Evaluation of Uterine Artery Embolisation on Size and Symptomatology of Leiomyoma Under Patient Controlled Analgesia with Meperidine

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Abstract: *Aim*: We aimed to present our experience on uterine artery embolization (UAE) under intravenous (iv) patient controlled analgesia (PCA) with meperidine. *Methods***:** Twelve patients, aged between 30 to 45 years with solitary leiomyoma having pelvic pain or heavy menstruel bleeding were included. The size and location of uterine leiomyomas were determined by transvaginal ultrasound. The UAE was performed after angiography of the uterine artery blood supply by percutaneous unilateral common femoral arterial access under iv PCA with meperidine. Both uterine arteries were catheterized with co-axial microcatheter system through this route and embolized between 300 to 900 µm microspheres under fluoroscopic guidance. *Results***:** The fibriod volumes measured after 3 and 6 months significantly decreased when compared to the pre-embolization volumes. Symptoms of irregular excessive menstruel bleeding, pelvic discomfort, bowel and bladder dysfunction, pressure sensation in the lower abdomen and pain during intercourse markedly regressed. Pain relief was provided by iv PCA from the onset of the procedure until 24 hours after the procedure. **Conclusion:** The UAE procedure under iv PCA with meperidine has been shown to be a comfortable technique that might be offered to patients with symptomatic fibroids in non-reproductive age or desire for not having a child.

Keywords: Interventional radiology, Uterine leiomyoma, embolization, pain relief.

INTRODUCTION

Uterine leiomyoma, which has an incidence about 20–40% in women during their reproductive years shows symptoms varying from common irregular excessive menstruel bleeding due to endometrial venule ectasia, increased endometrial surface area, dysregulation of local growth factors and aberrant angiogenesis to pelvic discomfort, bowel and bladder dysfunction, pressure sensation in the lower abdomen and pain during intercourse [1-4]. Either solitary or multiple size tumours display clear association with exposure to circulating estrogen [5]. Medical treatment consists of non-steroidal anti-inflammatory drugs, progesterones, progesterone releasing intrauterine devices and gonadotrophine releasing hormone analogues. However, they did not demonstrate long-term efficacy and therapies like hysteroscopic endometrial ablation and transcervical resection of submucous fibroid, laparoscopic or open myomectomy / myolysis, bipolar coagulation and/or dissection of uterine vessels, myomectomy and hysterectomy that might be related to increased morbidities [6,7]. After angiographic embolization in 1987, uterine artery embolization (UAE) has gained popularity [8-10]. Although UAE is a minimally invasive procedure, pain due to fibroid ischemia has been managed either by epidural or intravenous (iv) patient controlled analgesia (PCA) [11,12]. Therefore, we aimed to present our experience on UAE under iv PCA with meperidine.

MATERIALS AND METHODS

Twelve patients aged between 30 to 45 years with solitary uterine fibroid with symptomatic leiomyomas admitted to the Department of Gynecology in Medical School of Gazi University were enrolled in the study. The study protocol was approved by the institutional review board and written consent was obtained from each patient after all patients were informed about the rationale procedural details and risks of UAE under iv PCA as well as the possible treatment alternatives.

Patients with solitary leiomyoma with pelvic pain or heavy menstruel bleeding, being reluctant for future pregnancy were included after size and location of uterine leiomyomas were determined by transvaginal ultrasound (General Electric Logic 500, USA). The MR

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volumetric evaluations were done before and after the UAE procedure by the interventional radiologists.

The UAE Procedure

The UAE procedure was performed after angiography of the uterine artery by a 5-French percutaneous unilateral common femoral arterial access. Both uterine arteries were catheterized with a 2.8- French co-axial microcatheter system (Renegade, Boston Scientific Corp., USA) through this route and embolized with 300 to 900 µm microspheres (Embosphere, Biosphere Medical, France) under fluoroscopic guidance. Embolization was continued until the devascularization of the fibriod with obliteration of the perifibroid arterial plexus, sparing the main uterine artreries and the normal myometrium. The procedure including the angiography and embolization was done as described [13, 14]. Intravenous PCA for pain relief was performed according to our institution's pain management strategy and parenteral antibiotic prophylaxis.

