

Midterm Clinical and First Reproductive Results of a Randomized Controlled Trial Comparing Uterine Fibroid Embolization and Myomectomy

Michal Mara · Jana Maskova · Zuzana Fucikova · David Kuzel · Tomas Belsan · Ondrej Sosna

Received: 8 March 2007 / Accepted: 13 September 2007 / Published online: 18 October 2007
© Springer Science+Business Media, LLC 2007

Abstract The purpose of this study was to compare the midterm results of a radiological and surgical approach to uterine fibroids. One hundred twenty-one women with reproductive plans who presented with an intramural fibroid(s) larger than 4 cm were randomly selected for either uterine artery embolization (UAE) or myomectomy. We compared the efficacy and safety of the two procedures and their impact on patient fertility. Fifty-eight embolizations and 63 myomectomies (42 laparoscopic, 21 open) were performed. One hundred eighteen patients have finished at least a 12-month follow-up; the mean follow-up in the entire study population was 24.9 months. Embolized patients underwent a significantly shorter procedure and required a shorter hospital stay and recovery period. They also presented with a lower CRP concentration on the second day after the procedure ($p < 0.0001$ for all parameters). There were no significant differences between the two groups in the rate of technical success, symptomatic effectiveness, postprocedural follicle stimulating hormone levels, number of reinterventions for fibroid recurrence or regrowth, or complication rates. Forty

women after myomectomy and 26 after UAE have tried to conceive, and of these we registered 50 gestations in 45 women. There were more pregnancies (33) and labors (19) and fewer abortions (6) after surgery than after embolization (17 pregnancies, 5 labors, 9 abortions) ($p < 0.05$). Obstetrical and perinatal results were similar in both groups, possibly due to the low number of labors after UAE to date. We conclude that UAE is less invasive and as symptomatically effective and safe as myomectomy, but myomectomy appears to have superior reproductive outcomes in the first 2 years after treatment.

Keywords Comparison · Myomectomy · Reproduction · Uterine fibroid embolization

Embolization of uterine fibroids, which was first introduced by Ravina et al. [1] in 1995, is now a well-established therapeutic procedure. Uterine artery embolization (UAE) is mostly performed in women with symptomatic fibroids who do not plan further pregnancy. Its use in women with reproductive plans is still controversial. Evidence exists that there is a possible risk of infection, which may lead to sepsis and hysterectomy and premature ovarian failure in these patients [2–4].

Myomectomy is considered to be a standard treatment procedure for the removal of myomas in patients of fertile age [5]. This procedure can also be associated with dramatic complications such as perioperative bleeding and uterine rupture during subsequent gravidity, which may require hysterectomy. We thus decided to compare the efficacy and safety of these two approaches in women with reproductive plans who presented with intramural uterine fibroids. The first results of this trial have already been

M. Mara · Z. Fucikova · D. Kuzel · O. Sosna
Department of Obstetrics and Gynecology, General Faculty Hospital and First Medical Faculty of Charles University, Apolinarska 18, 128 00 Prague 2, Czech Republic

J. Maskova · T. Belsan
Department of Radiology, Central Military Hospital, U Vojenske nemocnice 1200, 169 02 Prague 6, Czech Republic

M. Mara (✉)
Department of Obstetrics & Gynecology, 1st Medical Faculty of Charles University, Apolinarska 18, 128 00 Prague 2, Czech Republic
e-mail: michal.mara@quick.cz

published [6]. The aim of this paper is to present midterm clinical and first reproductive results obtained in a larger group of patients.

Materials and Methods

Trial Design

The trial was approved by the Ethics Committee of the First Medical Faculty of Charles University. It was designed as prospective and randomized. Every newly recruited patient was randomly assigned a computer-generated integral number from 1 to 100 (using a random number generating program available at <http://www.random.org>, by Mads Haahr, Distributed Systems Group, Department of Computer Science, University of Dublin, and Trinity College, Ireland). This was always done at the point of randomization, so that no researcher could know or predict any subsequent number. Patients who were assigned an odd number were included in group E (embolization), and patients who were assigned an even number in group M (myomectomy). The researcher in charge of patient recruitment and detailed instruction has always been different from the researcher accomplishing randomization. This second doctor did not know any patient details at the time of randomization and was only notified that the patient met the criteria for trial entry.

Study Population

One hundred forty-nine women with uterine fibroid or fibroids and unfinished reproductive plans were examined from November 2001 to December 2005. All patients entering the trial underwent gynecological examination and abdominal and transvaginal ultrasonography (US) examination of the small pelvis, including Doppler examination of uterus and fibroids. Serum levels of follicle stimulating hormone (FSH) luteinizing hormone (LH), and estradiol were measured on the third day of the cycle in all patients. Additionally, pelvic magnetic resonance imaging (MRI) was performed (i) when clinical examination or US was suspicious for adenomyosis or uterine sarcoma, (ii) in virgins where vaginal US was impossible, and (iii) starting in April 2004, in all patients before UAE. Other possible causes of infertility were systematically investigated in couples with primary or secondary sterility or a history of consecutive abortions.

All patients completed a questionnaire relating to myoma-related symptoms before the start of the therapeutic procedure. Each patient had to define the intensity of symptoms on a scale from 1 to 10, where 1 = absence of

symptoms and 10 = maximal intensity of symptoms. The following symptoms were evaluated: (i) menorrhagia and/or hypermenorrhea, (ii) dysmenorrhea, (iii) dyspareunia, (iv) pelvic pain, (v) dysuria and/or urinary frequency, and (vi) pressure symptoms.

The following inclusion criteria were set: (i) US-verified intramural fibroid at least 4 cm at its largest diameter (in the case of multiple fibroids, at least one with a size of 4 cm), (ii) age <40 years, (iii) serum FSH concentration <30 IU/L (on the third day of menstrual cycle), and (iv) planned pregnancy. Intramural fibroids were defined using US as a uterine wall expansion of typical echo structure with the prevalent part of its volume inside the myometrium.

Exclusion criteria included (i) nonintramural localization of the main fibroid (submucosal and subserous); (ii) size of the dominant myoma >12 cm in its largest diameter (according to US) or uterus enlarged to the size corresponding to >4 months of pregnancy (according to bimanual pelvic examination); (iii) previous myomectomy, embolization, or hormonal therapy of fibroids with GnRH agonists or Danazol; (iv) suspected uterine sarcoma or diffuse adenomyosis (according to US or MRI); and (v) serious disease contraindicating gravidity.

Embolization Procedure

Patients included in group E underwent bilateral UAE. The access for the procedure was from the right groin via the right common femoral artery. The aim was to bilaterally embolize the ascending branches of the uterine artery supplying the fibroid in order to achieve a complete loss of fibroid perfusion and, at the same time, leave free flow in the main stems and in cervico-vaginal branches of both uterine arteries. We refrained from embolization of sites displaying significant utero-ovarian anastomoses of type III (main ovarian blood supply arises from the uterine artery) [7], which could not be overcome by microcatheter.

