		6	69.23 ± 4.93	
Mild	4		5	50.90 ± 5.35	
				P<.01	

Zupi. Artery embolization in uterine myoma. Fertil Steril 2003.

and vomiting. Two patients discharged myoma debris and blood from the vagina 4 weeks after the procedure; 3 women experienced oligomenorrhea for a 3-month period. No other major discomfort was observed. 13.78 cGy). On the skin the dose ranged between 54.66 and 767.11 cGy (126.71 \pm 71.17 cGy).

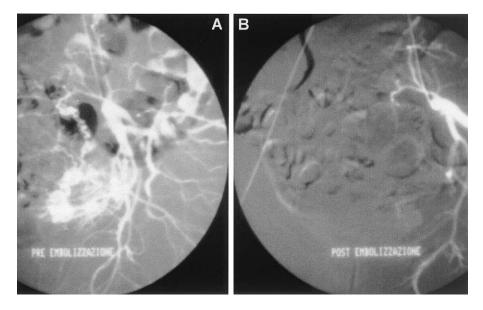
DISCUSSION

The radiation dose absorbed by the ovaries of the patients was calculated to be between 3.76 to 55.82 cGy (18.75 \pm

In our study all patients treated with selective uterine artery embolization did well, and we observed a low rate of

FIGURE

Variation in the arteriographic imaging after uterine artery embolization. (A), Uterine angiographic imaging before treatment showing the intense blood supply to the myoma region. (B), Uterine angiographic imaging after treatment showing the complete absence of blood supply to the myoma region.



Zupi. Artery embolization in uterine myoma. Fertil Steril 2003.

complications after the procedure, such as fever and pelvic pain, vaginal discharge of necrotic tissue, and amenorrhea. The procedure seems to be safe and allows a rapid, complete recovery of patients in a mean time of 2.3 days. The rate of disease relapse after 1-year follow-up in our study was close to 0, and we observed a reduction of myoma dimension with consequent symptom relief in 96% of cases.

In our group of patients, the dose of radiation absorbed by the ovary was higher than the dose absorbed during hysterosalpingography (range: 0.20 to 2.75 cGy), but dramatically lower than the dose used for radiotherapy (range: 263 to 3,500 cGy). However, the dose of radiation absorbed during the procedure seems to be within the range of safety (<80 cGy) and is not contraindicated for patients desiring to become pregnant, in accordance with published data (16– 17).

The evolution of materials has allowed the procedure to be conducted safely: the use of the coaxial 3G catheter allows a highly selective embolization of uterine artery branches supplying the blood flow to the myoma, preserving neighboring healthy areas of uterus. Furthermore, the pulsed fluoroscopy, using collimated x-rays, markedly reduces the patient's time of exposure (up to 50%) to x-rays (18). The limitation of the technique is that it is operator dependent and must be performed by radiologists who are experienced in these techniques. The technique gave better results in the case of myomas with high blood flow supply or with higher cellularity as they appeared on Doppler velocimetry and MRI.

These data show the reliability and the safety of this procedure. It allows the fast and complete recovery of patients without invasive surgery, with a relevant relief and resolution of symptoms. This procedure avoids surgery and the use of long-standing therapy with antiestrogen drugs. However, it has some disadvantages.

First, the women in our study experienced pain in the immediate postprocedure period and required peridural anesthesia for 24 hours. After the discontinuation of anesthesia, the women needed NSAID medication.

Second, overextensive embolization could result in fibrosis of the uterus and consequent infertility. A case has been brought to our attention of a 30-year-old woman in France who underwent uterine embolization for uterine myoma. She had necrosis and consequent fibrosis of the uterus, with obliteration of the endometrial cavity, resulting in definitive infertility. Thus, this procedure could be dangerous for women with myoma who aspire to have children. It should be performed only in cases of a single large intramural myoma with clear and distinct vascularization with an evident branch of the uterine artery supplying the myoma with blood.

Despite the high number of patients treated—an estimated 2,000 to 6,000 procedures performed yearly (14) with a high

rate of success(19-25)—several complications and side effects have been recorded. Premature ovarian failure, infections, hemorrhages, uterine discharge, necrosis, and also death from sepsis have been reported after this procedure (26-30). The procedure also may fail to result in the myoma shrinking (31). These complications would argue against using uterine artery embolization in women of childbearing age or those who are seeking treatment for infertility due to myomatosis.

Our study treated only patients with single myomas with high blood flow supplied by a single branch of the uterine artery without collateral circle. The selective uterine artery embolization in these cases promoted a definitive reduction blood flow in the myoma (32). Our data are encouraging and suggest that the technique could be used in a larger population of women of childbearing age. A randomized controlled trial is needed to validate the use of this technique in women of fertile age and to ascertain how this technique's success rate compares with surgery.