After preoperative evaluation of each patient, an 18 G iv cannula was inserted on the dorsum of the hand to infuse Ringer's lactate solution. No premedication was applied except routine iv aspiration prophylaxis with metochlopramide 10 mg and ranitidine 50 mg. Standart monitorization including heart rate, blood pressure and peripheral oxygen saturation were performed (GE Medical Systems, Model No. USE1913A Freiburg, Germany).

Analgesia Regimen

The PCA solution consisting meperidine 1 mg mL^{-1} was prepared (250 mg of meperidine was administered into 250 mL of saline). After an iv bolus dose of meperidine 20 mg, the PCA pump (Abbott Pain Management Provider, Abbott Laboratories, North Chicago IL, USA) was set to deliver 1 mg h^{-1} continuous background (basal) infusion with a 5 mg bolus on demand, 10 min lock-out interval and 2 $mgkg^{-1}$ of 4-h limit. Then, the PCA device was connected to the patient to deliver the drug from the beginning of the procedure until 24 hours after the procedure.

Patients were told to assess their pain with an 11 point verbal analogue scale (VAS) where 0 represents no pain and 10 represents the worst pain imaginable. Then, they were instructed to keep their VAS between zero to three by pushing the demand button of PCA in addition to the background infusion.

Statistical Analysis

Data were analyzed using SPSS 17.0 (Chicago USA) statistical software. Quantitative and qualitative data were expressed as mean, standard deviation, median or range, frequency and percentage where appropriate. Cumulative rates of treatment failure and re-intervention were estimated by Friedman and Spearman analysis. Results were compared by log-rank tests with baseline variables. Uterine volume was calculated by using the formula for a prolate ellipse (length X depth X width X 0,52), in cm^3. Cox regression (full model) analysis was applied for a possible predictor of failure by stepwise variable selection for confounders. A p value less than 0.05 was considered as statistically significant.

RESULTS

Findings of the UAE Procedure

No complications during the UAE procedure or after the procedure were observed. The mean age of the patients was 38.5±7.8 years and mean duration of the procedure was 50.4±11.7 minutes. Demographic characteristics of fibroid volumes before and after embolization and statistical volume difference before and 3 and 6 months after embolization were presented in Table **1**. The fibriod volumes measured after 3 and 6 months significantly decreased in comparison to pre-embolization volumes ($p<0.05$). However, there were no significant differences in the decrease of the fibroid volumes between 3 and 6 months (Table **1**). The fibroids before and after the UAE procedure were displayed (Figures **1**, **2**, **3** and **4**).

Table 1: Fibroid Volumes before and after Embolisation (Mean±SD) (Minimum-Maximum (cm^3)

Initial (control) volume	320.12±399.20 (33.63-1186.38)
Third month volume	47.39±58.73 (3.96-144.79)*
Sixth month volume	33.40±36.05(0.00-84.24)*

*:P<0.012 *vs*. control volume.

Only one patient underwent hysterectomy due to persisting pelvic discomfort despite her fibroid markedly regressed. Symptoms including irregular excessive menstruel bleeding, pelvic discomfort, bowel and bladder dysfunction, pressure sensation in the lower abdomen and pain during intercourse markedly regressed in the remaining 7 patients.