The technique of “free flow embolization” was employed to perform all procedures, using a 5-Fr catheter (RUC, COOK; William Cook Europe, Bjeverskov, Denmark) and always with the aid of a coaxially introduced microcatheter (Embocath; BioSphere Medical Inc., Rockland, MA, USA). Trisacryl gelatin microspheres (Embospheres; BioSphere Medical, S.A., Roissy, France) were used for embolization in all cases. At the start of the study (first five patients), we chose particles 300 to 900 μm in diameter. Later, in accordance with data published in the literature, particles larger than 500 μm were used exclusively, to prevent possible nontargeted ovarian embolization via utero-ovarian anastomoses [8].

A single dose of antibiotics (sultamicillin; 1.5 g intravenously) was administered to every patient 30 min before

the embolization. For pain management during the first 24 h after the procedure patients were given either epidural analgesia (10 ml of 0.5% bupivacain plus 5 µg of sufentanyl in 50 ml of normal saline, administered continually at 5 to 10 ml per hour) or intravenous analgesia (5 µg of sufentanyl plus 0.15 mg of clonidin in 50 ml of normal saline as a continual infusion at 5 to 10 ml per hour). Nausea and postembolization discomfort during subsequent days were treated by thiethylperazin, diclofenac, and paracetamol. The minimal length of hospitalization after the procedure was 48 h.

Embolization leading to bilateral occlusion of ascending branches of urinary arteries and a complete loss of fibroid perfusion, as detected by angiography, was considered technically successful. Dissection or spasm of uterine arteries, adverse reaction to administered drugs, hematoma in the groin, and other complications of angiography were considered periprocedural complications. All procedures were performed by the same interventional radiologist.

Myomectomy

The myomectomy procedure was always initiated with hysteroscopy: a finding of a submucous fibroid of type 0 or type I (according to the classification of European Society for Hysteroscopy) would eliminate the relevant patient from the study. Hysteroscopy was followed by laparoscopy and the access for myomectomy was chosen according to predefined criteria. Open myomectomy (OM) was preferred when a fibroid was larger than 8 cm, in the case of a finding of multiple intramural fibroids, and in the case of a very unfavorable localization of a fibroid (e.g., in uterine edges reaching the pelvic wall or deep in the posterior uterine wall reaching the insertions of sacro-uterine ligaments). In all other cases myomectomy was performed by laparoscopy. The suture of the uterine wall defect required after myoma enucleation was performed using atraumatic stitches in two layers (vicryl 2/0, polyglactin 910; Ethicon, Brussels, Belgium). Myomectomy was also covered by a single dose of antibiotics (sultamicillin, 1.5 g i.v. 30 min before the procedure), by the corresponding protocol of continuous intravenous analgesia (sufentanyl plus clonidin for the first 24 h after the procedure), and by the same symptomatic therapy (antiemetics, antipyretics, analgesics) such as UAE. The minimal length of hospital stay was 48 h after LM and 120 h (5 days) after OM.

Myomectomy was evaluated as successful when all detectable fibroids larger than 4 cm were completely removed. The following were considered to be perioperative complications: (i) injury of organs in the abdominal cavity (fallopian tube, ovaries, urinary bladder, intestines) or major pelvic vessels, (ii) blood loss exceeding 1000 ml,

(iii) unexpected penetration of the uterine cavity (in women in whom fibroid prominence in the cavity was not previously detected by hysteroscopy), (iv) unplanned conversion from LM to laparotomy (during myoma enucleation), and (v) early reoperation because of uterine bleeding, hemo-peritoneum, or hematoma. The same two surgeons performed all myomectomies.

Follow-up

The occurrence of the following early postoperative complications were monitored during the first 30 days: fever, signs of pelvic infection, severe vaginal bleeding, severe pain not responsive to analgesics, prolonged hospital stay (>48 h after UAE, 72 h after LM, and >144 h after OM), the necessity for antibiotics or blood transfusion, rehospitalization, allergic reactions, wound complications after myomectomy, ischemic phenomena after UAE, surgical intervention due to hematoma (pelvic, subfascial, retro-peritoneal, or inguinal) or infection, thromboembolic complications, and hysterectomy.

Patients were examined (clinically and using ultrasonography) 1 month and 6 months postprocedurally and subsequently every 6 months. The levels of FSH, LH, and estradiol (on the third day of the cycle or at another time in the case of amenorrhea) were measured and myoma-related symptoms were again evaluated (the same questionnaire) 6 months after the procedure. The FSH level was monitored in the subsequent course of follow-up in women with signs of ovarian failure. Patients were examined immediately in the case of difficulties, complications, or signs of pregnancy.

The following late complications were assessed more than 30 days after the procedure: (i) signs of uterine infection or sepsis; (ii) permanent or transient signs of ovarian failure (clinical, i.e., amenorrhea not related to pregnancy, with or without vasomotor symptoms of menopause, requiring hormone replacement therapy [HRT]; or laboratory, in the case of FSH increase by >5 IU/L, compared to pretreatment values); (iii) ischemic phenomena after UAE; (iv) chronic pelvic pain or dyspareunia; (v) sudden severe uterine bleeding; (vi) chronic malodorous vaginal discharge; (vii) loss of libido; (viii) emergency myomectomy or hysterectomy; (ix) vaginal fibroid expulsion; and (x) uterine rupture.

Great emphasis was placed on ultrasonographical scan of the uterus 6 months after the procedure. The following outcomes were evaluated as favorable, with regard to planned gravity: (i) absence of a fibroid larger than 5 cm or a fibroid deforming the uterine cavity and (ii) absence of a hematoma or thinning of the myometrium in place of previous myomectomy. MRI was performed 6 months after

embolization in patients who underwent MRI before UAE (all patients starting from April 2004) and also in patients who showed no sign of a fibroid decrease by US. The main benefit of MRI in these patients was confirmative determination of fibroid reperfusion or its insufficient infarction.

Reproductive Follow-up and Reinterventions

All patients with reproductive plans were recommended to wait for at least 6 months after the therapy. Women with a history of infertility who had a favorable outcome of a US uterus scan 6 months after the procedure were referred to a center of assisted reproduction to undergo causal infertility treatment (according to associated factors), including in vitro fertilization (IVF). History of reproductive attempts and results of all patients were systematically recorded during regular checkups (every 6 months). In the case of pregnancy, prenatal monitoring and delivery at our hospital were offered to all patients. The type of delivery and possible indications for operative delivery were subjected to standard rules: cesarean section was not primarily indicated (only if other indications were also present) except for cases where persisting fibroid formed an obstetric obstruction and in patients who underwent intrauterine penetration during myomectomy.