References

- 1. Stewart EA. Uterine fibroids. Lancet 2001;357:293-8.
- Carlson KJ, Miller BA, Fowler FJ Jr. The Maine Women's Health Study: I. Outcomes of hysterectomy. Obstet Gynecol 1994;83:556–65.
- Carlson KJ, Schiff I. Alternatives to hysterectomy for menorrhagia. N Engl J Med 1996;335:198–9.
- Hoffman MS, Lynch CM. Minilaparotomy hysterectomy. Am J Obstet Gynecol 1998;179:316–20.
- Dubuisson JB, Chapron C, Fauconnier A, Kreiker G. Laparoscopic myomectomy and myolisis. Curr Opin Obestet Gynecol 1997;9:233– 38.
- Derman SG, Rehnstrom J, Neuwirth RS. The long term effectiveness of hysteroscopic treatment of menorrhagia and leiomyomas. Obstet Gynecol 1991;77:591–94.
- DeCherney AH, Diamond MP, Lavy G, Polan ML. Endometrial ablation for intractable uterine bleeding: hysteroscopic resection. Obstet Gynecol 1987;70:668–70.
- Filicori M, Hall DA, Loughlin JS, River J, Vale W, Crowley WF Jr. A conservative approach to the management of uterine leiomyoma: pituitary desensitization by a luteinizing hormone-releasing hormone analogue. Am J Obstet Gynecol 1983;147:726–27.
- Fedele L, Parazzini F, Luchini L, Mezzopane R, Tozzi L, Villa L. Recurrence of fibroids after myomectomy: a transvaginal ultrasonographic study. Hum Reprod 1995;10:1795–96.
- Ravina JH, Herbreteau D, Ciraru-Vigneron N, Bouret JM, Houdart E, Aymard A, et al. Arterial embolisation to treat uterine myomata. Lancet 1995;346:671–2.
- Heaston DK, Mineau DE, Brown BJ, Miller FJ. Transcatheter arterial embolization for control of persistent massive puerperal hemorrhage after bilateral surgical hypogastric artery ligation. Am J Roentgnol 1979;133:152–4.
- Oliver JA, Lance JS. Selective embolization to control massive hemorrhage following pelvic surgery. Am J Obstet Gynecol 1979;135: 431–2.
- Vedantham S, Goodwin SC, McLucas B, Mohr G. Uterine artery embolization: an undersused method of controlling pelvic hemorrhage. Am J Obstet Gynecol 1997;176:938–48.
- Hurst BS, Stackhouse DJ, Matthews ML, Marshburn PB. Uterine artery embolization for symptomatic uterine myomas. Fertil Steril 2000;74: 855–69.
- Ravina JH, Vigneron NC, Aymard A, Le Dref O, Merland JJ. Pregnancy after embolization of uterine myoma: report of 12 cases. Fertil Steril 2000;73:1241–3.
- Hayard MY, Cornella JL, Grado GL, Rizzo NR. Prolonged amenorrhea associated with total nodal irradiation for Hodgkin's disease. J Natl Med Assoc 1996;88:391–3.
- Nikolic B, Spies JB, Lundsten MJ, Abbara S. Patient radiation dose associated with uterine artery embolization. Radiology 2000;214:121–5.
- Nikolic B, Abbara S, Levy E, Imaoka I, Lundsten ML, Jha RC, et al. Influence of radiographic technique and equipment on absorbed ovarian

dose associated with uterine artery embolization. J Vasc Interv Radiol 2000:11:1173-8

- 19. Goodwin SC, Vedantham S, McLucas B, Forno AE, Perrella R. Preliminary experience with uterine artery embolization for uterine fibroids. J Vasc Interv Radiol 1997:8:517-26.
- 20. Bradley EA, Reidy JF, Forman RG, Jarosz J, Braude PR. Transcatheter uterine artery embolisation to treat large uterine fibroids. Br J Obstet Gynaecol 1998;105:235-40.
- 21. Goodwin SC, McLucas B, Lee M, Chen G, Perrella R, Vedantham S, et al. Uterine artery embolization for the treatment of uterine leiomyomata midterm results. J Vasc Interv Radiol 1999;10:1159-65.
- 22. Hutchins FL, Worthington-Kirsch R, Berkowitz RP. Selective uterine artery embolization as primary treatment for symptomatic leiomyomata uteri. J Am Assoc Gynecol Laparosc 1999;6:279-84.
- 23. Ravina JH, Aymard A, Ciraru-Vigneron N, Ledreff O, Merland JJ. Arterial embolization of uterine myoma: results apropos of 286 cases [in French]. J Gynecol Obstet Biol Reprod (Paris) 2000;29:272-5.
- 24. Brunereau L, Herbreteau D, Gallas S, Cottier JP, Lebrun JL, Tranquart F, et al. Uterine artery embolization in the primary treatment of uterine leiomyomas: technical features and prospective follow-up with clinical and sonographic examinations in 58 patients. Am J Roentgenol 2000; 175:1267-72.

- 25. Siskin GP, Stainken BF, Dowling K, Meo P, Ahn J, Dolen EG. Outpatient uterine artery embolization for symptomatic uterine fibroids: experience in 49 patients. J Vasc Interv Rádiol 2000;11:305–11. Vashisht A, Studd J, Carey A, Burn P. Fatal septicaemia after fibroid
- 26. embolisation. Lancet 1999;354:307-8.
- 27. Berkowitz RP, Hutchins FL, Worthington-Kirsch RL. Vaginal expulsion of submucosal fibroids after uterine artery embolization. A report of three cases. J Reprod Med 1999;44:373-6.
- 28. Abbara S, Spies JB, Scialli AR, Jha RC, Lage JM, Nikolic B. Transcervical expulsion of a fibroid as a result of uterine artery embolization for leiomyomata. J Vasc Interv Radiol 1999;10:409-11.
- 29. Stringer NH, Grant T, Park J, Oldham L. Ovarian failure after uterine artery embolization for treatment of myomas. J Am Assoc Gynecol Laparosc 2000;7:395–400. Vashisht A, Studd JW, Carey AH, McCall J, Burn PR, Healy JC, et al.
- 30. Fibroid embolisation: a technique not without significant complications. Br J Obstet Gynecol 2000;107:1166-70.
- 31. Nikolic B, Spies JB, Abbara S, Goodwin SC. Ovarian artery supply of uterine fibroids as a cause of treatment failure after uterine artery embolization: a case report. J Vasc Interv Radiol 1999;10:1167-70.
- Worthington-Kirsch RL. Flow redistribution during uterine artery em-32. bolization for the management of symptomatic fibroids. J Vasc Interv Radiol 1999;10:237-8.