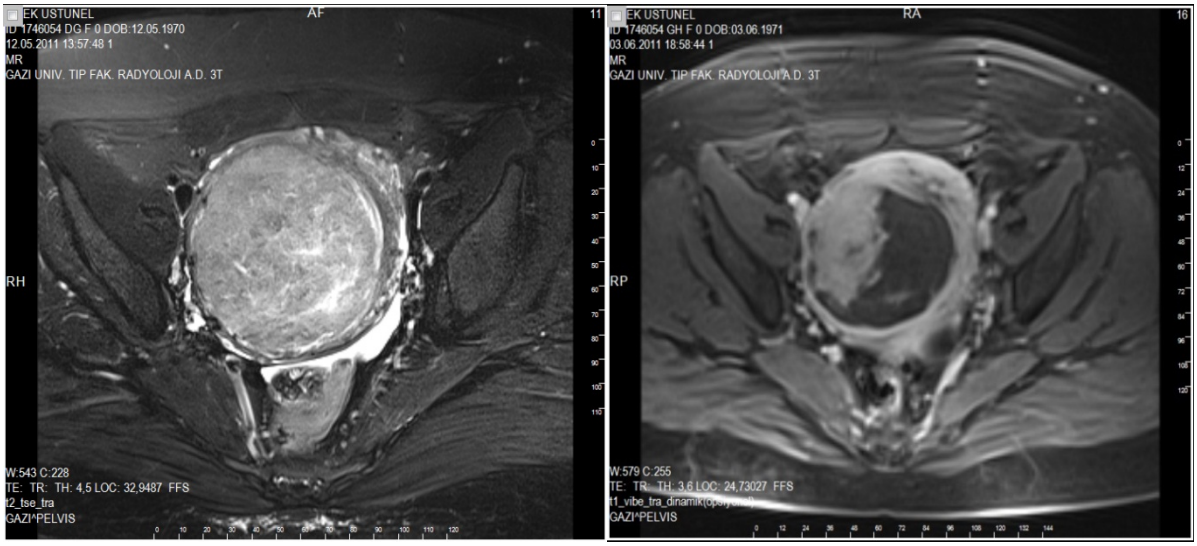

Figure 1.Patient DU: MR image of the pre and post-embolization leiomyoma

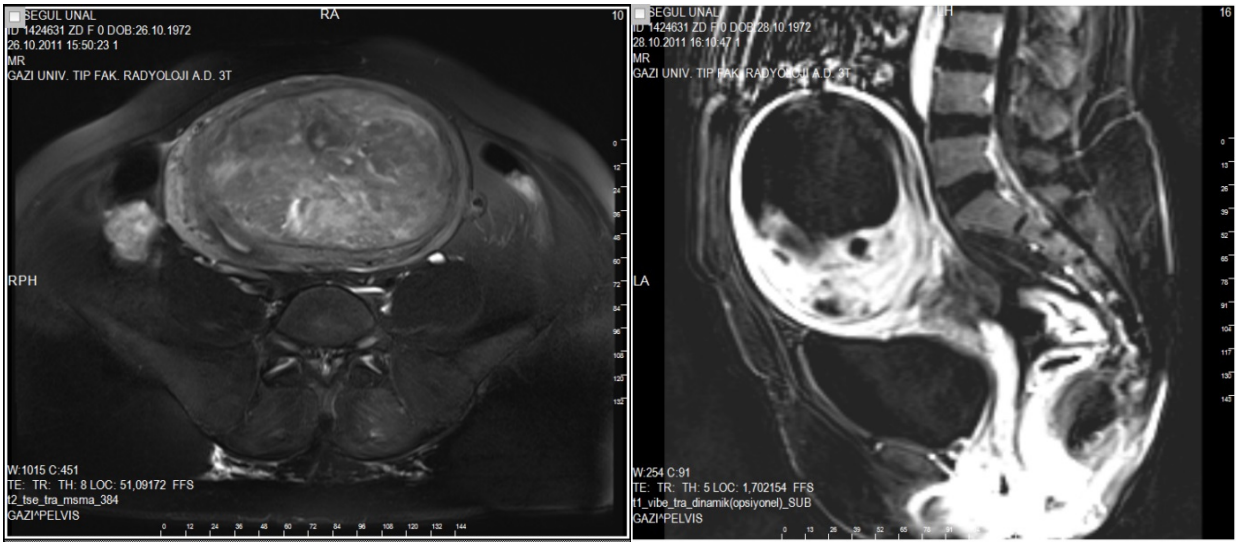

Figure 2. Patient AU: MR image of the pre and post-embolization leiomyoma.