Secondary myomectomy was recommended in the case of undetectable fibroid shrinkage at 6 months after UAE and/or in the case of a persisting fibroid >5 cm. Similar reintervention was recommended anytime later (except during pregnancy) when fibroid regrowth after UAE (over 5 cm) or recurrent fibroid >5 cm after myomectomy was detected. The intervals between checkups after surgical reintervention were also 6 months, and patients were recommended to delay their pregnancy plans for at least another 6 months.

Analysis of the Results

The results were analyzed on an intent-to-treat basis. For statistical comparison of qualitative parameters from both groups (e.g., rehospitalization: yes or no), chi-square test and Fischer's test were used. For comparison of quantitative parameters (e.g., FSH level), Student's t-test and Mann-Whitney test were used. $p < 0.05$ was determined to be statistically significant.

Results

Twenty-one patients (15.4%) of 149 refused to participate in the trial and 7 patients were excluded from the study

based on the elimination criteria; the remaining 121 women were randomized into one of the two groups (58 for UAE and 63 for myomectomy) and they underwent appropriate therapy (Table 1). Of this count, 120 patients have finished a 6-month follow-up and 3 patients have dropped out of the trial: 1 patient did not turn up for the checkup at 6 months after myomectomy and 2 patients did not turn up at 12 months after UAE.

Of the total number of 121 patients, 110 patients were symptomatic (90.9%). The mean age of women was 32.4 and 32.0 years in groups E and M, respectively. Sixty-six patients were nulligravidae (54.5%), 35 were sterile (28.9%; 11 in group E and 24 in group M; $p < 0.05$), 18 had miscarried in the past (14.9%), and 51 had another subfertility factor other than myoma (42.1%). Mean FSH levels before the procedure were 6.98 ± 2.9 IU/L in group E and 6.73 ± 1.9 IU/L in group M. Six patients had a FSH value >10 IU/L before embolization, and four women before myomectomy. Except for the rate of sterility, there were no statistically significant differences in any aforementioned factors or in other entry parameters (size of dominant fibroid, number of fibroids) between the two groups. A detailed summary of US scan findings prior to both procedures is given in Table 2.

Periprocedural results are shown in Table 3. The rate of technical failures was about 10% in both groups. Six patients were embolized unilaterally (four due to atypical branching or spasms of uterine arteries not responding to vasodilators and two because of large utero-ovarian anastomoses). In five women myomectomy was incomplete due to unfavorable localization, resulting in the retention of a fibroid larger than 4 cm. Forty-two (67%) myomectomies of 63 were performed by LM. The frequency of laparoconversions, i.e., myomectomies started by LM which had to be completed as an open surgery because of complications (i.e., bleeding and/or difficult tumor enucleation from the uterus), was 4.5%. The following complications have occurred: in group E, one case of artery dissection and three cases of uterine artery spasms; and in group M, three myomectomies with unexpected intrauterine penetration and two nonelective laparoconversions.

There were no significant differences in most monitored parameters of early postprocedural results between the two groups (Table 4). The average length of hospitalization and postoperative recovery were significantly longer and the mean serum C-reactive protein concentration was significantly higher in the group of women treated by surgery. There were no significant differences in the frequency of early complications between the two groups. All these complications can be considered as mild or moderately serious. It was the febrile status in most cases which required therapy with antibiotics (eight patients in group E, five patients in group M). After UAE 1 patient required a

Table 1 Flowchart of 142 patients (pt) eligible (according to inclusion criteria) to enter the trial

Pt no.	Pt initials	Year of birth	Date of randomization	Randomized into group	Date of procedure	Type of procedure
1	Z.I.	1969	2.11.2001	E	20.11.2001	UAE
2	M.H.	1967	2.11.2001	E	22.11.2001	UAE
—	K.S.	1965	—	Refused	—	—
3	L.N.	1973	7.12.2001	M	9.1.2002	OM
4	D.D.	1965	14.12.2001	E	24.1.2002	UAE
5	D.K.	1964	11.1.2002	M	21.2.2002	OM
—	J.B.	1973	—	Refused	—	—
6	M.M.	1976	8.2.2002	E	28.3.2002	UAE
—	B.C.	1970	—	Refused	—	—
7	M.L.	1974	15.3.2002	M	11.4.2002	OM
8	D.L.	1973	22.3.2002	M	15.4.2002	OM
9	V.H.	1976	22.3.2002	E	3.5.2002	UAE
10	K.S.	1968	12.4.2002	M	22.5.2002	LM
—	P.K.	1964	—	Refused	—	—
—	M.P.	1976	—	Refused	—	—
11	M.M.	1972	31.5.2002	M	4.7.2002	OM
—	L.H.	1977	—	Refused	—	—
12	L.B.	1971	21.6.2002	M	7.8.2002	OM
13	D.M.	1975	6.9.2002	E	11.10.2002	UAE
14	E.M.	1976	13.9.2002	E	15.10.2002	UAE
15	M.K.	1973	27.9.2002	M	27.11.2002	OM
16	J.C.	1974	4.10.2002	E	14.11.2002	UAE
17	L.S.	1975	18.10.2002	M	27.11.2002	LM
18	A.H.	1970	25.10.2002	M	16.12.2002	OM
19	I.K.	1970	25.10.2002	E	21.11.2002	UAE
—	H.S.	1966	—	Refused	—	—
20	M.K.	1975	13.12.2002	M	22.1.2003	OM
21	M.C.	1966	20.12.2002	E	9.1.2003	UAE
22	D.H.	1976	20.12.2002	M	28.1.2003	LM
23	D.V.	1967	10.1.2003	E	30.1.2003	UAE
24	J.B.	1971	24.1.2003	E	6.3.2003	UAE
—	S.B.	1968	—	Refused	—	—
25	V.H.	1970	7.2.2003	E	20.3.2003	UAE
26	M.O.	1967	21.2.2003	M	2.4.2003	OM
27	I.T.	1968	28.2.2003	M	14.5.2003	OM
28	H.A.	1964	28.3.2003	E	30.4.2003	UAE
29	L.V.	1969	4.4.2003	E	7.5.2003	UAE
30	J.M.	1963	25.4.2003	M	3.6.2003	OM
31	M.K.	1974	25.4.2003	E	19.5.2003	UAE
32	L.T.	1968	2.5.2003	M	17.6.2003	OM
33	S.B.	1971	2.5.2003	E	29.5.2003	UAE
34	E.T.	1968	23.5.2003	E	3.7.2003	UAE
35	B.P.	1973	13.6.2003	M	9.9.2003	OM
36	L.K.	1974	13.6.2003	E	3.7.2003	UAE
—	I.S.	1964	—	Refused	—	—
37	M.S.	1966	10.10.2003	M	26.11.2003	LM
38	M.H.	1964	24.10.2003	E	4.12.2003	UAE
—	A.H.	1965	—	Refused	—	—

