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Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids (EMMY trial): Peri- and postprocedural results from a randomized controlled trial

Wouter J. K. Hehenkamp, MD,[a,*] Nicole A. Volkers, MD,[b] Peter F. J. Donderwinkel, MD,[c] Sjoerd de Blok, MD, PhD,[e] Erwin Birnie, PhD,[d] Willem M. Ankum, MD, PhD,[a] Jim A. Reekers, MD, PhD[b]

Department of Gynecology,[a] Department of Radiology,[b] Department of Public Health Epidemiology,[d] Academic Medical Center, Amsterdam, The Netherlands; Department of Gynecology,[c] Martini Hospital, Groningen, The Netherlands; Department of Gynecology,[e] Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

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KEY WORDS
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Objective: This was a randomized controlled trial to evaluate the safety of uterine artery embolization (UAE) compared with hysterectomy.

Study design: Twenty-eight Dutch hospitals recruited 177 patients with symptomatic uterine fibroids and menorrhagia who were eligible for hysterectomy. Patients were randomized to UAE (n = 88) or hysterectomy (n = 89). In this paper we evaluate the peri- and postprocedural complications, length of hospital stay, unscheduled visits, and readmission rates up to 6 weeks' post-intervention. Analysis was by intention to treat.

Results: Bilateral UAE failure occurred in 4 patients (4.9%). Major complications occurred in 4.9% (UAE) and 2.7% (hysterectomy) of cases ($P = .68$). The minor complication rate from discharge until 6 weeks after was significantly higher in the UAE group than in the hysterectomy group (58.0% vs 40.0%; RR 1.45 [1.04-2.02]; $P = .024$). UAE patients were more often readmitted (11.1% vs 0%; $P = .003$). Total length of hospital stay was significantly shorter in UAE patients (mean [SD]: 2.5 [2.7] vs 5.1 [1.3], $P < .001$).

Conclusion: UAE is a procedure similar to hysterectomy with a low major complication rate and with a reduced length of hospital stay. Higher readmission rates after UAE stress the need for careful postprocedural follow-up.

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Drs Hehenkamp and Volkers contributed equally to this paper.

* Reprint requests: W. J. K. Hehenkamp, MD, Academic Medical Center, Department of Gynecology, Meibergdreef 9; 1105 AZ Amsterdam, The Netherlands.

E-mail: w.j.k.hehenkamp@amc.uva.nl

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Uterine artery embolization (UAE) for the treatment of heavy menstrual bleeding caused by uterine fibroids was first described in 1995.[1] Since then, several large case series have been published describing the risks and benefits of UAE.[2-6] These reports suggest that UAE may have advantages over surgery, but are hampered by the inclusion of patients with strong treatment preferences and the lack of a control group. Obviously, this seriously affects the validity and generalizability of their results.

To evaluate the safety and efficacy of UAE in comparison to the standard treatment, ie, hysterectomy, we initiated a prospective, multicenter, randomized controlled trial comparing UAE with hysterectomy for the treatment of menorrhagia caused by uterine fibroids. In the trial, patients were followed until 2 years after the intervention. In this report, we present the baseline and procedural characteristics, peri- and postprocedural complications, duration of hospital stay, unscheduled visits, and readmissions up to 6 weeks' post-intervention.

Material and methods

Study design

The EMbolization versus hysterectoMY (EMMY) study is a multicenter, randomized controlled trial, conducted in The Netherlands. Five university hospitals and 29 general hospitals participated in the trial.

Patients visiting the gynecologic outpatient clinics were asked to participate if they met the following criteria: 1) the clinical diagnosis of uterine fibroids had been confirmed by ultrasonography; 2) menorrhagia (subjectively reported by the patient as increased or prolonged menstrual blood loss which causes dysfunction in daily life) was their predominant complaint, among other possibly fibroid-related signs and symptoms; 3) they were premenopausal; and 4) they were to be scheduled for a hysterectomy. Whenever other treatment options were still available, women were not asked to participate, but were treated otherwise.