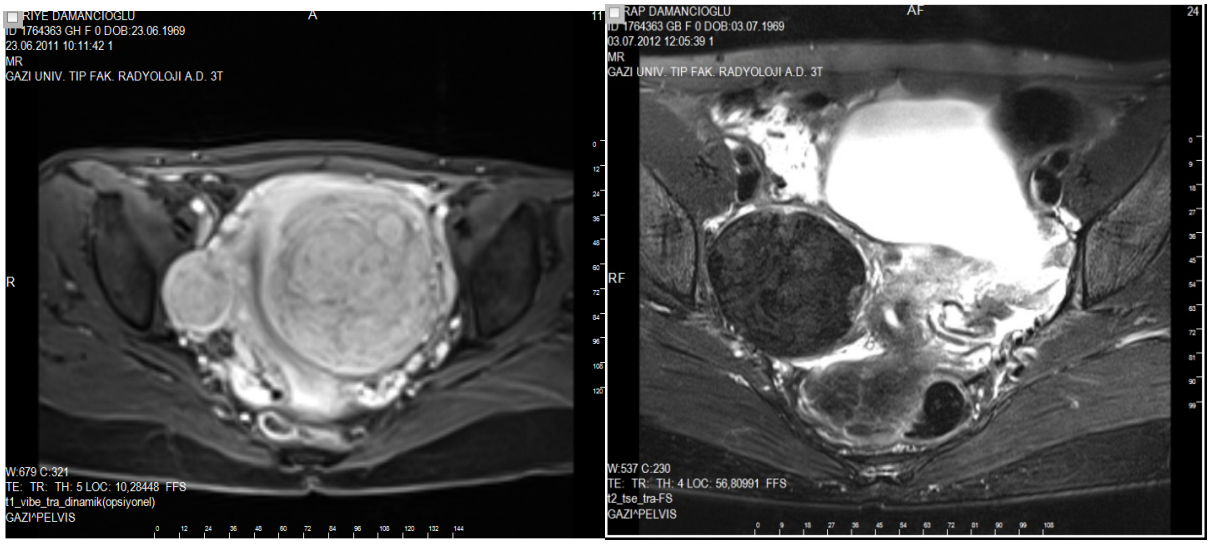

Figure 3. Patient SD: MR image of the pre and post-embolization leiomyoma.

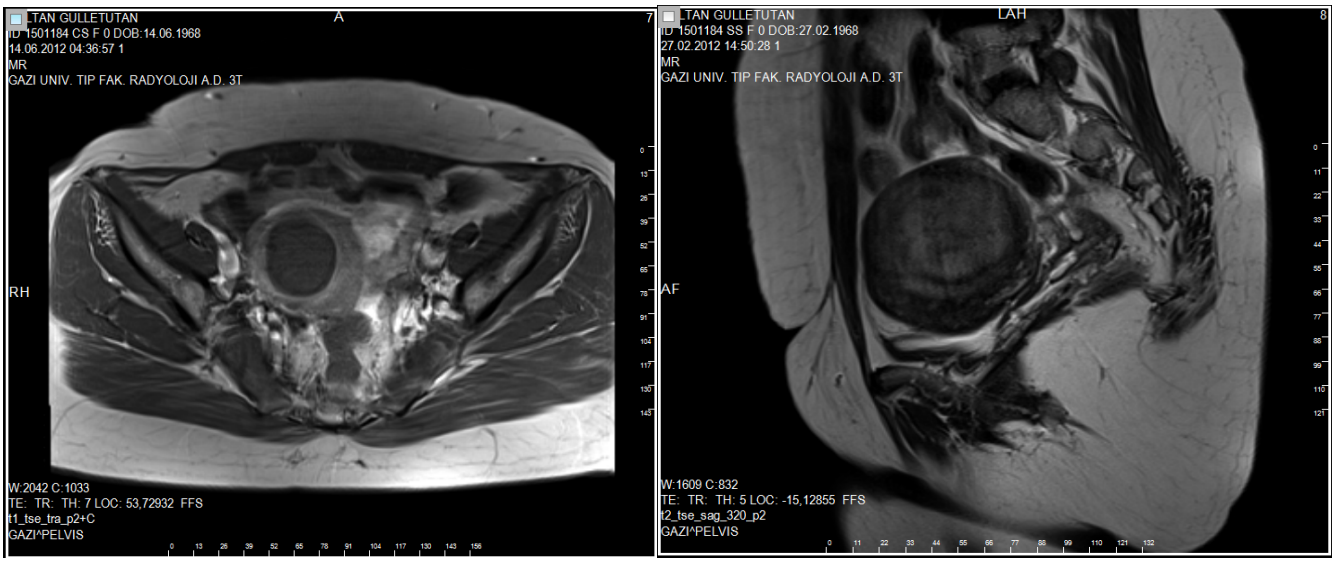

Figure 4. Patient SG: MR image of the pre and post-embolization leiomyoma.

Findings of Pain Relief Regimen

The PCA device was kept until the whole solution finishes. Seven out of 8 patients were able to keep their VAS ≤3 throughout this period. Only one patient who had VAS >3, received supplemental iv paracetamol (1 g) and nonsteroid antiinflammatory drug (diclophenac sodium 20 mg). None of the patients have suffered from nausea and vomiting during this period.