Table 1 continued

Pt no.	Pt initials	Year of birth	Date of randomization	Randomized into group	Date of procedure	Type of procedure
39	K.K.	1975	19.12.2003	M	10.2.2004	LM
40	L.J.	1967	19.12.2003	E	9.1.2004	UAE
41	I.F.	1971	9.1.2004	E	23.1.2004	UAE
42	D.L.	1977	16.1.2004	M	17.2.2004	LM
43	J.V.	1977	16.1.2004	E	17.2.2004	UAE
44	E.S.	1972	30.1.2004	M	2.3.2004	LM
45	R.K.	1966	6.2.2004	E	5.3.2004	UAE
46	J.H.	1972	13.2.2004	E	12.3.2004	UAE
47	M.M.	1967	13.2.2004	M	23.3.2004	LM
48	M.Z.	1970	20.2.2004	E	12.3.2004	UAE
49	E.S.	1970	5.3.2004	M	20.4.2004	LM
50	M.M.	1965	12.3.2004	M	20.4.2004	OM
51	K.K.	1968	12.3.2004	E	2.4.2004	UAE
52	D.M.	1968	19.3.2004	M	21.4.2004	OM
53	N.V.	1969	19.3.2004	M	21.4.2004	LM
54	M.T.	1970	26.3.2004	M	8.6.2004	LM
55	I.S.	1966	26.3.2004	E	29.4.2004	UAE
—	E.Z.	1971	—	Refused	—	—
56	M.P.	1974	23.4.2004	M	7.7.2004	LM
57	E.K.	1972	23.4.2004	E	14.5.2004	UAE
58	P.S.	1967	7.5.2004	M	19.7.2004	OM
59	L.D.	1974	14.5.2004	M	21.7.2004	LM
60	J.S.	1968	14.5.2004	E	11.6.2004	UAE
61	H.K.	1965	21.5.2004	M	7.9.2004	OM
62	M.M.	1972	28.5.2004	M	12.10.2004	LM
63	A.M.	1970	28.5.2004	M	9.11.2004	LM
64	V.H.	1978	31.5.2004	E	11.6.2004	UAE
65	K.W.	1970	4.6.2004	E	9.7.2004	UAE
—	L.S.	1975	—	Refused	—	—
66	K.H.	1973	18.6.2004	E	20.8.2004	UAE
67	E.B.	1983	25.6.2004	E	20.8.2004	UAE
68	K.F.	1968	2.7.2004	E	9.9.2004	UAE
69	M.R.	1973	9.9.2004	M	16.11.2004	LM
70	M.H.	1967	9.9.2004	E	1.10.2004	UAE
—	J.P.	1976	—	Refused	—	—
—	D.R.	1965	—	Refused	—	—
71	K.F.	1976	23.9.2004	M	29.11.2004	LM
72	P.C.	1975	23.9.2004	E	22.10.2004	UAE
73	P.P.	1972	30.9.2004	E	22.10.2004	UAE
74	B.S.	1972	7.10.2004	M	19.1.2005	LM
75	P.H.	1969	14.10.2004	E	3.11.2004	UAE
76	J.L.	1979	14.10.2004	M	26.1.2005	LM
77	J.E.	1968	21.10.2004	M	27.1.2005	LM
78	L.A.	1969	21.10.2004	E	19.11.2004	UAE
79	M.D.	1975	4.11.2004	M	2.2.2005	LM
80	M.R.	1972	11.11.2004	E	10.12.2004	UAE
81	M.Z.	1966	18.11.2004	M	17.2.2005	LM
82	S.Z.	1971	9.12.2004	M	17.2.2005	LM

Table 1 continued

Pt no.	Pt initials	Year of birth	Date of randomization	Randomized into group	Date of procedure	Type of procedure
83	H.S.	1968	16.12.2004	E	21.1.2005	UAE
84	M.S.	1974	6.1.2005	E	18.2.2005	UAE
—	E.K.	1965	—	Refused	—	—
—	S.D.	1970	—	Refused	—	—
85	L.L.	1972	27.1.2005	E	18.3.2005	UAE
86	L.M.	1972	3.2.2005	M	21.3.2005	LM
87	I.C.	1970	17.2.2005	M	23.3.2005	LM
88	P.Z.	1971	24.2.2005	E	8.4.2005	UAE
89	M.K.	1969	24.2.2005	M	11.4.2005	LM
—	M.T.	1975	—	Refused	—	—
90	H.K.	1967	3.3.2005	M	26.4.2005	OM
91	B.Z.	1974	10.3.2005	E	6.5.2005	UAE
92	M.K.	1965	24.3.2005	M	4.5.2005	LM
93	A.G.	1977	31.3.2005	M	16.5.2005	LM
94	L.P.	1972	7.4.2005	M	17.5.2005	LM
95	L.H.	1977	7.4.2005	M	18.5.2005	OM
96	J.K.	1976	14.4.2005	E	13.5.2005	UAE
97	M.L.	1976	21.4.2005	M	23.5.2005	LM
—	H.V.	1965	—	Refused	—	—
98	M.K.	1974	12.5.2005	M	6.6.2005	LM
99	P.L.	1978	26.5.2005	E	1.8.2005	UAE
100	E.P.	1971	23.6.2005	E	1.8.2005	UAE
101	K.K.	1977	30.6.2005	M	7.9.2005	LM
102	L.F.	1969	14.7.2005	E	21.9.2005	UAE
—	E.S.	1966	—	Refused	—	—
103	J.R.	1980	8.9.2005	M	26.9.2005	LM
104	E.H.	1972	8.9.2005	E	23.9.2005	UAE
105	O.S.	1967	15.9.2005	M	5.10.2005	LM
106	I.K.	1970	15.9.2005	M	12.10.2005	LM
—	H.A.	1966	—	Refused	—	—
107	P.P.	1966	22.9.2005	E	14.10.2005	UAE
108	M.A.	1977	29.9.2005	M	26.10.2005	LM
109	E.Z.	1973	29.9.2005	M	2.11.2005	LM
110	I.S.	1979	29.9.2005	M	2.11.2005	LM
111	D.M.	1967	6.10.2005	E	21.10.2005	UAE
112	J.B.	1967	6.10.2005	M	2.11.2005	LM
113	A.G.	1983	13.10.2005	M	9.11.2005	OM
114	J.P.	1973	13.10.2005	E	15.11.2005	UAE
115	S.S.	1969	20.10.2005	M	16.11.2005	LM
116	H.D.	1974	27.10.2005	M	1.12.2005	LM
117	L.B.	1973	27.10.2005	E	2.12.2005	UAE
—	D.V.	1976	—	Refused	—	—
118	K.K.	1970	10.11.2005	E	2.12.2005	UAE
119	M.J.	1972	10.11.2005	M	1.12.2005	LM
120	R.L.	1977	10.11.2005	E	9.12.2005	UAE
121	D.R.	1975	24.11.2005	E	9.12.2005	UAE