Women were excluded if: 1) preservation of the uterus was warranted for future pregnancy; 2) renal failure (creatinine >150 mmol/L), active pelvic infection, or clotting disorders were clinically established; 3) they were allergic to contrast material; 4) uterine malignancy was suspected; 5) submucosal fibroids with 50% of their diameter within the uterine cavity or dominant pedunculated serosal fibroids were present.

After written informed consent had been obtained the attending gynecologist contacted the trial bureau by telephone, where the patient was registered and randomly assigned (1:1) to UAE or hysterectomy, using a computer-based minimization scheme ('balancing procedure'), and stratified for study center. The randomization result was recorded electronically.

According to Dutch guidelines, the study was approved by the Central Committee Involving Human Subjects (www.ccmo.nl) and by local ethics committees of participating hospitals.

Preassessment

All clinical data were prospectively recorded in a standardized case record form during the entire study period. All patients underwent a pelvic ultrasound either transvaginally or transabdominally. The uterus and the largest fibroid were measured in 3 dimensions, ie, longitudinal (D1), anterior-posterior (D2), and transverse (D3). Volumes were calculated using the formula $(0.5233 \times D1 \times D2 \times D3)$.[7]

Procedures

Uterine artery embolization

Patients were advised to discontinue any GnRH analogues treatment at least 1 month before the UAE.[8,9]

UAE was performed in all participating hospitals. The first 2 to 3 procedures were supervised by an interventional radiologist (J.R.) with ample experience in UAE. All radiologists were experienced in intervention radiology, including various embolization techniques in general. At the start of the study UAE was not a routine procedure for all radiologists. Seven radiologists were considered experienced in UAE group (having performed >10 UAE procedures), and 19 interventional radiologists had less experience in UAE (having performed <10 UAE procedures). Patients received an intravenous line and a Foley catheter before UAE. UAE was performed under local or epidural/spinal anesthesia. The use of analgesics and antibiotics was not standardized. Femoral artery access could be unilateral or bilateral. A 4-F or 5-F catheter was introduced into the femoral artery and advanced over the aortic bifurcation to the contralateral internal iliac artery to identify the origin of the uterine artery. In case of spasm, the policy was to wait, but a microcatheter and/or spasmolytics could be used within the study protocol. When catheters were placed correctly, the actual embolization was carried out. Polyvinyl alcohol particles (PVA, Contour, Boston Scientific, Beek, The Netherlands) with a size of 355 to 500 μm, were used. Only if an anastomosis with the ovarian artery was observed were 500 to 700 μm particles used. PVA, mixed with contrast medium and saline, was injected into each uterine artery until parenchyma filling of the fibroids had stopped (target embolization), or until the main uterine artery was blocked with stasis of contrast (selective embolization). After the procedure, groin pressure was applied for 10 to 15 minutes.

According to the Cardiovascular and Interventional Radiology Society of Europe guidelines, UAE was

considered successful whenever bilateral UAE was established; unilateral UAE was only considered a successful procedure if single-sided uterine arterial flow to the fibroids was present.[10]

If a uterine artery was absent and flow to the fibroids came solely from the ovarian artery, the procedure was stopped because of risk for ovarian damage, and considered unsuccessful. Also, in case of extensive collaterals to the cervix and vaginal wall, the procedure was stopped and considered unsuccessful.

Unsuccessful procedures may not always result from the technical inability to selectively catheterize the uterine artery. Therefore, we also calculated the true technical failure rate as the total number of arteries that could be embolized (ie, arteries were present without extensive collaterals with the cervico-vaginal vascular system), but which were not embolized because of technical inabilities to do so.