At the end of the entire follow-up, the patients free from any symptoms like nausea, vomiting or pain consulted by OBGYN were discharged. Patients were called for re-determining fibroid-size by ultrasound every 3 - month intervals within the first year. However, 4 patients were excluded from the study because of lack of follow-up records.

DISCUSSION

The UAE performed under iv PCA with meperidine via a multidisciplinary approach was presented in the current prospective observational study. Based on our experience, UAE procedure reduced symptoms and size of uterine fibroids in 2/3 of our patients with a successful pain relief regimen.

Available treatment options may vary from medical management to minimally invasive or major surgery [15]. The minimally invasive procedures like laparoscopic and hysteroscopic myomectomy include; endometrial ablation, UAE, magnetic resonance guided focussed ultrasound radiofrequency ablation, microwave ablation and cryoablation of fibroids, and UAE, which has been approved by FDA for treating larger or more complicated fibroids in a noninvasive manner against to the traditional options of hysterectomy and open myomectomy [9,10]. According to the short term results of the randomized controlled trials, UAE was more advantageous than open surgery because of resulting less blood loss, quicker return to work and less postoperative pain. However, the mid and long-term benefits were similar except higher re-intervention rate after UAE [16]. Also the failure rate of UAE at young age and/or having prior myomectomy was directly proportional with time (3%, 7%, 14% and 18% within 1, 3, 5 and 7 years, respectively) [17].

Despite promising results in terms of symptoms' relief, there are still some concerns about pain and embolization syndrome after the procedure, infection, premature ovarian failure (POF) and secondary amenorrhoea due to endometrial atrophy or intrauterine adhesions and the unknown effect on conception and pregnancy [18]. A recent study comparing epidural analgesia versus iv PCA analgesia to provide pain relief after UAE demonstrated that epidural analgesia was superior than iv PCA but cost of epidural analgesia was higher and had potentially greater risk of complications [11]. Therefore, we used iv PCA for the pain management during and after the UAE procedure. We started iv PCA in the beginning of the procedure and kept it until after procedure as well. Almost same amount of PCA solution which was approximately 255 mL was consumed by all the patients.

In the present study the patients underwent UAE for heavy menstruel bleeding did not have amenorrhea and ovarian failure due to impairment of ovarian blood flow, but they had regular mentsruel period and normal amount of menstrual bleeding. The UAE also caused no infection leading to fallopian tube damage in any patients. One patient out of 8 underwent hysterectomy because of pelvic discomfort which was not relieved with embolization even after 8 months. Rest of the patients' symptoms markedly regressed. The short-term results of our study appear to be similar with the literature in terms of efficiency on the symptomatic uterine leiomyomas.

Regarding new and novel analgesia modalities, dexmedetomidine plus fentanyl iv PCA has been compared with fentanyl iv PCA for UAE in a large prospective randomized study. The dexmedetomidine plus fentanyl combination provided better analgesia and fentanyl sparing effect with less nausea and vomiting [12]. However, our study has been the first study that demonstrated iv PCA with meperidine was effectively controlled pain without side effects in non-premedicated women not only after the UAE procedure but also during the procedure.

The limitation of the present study is having limited number of eligible patients for UAE in our institution. We presented our experience since iv PCA meperidine as a pain relief method has been a novel approach compared to the recently preferred pain relief regimens.

In conclusion the UAE procedure under iv PCA with meperidine might be offered as a first option before surgery in selected women in the non-reproductive period or having no children desire who are suffering from bleeding or pelvic pain due to symptomatic intramural fibroids because of fast recovery and discharge availability of the this minimal invasive treatment modality.

REFERENCES

[1] Wallach EE, Vlahos NF. Uterine myomas: An overview of development, clinical features, and management. Obstet Gynecol 2004; 104:393–406. http://dx.doi.org/10.1097/01.AOG.0000136079.62513.39

[2] Duhan N, Sirohiwal D. Uterine myomas revisited. Eur J Obstet Gynecol Reprod Biol 2010; 152: 119–125. http://dx.doi.org/10.1016/j.ejogrb.2010.05.010

[3] Marsh EE, Bulun SE. Steroid hormones and leiomyomas. Obstet Gynecol Clin North Am 2006; 33: 59–67. http://dx.doi.org/10.1016/j.ogc.2005.12.001

[4] Huyck KL, Panhuysen CI, Cuenco KT, Zhang J, Goldhammer H, *et al.* The impact of race as a risk factor for symptom severity and age at diagnosis of uterine leiomyomata among affected sisters. Am J Obstet Gynecol 2008; 198; 168.e1–168.e9.