Note. LM, laparoscopic myomectomy; OM, open myomectomy; UAE, uterine artery embolization. Dates given as day.month.year

Table 2 Ultrasound findings for 121 patients prior to uterine artery embolization (UAE) or myomectomy

	UAE (<i>n</i> = 58)	Myomectomy (<i>n</i> = 63)	<i>p</i>
Average size of dominant fibroid, mm ± SD (range)	62.3 ± 19.1 (42–107)	59.8 ± 16.5 (41–110)	NS ^a
No. women with myoma >80 mm	8 (13.8%)	7 (11.1%)	NS ^b
No. myomas >2 cm ± SD (range)	1.95 ± 1.8 (1–8)	1.84 ± 2.1 (1–16)	NS ^a
No. women with Solitary myomas	39 (67.2%)	40 (63.5%)	NS ^b
2–5 fibroids	15 (25.9%)	21 (33.3%)	NS ^b
>5 fibroids	4 (6.9%)	2 (3.2%)	NS ^c
Uterine cavity deviated by fibroid(s)	30 (51.7%)	22 (34.9%)	NS ^b

Note. NS, nonspecific difference; SD, standard deviation. Tested by: ^a Mann-Whitney test; ^b chi-square test; ^c Fisher's test

Table 3 Periprocedural evaluation

	UAE (<i>n</i> = 58)	Myomectomy (<i>n</i> = 63)	<i>P</i>
Technical success	52 (89.7%)	58 (92.1%)	NS ^b
Average time of procedure, min ± SD (range)	59.2 ± 23.1 (30–140)	108.9 ± 27.7 (54–173)	<0.0001 ^a
Fluoroscopy time, min ± SD (range)	16.8 ± 6.3 (5–33)	—	
No. women with utero-ovarian anastomoses	25 (43.1%)	—	
Average perioperative blood loss, ml ± SD (range)	—	296.0 ± 122.6 (100–700)	
Type of analgesia	38 EDA/20 IVA	63 IVA	
Complications	4 (6.9%)	5 (7.9%)	NS ^c

Note. UAE, uterine artery embolization; NS, nonspecific difference; SD, standard deviation; EDA, epidural analgesia; IVA, intravenous analgesia. Tested by: ^a Mann-Whitney test; ^b chi-square test; ^c Fisher's test

Table 4 Early postprocedural results (from day 1 to day 30 after procedure)

	UAE (<i>n</i> = 58)	Myomectomy (<i>n</i> = 63)	<i>P</i>
Average hospital stay, h ± SD (range)	60.2 ± 32.3 (36–216)	86.1 ± 40.4 (48–192)	<0.0001 ^a
Prolonged hospital stay*	9 (15.5%)	6 (9.5%)	NS ^b
Hospital stay >7 days	1 (1.7%)	3 (4.8%)	NS ^c
Readmissions to hospital	2 (3.4%)	1 (1.6%)	NS ^c
Febrile morbidity	7 (12.1%)	7 (11.1%)	NS ^b
Day 2 serum CRP, mg/L ± SD (range)	23.8 ± 27.3 (3–168)	36.9 ± 28.1 (6–137)	<0.0001 ^a
Need for antibiotics	8 (13.8%)	6 (9.5%)	NS ^b
Necessity for transfusion	0	2 (3.2%)	NS ^c
Recovery period, days ± SD (range)	11.9 ± 5.9 (3–30)	22.1 ± 12.3 (7–65)	<0.0001 ^a
Disability >2 wk	13 (22.4%)	36 (57.1%)	<0.0001 ^b
Complications	12 (20.7%)	10 (15.9%)	NS ^b

Note. UAE, uterine artery embolization; NS, nonspecific difference; SD, standard deviation; CRP, C-reactive protein. Tested by: ^a Mann-Whitney test; ^b chi-square test; ^c Fisher's test

*Longer hospital stay than usual (i.e., more than 48 h after UAE, 72 h after laparoscopic myomectomy, and 144 h after open myomectomy)

prolonged hospital stay due to severe vaginal bleeding (treated by pharmacotherapy), one patient developed a rash as a probable reaction to analgesics, and one woman was treated for postpuncture headache after epidural anesthesia. Additionally, a subcutaneous hematoma of approximately 5 cm developed in one woman at the site of puncture in the

right groin and was managed by conservative therapy. After myomectomy two patients (one after LM and one after OM) required transfusion due to severe anemia, one woman developed a urinary tract infection, and one woman a wound infection. One patient underwent surgical evacuation of subfascial hematoma 1 day after OM.

Table 5 Late postprocedural results

	UAE (<i>n</i> = 58)	Myomectomy (<i>n</i> = 62)	<i>P</i>
Mean follow-up, mo ± SD (range)	26.2 ± 14.2 (6–55)	23.7 ± 13.9 (6–54)	NS ^a
Relief from symptoms*	88.5% (46/52)	87.9% (51/58)	NS ^b
6 mo after procedure Serum FSH, IU/L ± SD (range)	7.89 ± 6.0 (4.0–48.9)	6.49 ± 2.0 (3.6–12.3)	NS ^a
FSH >10 IU/L	8 (13.8%)	2 (3.2%)	<0.05 ^c
Significant elevation of FSH [†]	3 (5.2%)	0	NS ^c
Regrowth or recurrence of fibroid(s)	6 (10.3%)	5 (8.1%)	NS ^b
Reinterventions	19 (32.8%)	2 (3.2%)	<0.0001 ^b
Reinterventions for regrowth or recurrence of fibroid(s)	4 (6.9%)	2 (3.2%)	NS ^c
Complications	8 (13.8%)	5 (8.1%)	NS ^b

Note. UAE, uterine artery embolization; NS, nonspecific difference; SD, standard deviation. Tested by: ^a Mann-Whitney test; ^b chi-square test; ^c Fisher's test

*Lower sum of six followed symptoms at 6 months after procedure than preprocedurally (based on the questionnaire)

[†] At least 5 IU/L increase at 6 months after procedure (compared with preprocedural level)

Tables 5 and 6 summarize late clinical results and results of imaging studies at 6 months after the procedure. The mean length of follow-up was approximately 2 years in both groups; 81% of women after embolization and 79% after surgery have been followed for more than 1 year, and 50% of patients in group E and 43% in group M have been followed for at least 2 years. Both methods were similarly effective when cumulative evaluation of all symptoms at 6 weeks after the procedure was considered. While it seemed at preliminary evaluation of results that representation of patients with total relief from all myoma-related symptoms would be significantly higher in group M, it now appears that their number is only insignificantly higher (32 of 58 women, i.e., 55 %) in this group than after embolization (26 of 52 women, i.e., 50%).