The type of anesthesia, type of UAE, the amount of PVA vials used, the amount of blood loss, the procedural complications, and the duration of the procedure were recorded. After the procedure, women were admitted to the gynecology ward for further care. All patients were advised to stay in hospital for at least 1 night. At discharge, all patients were no longer using opiates and received clear instructions on pain medication regiments. They also received written instruction with contact numbers to contact their gynecologist whenever uncontrollable pain, persistent fever, or expulsion of fibroids occurred.

Hysterectomy

The type of hysterectomy and the route of access were left at the discretion of the attending gynecologist in order to keep as close to daily practice as possible. The following procedures were allowed: abdominal hysterectomy, either by median or a pfannenstiel incision, vaginal hysterectomy, laparoscopically assisted vaginal hysterectomy (LAVH), and laparoscopic hysterectomy. Both supravaginal and total hysterectomies were allowed. We used no guidelines for: antibiotic prophylaxis; type of anesthesia; removal or ablation of endocervical tissue in the supravaginal hysterectomy group; concomitant adnexal surgery; wound closure; evaluation and treatment of fever; or hospital discharge criteria. Prospectively recorded were: prescription of antibiotics, type of anesthesia, type of hysterectomy, removal of the cervix, ovaries, or other procedures, complications, blood loss, and duration of procedure. At discharge, patients were instructed in a similar fashion as for the UAE patients.

Follow-up

Complications were classified as "major" when the events were potentially life-threatening, could lead to permanent sequelae, or required surgical intervention. Other complications were listed as "minor." Nausea, pain, and fever were considered "general" complications. Whenever a definite cause of fever was identified (eg, urinary tract infection), this was listed under minor or major complications, using the criteria described above.

Complications were separately listed for 2 time intervals: the hospitalization period (ie, occurring during and after the procedure) and the first 6 weeks thereafter (ie, between discharge and first routine visit at 6 weeks after the procedure). Complication rates were expressed as the occurrence of at least 1 complication within a patient and calculated for minor and major complications separately in both time intervals and overall.

All UAE patients were routinely telephoned by the gynecologist 1 week after discharge to inquire about their health status.

At the first routine visit (6 weeks after the procedure), complications after discharge, unscheduled visits, readmissions, and reinterventions were recorded.

Sample size and end points

The primary end point of this trial was the elimination of menorrhagia after a follow-up period of 2 years. UAE was considered equivalent to hysterectomy when menorrhagia resolved in at least 75% of patients,[11,12] with preservation of the uterus and no significant differences in major complications between both procedures. To reject the null hypothesis that UAE and hysterectomy are not clinically equivalent (expected effectiveness of UAE = 0.875[13-16]; expected effectiveness of hysterectomy = 0.999; threshold value $\Delta = 0.25$; $\alpha = 0.05$ (one-sided); $1\text{-}\beta = 0.90$), at least 2×60 ($=120$) analyzable patients had to be included.

The objective of the present study was to compare the following end points between both interventions: technical failures, procedure safety, complications, duration of hospital stay (discharge date minus procedure date), and the occurrence of unscheduled visits, readmissions, and reinterventions. For this analysis, no separate power calculation was made.

Statistical analysis

All data entries were visually double checked by an independent second investigator. Analyses were done using SPSS statistical software (version 11.5.1, Chicago, IL).

Study outcomes were analyzed according to original treatment assignment (intention to treat). Differences in baseline characteristics were tested with multiple logistic regression analysis. Differences in complications between groups were expressed in absolute numbers, rates, and relative risks (RR) with 95% CI. Confidence intervals were calculated with Statcalc (EpiInfo version 5, Centers for Disease Control and Prevention, Atlanta, GA). Differences in hospital stay were tested with the