[5] Valladares F, Frias I, Baez D, Garcia C, Lopez FJ, Fraser JD, *et al.* Characterization of estrogen receptors alpha and beta in uterine leiomyoma cells. Fertil Steril 2006; 86: 1736–43. http://dx.doi.org/10.1016/j.fertnstert.2006.05.047

[6] Gupta JK, Sinha A, Lumsden MA, Hickey M. Uterine artery embolization for symptomatic uterine fibroids.Conchrane Database Syst Rev 2012; 16; 5: CD005073.

[7] Garry R, Fountain J, Mason S, Hawe J, Napp V, Abbott J, *et al.* The Evaluate study: two parallel randomised trials, one comparing laparoscopic with abdominal hysterectomy, the other comparing laparoscopic with vaginal hysterectomy. BMJ 2004; 328 (7432): 129. http://dx.doi.org/10.1136/bmj.37984.623889.F6

[8] Greenwood LH, Glickman MG, Schwartz PE, Morse SS, Denny DF. Obstetric and non malignant gynecologic bleeding: treatment with angiographic embolization. Radiology 1987; 164: 155–9.

[9] 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. http://dx.doi.org/10.1016/S1051-0443(97)70603-1

[10] Ravina JH, Bouret JM, Ciraru-Vigneron N, Repiquet D, Herbreteau D, Aymard A, *et al.* Recourse to particular arterial embolization in the treatment of some uterine leiomyoma. Bull Acad Nat Med 1997; 18:233–43.

[11] Van der Kooij SM, Moolenaar LM, Ankum WM, Rekeers JA, Mol BWJ, Hehenkamp WJK. Epidural analgesia versus patient controlled analgesia for pain relief im uterine artery embolization for uterine fibroids: A decision analysis. Cardiovasc Intervent Radiol 2013; 36: 1514-20. http://dx.doi.org/10.1007/s00270-013-0607-1

[12] Kim SY, Chang CH, Lee JS, Kim MD, Han DW. Comparison of the efficacy of dexmedetomidine plus fentanyl patient controlled analgesia with fentanyl patient controlled analgesia for pain control in uterine artery embolization for symptomatic fibroid tumours or adenomyosis: A prospective, randomized study. J Vasc Intervent Radiol 2013; 24: 779-86. http://dx.doi.org/10.1016/j.jvir.2013.02.034

[13] Worthington-Kirsch RL, Andrews RT, Siskin GP, Shlansky-Goldberg R, Lipman JC, Goodwin SC, Bonn J, Hovsepian DM. II. Uterine fibroid embolization: technical aspects. Tech Vasc Interv Radiol 2002; 5: 17-34. http://dx.doi.org/10.1053/tvir.2002.124101

[14] Pelage JP, Cazejust J, Pluot E, Le Dref O, *et al.* Uterine fibroid vascularization and clinical relevance to uterine fibroid embolization. Radiographics 2005; 25: S99-S117. http://dx.doi.org/10.1148/rg.25si055510

[15] Mukhopadhaya N, De Silva C, Manyonda IT. Conventional myomectomy. Best Pract Res Clin Obstet Gynaecol 2008; 22:677-705. http://dx.doi.org/10.1016/j.bpobgyn.2008.01.012

[16] van der Kooij SM, Bipat S, Hehenkamp WJ, Ankum WM, Reekers JA. Uterine artery embolization versus surgery in the treatment of symptomatic fibroids: a systematic review and meta-analysis. Am J Obstet Gynecol 2011; 205: 317.e18.

[17] Tropeano G, Di Stasi C, Amoroso S, Vizzielli G, Mascilini F, Scambia G. Incidence and risk factors for clinical failure of uterine leiomyoma embolization. Obstet Gynecol 2012; 120: 269-276. http://dx.doi.org/10.1097/AOG.0b013e31825cb88e

[18] Spies JB, Warren EH, Mathias SD, Walsh SM, Roth AR, Pentecost MJ. Uterine fibroid embolization: measurement of health-related quality of life before and after therapy. J Vasc Interv Radiol 1999; 10: 1293–303. http://dx.doi.org/10.1016/S1051-0443(99)70235-6

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