With respect to the main goal of the therapy (gravidity) and trial design, both groups differed significantly in the frequency of reinterventions. Secondary myomectomy was performed in 19 cases in group E: 9 by LM, 8 by laparotomy, and 2 by hysteroscopy. The mean interval from UAE to reintervention was 12.4 months (±12.2 months; median, 7.0 months). The persistence of a large fibroid (>5 cm) at 6 months after UAE was the most frequent indication (15 cases, including 5 patients with UAE technical failure), and in 4 cases we reintervened due to regrowth of a fibroid (see Table 5). In group M, the reintervention was indicated only in cases of clinically significant recurrence. Remyomectomy was performed in two women (one by LM and one by open surgery) at a 15- and 30-month interval from primary therapy, respectively.

We recorded a relatively low frequency of late complications. All these incidents (dyspareunia, pelvic pain, endometritis, and one episode of metrorrhagia) after myomectomy were regarded as mild and nonserious. No

Table 6 Results of imaging studies 6 months after uterine artery embolization (UAE)

Mean shrinkage of diameter of dominant fibroid on US (58 patients)	31.7%
Mean shrinkage of volume of dominant fibroid on MRI*	58.7%
Mean volume of dominant fibroid on MRI*	69 cm ³ (pre-UAE: 166 cm ³)
Partial infarction of dominant fibroid on MRI*	28.9% (11 / 38)
No infarction of dominant fibroid on MRI*	2.6% (1 / 38)

*Calculated from only 38 patients with both (pre- and post-UAE) MRI scans

serious or life-threatening complications have occurred after UAE either, but in four women there were complications related to ovarian function. One patient with 6 weeks of amenorrhea had no further menopausal symptoms, had a normal FSH level (6.4 IU/L) at 6 months after UAE, and is pregnant now. A transitory, but significant FSH elevation, to 15.0, 30.4, and 48.9 IU/L, respectively, occurred in three women with preprocedural FSH <10 IU/L (Table 5). One of these women suffered amenorrhea for 2 months and did not respond to progesterone, but her cycle adjusted spontaneously. This woman has not tried to conceive to date. Another two patients with FSH elevation were clinically asymptomatic (from the time of embolization until now, which is 53 and 35 months, respectively), but they both underwent unsuccessful therapy for sterility, including two and three IVF cycles, respectively, to date. Low response to ovarian stimulation with gonadotropins (high consumption of FSH, low number of reacting follicles) and poor development of most embryos were common for their cycles.

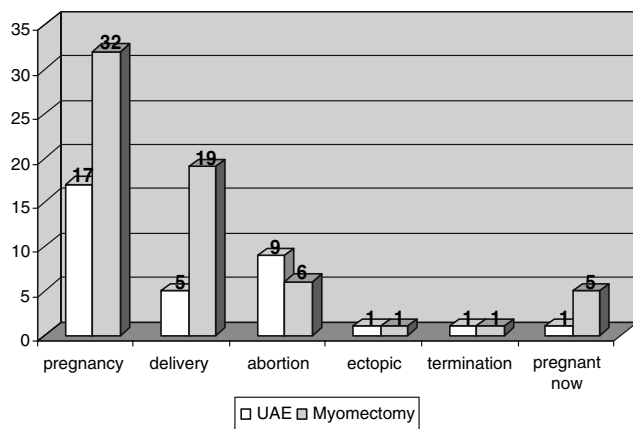


Fig. 1 Reproductive results of 26 women after uterine artery embolization (UAE) and 40 women after myomectomy. Statistical difference between the groups (p value): pregnancy, NS^b; delivery, <0.05^b; abortion, <0.05^b; ectopic gestation, NS^c; pregnancy termination, NS^c; pregnant now, NS^c. Tested by: ^bchi-square test; ^cFisher's test. NS, nonsignificant

Overall there were eight patients with a FSH concentration >10 IU/L at 6 months after UAE (including four women with a pre-UAE value >10 IU/L and three with an increase of >5 IU/L) and two patients with FSH > 10 IU/L at 6 months after myomectomy (including one with pre-procedural FSH > 10 IU/L and no case of significant increase). No patients had climacteric vasomotor symptoms and no patient required HRT. Two patients complained of temporarily decreased sexual appetite after embolization (this improved within 12 months): 1 of them in connection with noticeable hypomenorrhea and the other patient in connection with the feeling of "vaginal dryness." No case of uterine rupture, urgent hysterectomy or other emergency surgery, or hospitalization for late complications after embolization or myomectomy has occurred in the whole cohort to date.

Existing reproductive and first perinatal results are summarized in Fig. 1 and Table 7. From the limited cohort of patients who have already tried to conceive (26 after UAE and 40 after myomectomy), 13 from group E (mean age, 32.8 years; range, 22 to 40 years) and 31 from group M (mean age, 34.3 years; range, 27–42 years) have already become pregnant. Four women after embolization and one patient after myomectomy have already become pregnant two times; one woman after myomectomy gave birth to twins (after IVF). The mean interval between the procedure and gravidity was 18 and 13 months in groups E and M, respectively. This difference could be partially influenced by the rate of secondary myomectomy in the two groups of pregnant women: it was performed in 5 of 13 pregnant women after UAE but in 1 only patient of 31 pregnant patients in group M. Presenting the results in the language of reproductive medicine, the pregnancy rate after UAE

was 50% to date, delivery rate 19%, and abortion rate 64%, while after myomectomy the pregnancy rate was 78%, delivery rate 48%, and abortion rate 23%. The differences in all these parameters were statistically significant ($p < 0.05$, χ^2 test). Relative risk (RR) of women treated with UAE not to get pregnant was 2.22 (95% confidence interval, 1.11 < RR < 4.44); not to deliver, 1.54 (1.08 < RR < 2.18); and to abort, 2.79 (1.25 < RR < 6.22).

Discussion

Comparison of myomectomy and UAE, two very different therapeutic approaches, is difficult and could appear misleading, particularly in some parameters (invasiveness, complication rate, reinterventions). Nevertheless, the question of possible use of uterine fibroid embolization in young women with active reproductive plans is very important from the point of view of gynecology and reproductive medicine. The surgical therapy is, especially in some patients, technically difficult, invasive, and risky, and therefore comparison of UAE with myomectomy as a possible alternative to existing standard therapy is most desirable [9].