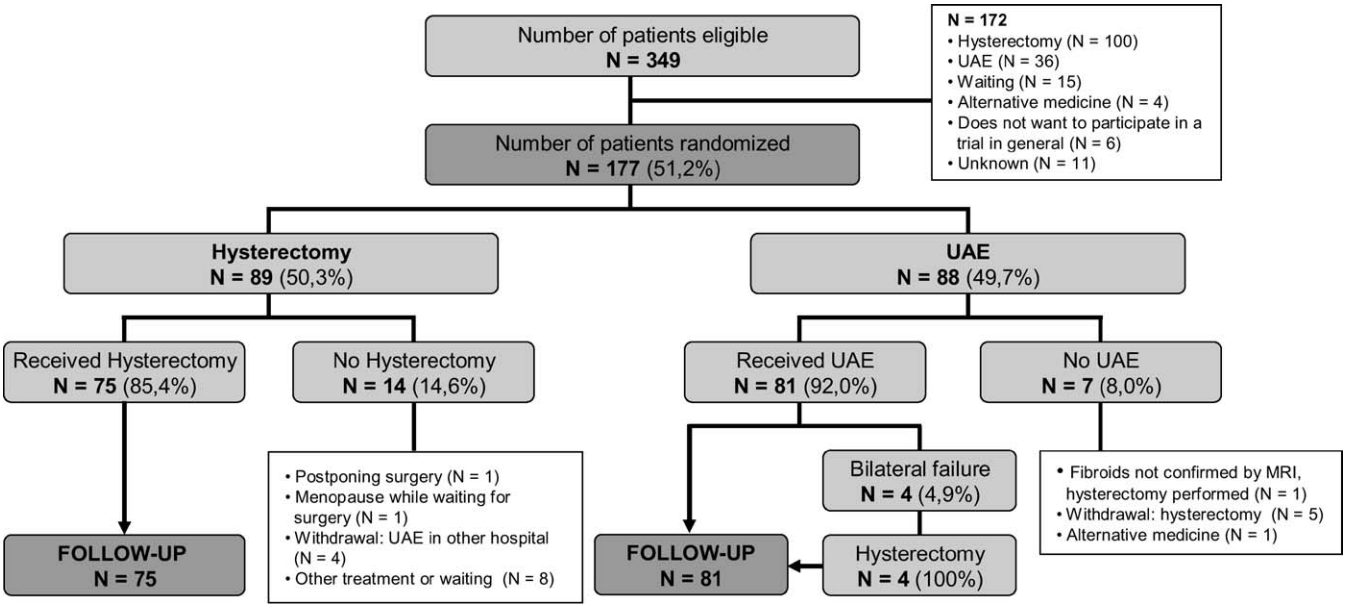

Figure Trial profile.

Mann-Whitney *U* test. Differences in categorical data were compared with χ^2-tests or Fisher exact tests if appropriate. We also investigated the effect of experience of the radiologist and hospitals perfoming UAE on technical failure, complications, and readmissions. A *P* value of $< .05$ was considered statistically significant.

Results

Patients

Patients were enrolled between March 2002 and February 2004. Twenty-eight of the 34 participating hospitals included patients. Of 349 eligible patients, 177 were randomized: 88 were allocated UAE and 89 hysterectomy (Figure). The majority of patients refusing participation did so for a strong preference for hysterectomy (58%) or for UAE (21%). After randomization 7 patients in the UAE group and 14 patients in the hysterectomy group refused the allocated treatment. Patients who refused the assigned treatment were comparable to participating patients in terms of: age, race, BMI, parity, symptoms, and duration of symptoms (data not shown). The mean age was 44.6 years (UAE group) and 45.4 years (hysterectomy group). Participants were predominantly white: 61.4% and 64.0% for UAE and hysterectomy respectively (Table I). Table II shows that most patients (85.3%) had already received 1 or more treatments for symptomatic uterine fibroids before study enrollment. Patients suffered from menorrhagia for a median of 24 months. Other symptoms besides menorrhagia were prevalent. The majority of women had multiple fibroids. Fibroid volumes were higher in the hysterectomy group. Logistic regression analysis did not reveal baseline characteristics that could predict randomization outcome, confirming successful randomization.