There are many reports about gravidities and reproductive results after embolization in the literature today [10–15]. Surprisingly, there is an apparent nearly absolute lack of prospective studies comparing not only myomectomy and UAE, but also different fibroid treatments in relation to fertility (e.g., myomectomy with expectation). Only four papers [16–19] compare clinical results of embolization and myomectomy. But they are not randomized studies, only one is prospective [19], and only one is aimed at obstetrical, not *just* reproductive results [17].

In this study we confirmed in a midterm time horizon and in a larger cohort of patients most of the results from our preliminary evaluation [6]. Myomectomy and embolization were comparable as far as technical success rate, frequency of early and late complications, and symptomatic effectiveness are concerned. We also verified lower invasiveness of the radiological approach compared to myomectomy (hospital stay, recovery period, acute phase markers). The rate of serious complications was very low in both groups. The trial does not give the answer to the management of large or recurrent fibroids (see exclusion criteria) but our goal was to keep the study group as homogeneous as possible, which is always difficult in uterine fibroid patients. Unlike other studies, we did not focus on economical comparisons between the two treatment methods [20], mainly because the cost of UAE is many times higher than that of myomectomy at the site of this study, and there are significant differences between *open* and laparoscopic myomectomy.

Table 7 Perinatal results

	UAE (<i>n</i> = 5)	Myomectomy (<i>n</i> = 19)	<i>p</i>
Mean age of mothers, yr ± SD (range)	32.2 ± 4.1 (29–39)	34.4 ± 4.4 (27–42)	NS ^a
Mean birth weight, g ± SD (range)	3042 ± 316 (2830–3600)	3035 ± 538 (1600–3940)	NS ^a
Mean completed gestational weeks ± SD (range)	38.8 ± 0.6 (38–40)	37.5 ± 2.4 (31–40)	NS ^a
Preterm delivery (<37th week)	0	5 (26.3%)	NS ^b
Cesarean section	3 (60.0%)	13 (68.4%)	NS ^b
Postpartum hemorrhage	1 (20.0%)	0	NS ^b
Perinatal hypoxia of neonate	0	0	—
Pre-eclampsia	0	2 (10.5%)	NS ^b
Fetal intrauterine growth restriction	0	2 (10.5%)	NS ^b

Note. UAE, uterine artery embolization; NS, nonspecific difference; SD, standard deviation. Tested by: ^a Mann-Whitney test; ^b Fisher's test

The relatively high rate of LMs (two-thirds) might seem surprising and it certainly does not represent a typical picture of a broad gynecological practice. But we believe that these patients should always be referred to centers of reproductive surgery with experienced endoscopic surgeons. With respect to certain limits for LM (mentioned under Materials and Methods), many studies have already proved the equal safety and potency of the laparoscopic approach in comparison to the open procedure [21, 22].

The technical failure rate of UAE was higher than the rates reported in other studies [23, 24], mainly as a result of the unusual or unfavorable anatomy (anastomoses to ovarian artery) present. Another reason for the higher failure rate could be the nature of our patient group, comprised of young women desiring pregnancy. This might account for a particularly careful approach to their treatment. Only the results of the EMMY trial showed a similar frequency of technical failures [25], but in their case, in addition to difficult anatomy, the absence of one of the uterine arteries was the most common reason.

In accordance with our expectations, there were far more reinterventions in the group treated by embolization (Table 5). But these numbers do not reflect the frequency of method failure or the rate of recurrence. Instead, they seem to be the logical consequences of the different character of the two procedures (UAE leaves fibroids in situ), of the main goal of the therapy (to optimize the uterine condition before planned conception), and of methods adapted to it (specific strategy for indications of reinterventions).

The fact that in the initial study postprocedural MRI was performed only in patients where significant shrinkage of fibroid had not occurred (including 6 patients with unilateral embolization only) could account for the relatively high number of cases with at least partially maintained fibroid perfusion at 6 months after UAE (12 patients of 38 evaluated; see Table 6). If we had performed this examination in all women, including those with a good clinical response

and Doppler US evidence of infarcted fibroid, this number would have been expected to be significantly lower.

Existing reproductive results could be partially influenced by the short duration of the follow-up and mainly by the unequal number of patients who tried to conceive in each group: 40 after myomectomy and only 26 after embolization ($p < 0.05$, χ^2 test). Nevertheless, the statistically significant differences observed in the number of successful deliveries (19 after myoma enucleation and only 5 after UAE) and in the number of early pregnancy losses (6 after myomectomy and 9 after embolization; in all cases spontaneous or missed miscarriage in the first trimester) were in support of the surgical approach. We can only speculate whether these reproductive results are due to an error of small numbers, whether they reflect the influence of UAE on ovarian function, uterine perfusion, and implantation quality, or whether they reflect a direct influence of embolization on the uterine cavity and endometrium [26–28].

The fact that the rate of abortions after UAE was higher than 60% (in contrast with 23% after myomectomy) is the most alarming result of the study to date, in contrast to existing reports from other authors [10, 12, 17]. The post-UAE abortion rate was 16.7% in the Ontario multicenter, prospective trial (24 pregnancies in 21 women of mean age 34 years), 27% in the retrospective trial of Carpenter and Walker (26 pregnancies; mean age of patients, 37 years), and 24% after UAE and 15% after laparoscopic myomectomy in the controlled retrospective multicenter trial of Goldberg et al. (53 pregnancies; mean age, 38 years), but the difference was not statistically significant. In our cohort, the mean age of pregnant women after UAE was lower (32.8 years) than that of pregnant women after myomectomy (34.3 years), and at the same time, it was lower than in the aforementioned trials. The mean age of women who aborted after embolization was only slightly higher (33.0 years), and that is why the age factor does not explain the frequency of abortions after UAE. The abortion rate was

expressed as a quotient of all abortions in all begun pregnancies, thus including two patients with terminations in early gravidity (one termination due to extrauterine gravidity and one termination in the eighth week of gestation). Even when excluding these two cases from the overall abortion rate, this number would still be notably higher (53%). On the other hand, the pregnancy success rate after UAE is significantly higher in our cohort (50%) than the rate reported by Carpenter and Walker, where only 26 (33%) of 79 women conceived after embolization.

It is difficult to compare obstetrical results at the moment because only a small number of patients after embolization have passed the first trimester of pregnancy. The statistical analysis did not prove any significant differences in any of the parameters studied between the two groups, however, Table 6 provides an interesting summary of existing perinatal results and complications. It is remarkable to point out that, provided a pregnant woman after UAE successfully passed the first trimester, we subsequently did not record any of the serious pregnancy complications (e.g., gestational hypertension, fetal growth retardation, malpresentation, or prematurity) repeatedly described in other trials [10, 12, 17].

At the beginning of this trial we asked ourselves the question whether the less invasive method of fibroid embolization in women with reproductive plans is as effective and safe as myomectomy. After more than 4 years of the trial duration it can be concluded that both methods are comparable in terms of technical success rate, safety, and symptomatic efficacy. UAE is a less invasive approach, but also, as it appears at this midterm following, it is less definitive if the aim is to maximally eradicate fibroids before gravidity. For a definitive case comparison of reproductive and perinatal results we need to analyze more patients who try to conceive after the procedures and use a longer follow-up. However, the existing results clearly indicate that myomectomy is a method with a greater chance of success in women who plan to get pregnant early after the procedure.

Acknowledgments The study was supported by a grant from the Internal Grant Agency (IGA) of the Ministry of Health of the Czech Republic (NR/8099-3). The authors wish to thank Mrs. Alena Dohnalova for statistical consultations and analysis of the results, Pavel Dundr, M.D., for histopathological examinations of all excised myomas, and Petr Kriz, M.D., for pain management of all treated patients.

References

- Ravina JH, Herbreteau D, Ciraru-Vigneron N, et al. (1995) Arterial embolization to treat uterine myomata. *Lancet* 346:671–672
- Payne JF, Robboy SJ, Haney AF (2002) Embolic microspheres within ovarian arterial vasculature after uterine artery embolization. *Obstet Gynecol* 100:883–886
- Stringer NH, Grant T, Park J, et al. (2000) Ovarian failure after uterine artery embolization for treatment of myomas. *J Am Assoc Gynecol Laparosc* 7:395–400
- Vashisht A, Studd JW, Carey AH, et al. (2000) Fibroid embolization: a technique not without significant complications. *Br J Obstet Gynaecol* 107:1166–1170
- Olive DL, Lindheim SR, Pritts EA (2004) Non-surgical management of leiomyoma: impact on fertility. *Curr Opin Obstet Gynecol* 16:239–243
- Mara M, Fucikova Z, Maskova J, et al. (2006) Uterine fibroid embolization versus myomectomy in women wishing to preserve fertility: preliminary results of a randomized controlled trial. *Eur J Obstet Gynecol Reprod* 126:226–233
- Razavi MK, Wolanske KA, Hwang G, et al. (2002) Angiographic classification of ovarian artery to uterine artery anastomoses: initial observations in uterine fibroid embolization. *Radiology* 224:707–712
- Pelage JP, Le Dref O, Beregi JP, et al. (2003) Limited uterine artery embolization with tris-acryl gelatin microspheres for uterine fibroids. *J Vasc Interv Radiol* 14:15–20
- Fauconnier A, Pelage JP, Lacombe P, et al. (2004) Embolization of uterine fibroids and infertility: Is a clinical trial conceivable? *Gynecol Obstet Fertil* 32:818–24
- Carpenter TT, Walker WJ (2005) Pregnancy following uterine artery embolisation for symptomatic fibroids: a series of 26 completed pregnancies. *Br J Obstet Gynaecol* 112:321–325
- McLucas B, Goodwin S, Adler L, et al. (2001) Pregnancy following uterine fibroid embolization. *Int J Gynaecol Obstet* 74:1–7
- Pron G, Mocarski E, Bennett J, et al. (2005) Pregnancy after uterine artery embolization for leiomyomata: the Ontario multicenter trial. *Obstet Gynecol* 105:67–76
- Ravina JH, Vigneron NC, Aymard A, et al. (2000) Pregnancy after embolization of uterine myoma: report of 12 cases. *Fertil Steril* 73:1241–1243
- Walker WJ, Pelage JP (2002) Uterine artery embolization for symptomatic fibroids: clinical results in 400 women with imaging follow up. *Br J Obstet Gynecol* 109:1262–1272
- Kim MD, Kim NK, Kim HJ, et al. (2005) Pregnancy following uterine artery embolization with polyvinyl alcohol particles for patients with uterine fibroid or adenomyosis. *CardioVasc Interv Radiol* 28:611–615
- Broder MS, Goodwin S, Chen G, et al. (2002) Comparison of long-term outcomes of myomectomy and uterine artery embolization. *Obstet Gynecol* 100:864–868
- Goldberg J, Pereira L, Berghella V, et al. (2004) Pregnancy outcomes after treatment for fibromyomata: uterine artery embolization versus laparoscopic myomectomy. *Am J Obstet Gynecol* 191:18–21
- Razavi MK, Hwang G, Jahed A, et al. (2003) Abdominal myomectomy versus uterine fibroid embolization in the treatment of symptomatic uterine leiomyomas. *AJR* 180:1571–1575
- Siskin GP, Shlansky-Goldberg RD, Goodwin SC, et al. (2006) A prospective multicenter comparative study between myomectomy and uterine artery embolization with polyvinyl alcohol microspheres: long-term clinical outcomes in patients with symptomatic uterine fibroids. *J Vasc Interv Radiol* 17:1287–1295
- Goldberg J, Bussard A, McNeil J, et al. (2007) Cost and reimbursement for three fibroid treatments: abdominal hysterectomy, abdominal myomectomy, and uterine fibroid embolization. *CardioVasc Interv Radiol* 30:54–58
- Dubuisson JB, Fauconnier A, Fourchette V, et al. (2001) Laparoscopic myomectomy: predicting the risk of conversion to an open procedure. *Hum Reprod* 16:1726–1731
- Seracchioli R, Rossi S, Govoni F, et al. (2000) Fertility and obstetric outcome after laparoscopic myomectomy of large

- myomata: a randomized comparison with abdominal myomectomy. *Hum Reprod* 15:2663–2668
23. Pron G, Bennett J, Common A, et al. (2003) Technical results and effects of operator experience on uterine artery embolization for fibroids: the Ontario Uterine Fibroid Embolization Trial. *J Vasc Interv Radiol* 14:545–554
 24. Kröncke TJ, Gauruder-Burmester A, Gronewold M, et al. (2004) Technical success rate, peri-interventional complications and radiation exposure of the transarterial embolization for leiomyomas of the uterus. *Rofo* 176:580–589
 25. Volkers NA, Hehenkamp WJ, Birnie E, et al. (2006) Uterine artery embolization in the treatment of symptomatic uterine fibroid tumors (EMMY trial): periprocedural results and complications. *J Vasc Interv Radiol* 17:471–480
 26. Honda I, Sato T, Adachi H, et al. (2003) Uterine artery embolization for leiomyoma: complications and effect on fertility. *Nippon Igaku Hoshasen Gakkai Zasshi* 63:294–302
 27. Tropeano G, Litwicka K, Di Stasi C, et al. (2003) Permanent amenorrhea associated with endometrial atrophy after uterine artery embolization for symptomatic uterine fibroids. *Fertil Steril* 79:132–135
 28. Tulandi T, Sammour A, Valenti D, et al. (2002) Ovarian reserve after uterine artery Embolization for leiomyomata. *Fertil Steril* 78:197–198