Procedures

UAE was successfully performed in 72 of 81 patients, 5 of whom had a unilateral procedure because of single-sided arterial blood flow to the fibroid (procedural success rate: 88.9%). The remaining 11.1% consisted of 5 patients (6.2%) with a unilateral procedure (caused by technical failure on the other side) and 4 patients (4.9%) with bilateral unsuccessful UAE. The bilateral impossibility to embolize resulted from bilateral absence of uterine artery flow to the fibroids (n = 2), bilateral technical failures (n = 1), and extensive anastomoses with the cervix/vagina on 1 side and a technical failure on the other (n = 1). These 4 patients subsequently underwent hysterectomy, but were analyzed in the UAE group. The total number of arteries that could potentially be embolized in the 88 UAE patients was 152. Of these, 8 arteries were not embolized because of technical inability (technical failure rate: 5.3%).

Table III displays the characteristics of both treatments. In most cases (86.1%), target embolization was carried out. For technically successful UAE, a median of 1 vial (range 0.1-3) of PVA was used for each artery.

In the hysterectomy group, all operations were technically successful. Four conversions took place: 3 procedures (1 LAVH, 1 vaginal, and 1 laparoscopic hysterectomy) were converted to a laparotomy. In 1 abdominal hysterectomy, the cervix could not be removed

Table I Baseline characteristics: patient demographics

	UAE (n = 88) No. (%)	Hysterectomy (n = 89) No. (%)
Age (y)		
< 35	1 (1.1)	0 (0)
35-40	17 (19.3)	9 (10.1)
40-45	28 (31.8)	29 (32.6)
45-50	33 (37.5)	40 (44.9)
>50	9 (10.2)	11 (12.4)
Mean (SD)	44.6 (4.8)	45.4 (4.2)
Body mass index (weight [kg]/length [m^2])		
<18.5	2 (2.3)	0 (0)
18.5-24.9	33 (37.5)	44 (50)
25-29.9	32 (36.4)	34 (38.6)
>30	21 (23.9)	10 (11.4)
Mean (SD)	26.7 (5.6)	25.4 (4.0)
Parity		
0	30 (34.1)	20 (22.5)
≥1	58 (65.9)	69 (77.5)
Ethnicity		
Black	24 (27.3)	20 (22.5)
White	54 (61.4)	57 (64.0)
Other	10 (11.4)	12 (13.5)
Marital status		
Single	16 (18.2)	13 (14.8)
Married	55 (62.5)	54 (61.4)
Living apart together	5 (5.7)	4 (4.5)
Divorced	12 (13.6)	15 (17.0)
Widow	0 (0)	2 (2.3)
Employment status		
Employed	68 (77.3)	69 (78.4)
Unemployed	20 (22.7)	19 (21.6)
Smoking status		
Current smoker	21 (23.9)	23 (25.8)
Former smoker	11 (12.5)	14 (15.7)
Nonsmoker	56 (63.6)	52 (58.4)
Highest educational level*		
Elementary school	3 (3.4)	6 (6.9)
Lower vocational, lower secondary school	29 (33.0)	32 (36.8)
Intermediate and higher vocational, higher secondary school	26 (29.5)	27 (31.0)
College/University	28 (31.8)	22 (25.3)
Other	2 (2.3)	0 (0)

Data were available for all or all but 1 patient, unless stated otherwise. Logistic regression analysis did not reveal baseline characteristics that could predict randomization outcome.

* Missing: 2

as planned because of adhesions, and a supravaginal hysterectomy was carried out instead. Furthermore, in 1 vaginal hysterectomy, morcellation was necessary for a large fibroid. Most hysterectomies were performed transabdominally (84.0%).

UAE procedures on average took shorter than hysterectomy procedures (79.0 vs 95.4 minutes, $P = .007$). Patients subject to UAE had significantly less blood loss than those undergoing hysterectomy (30.9 and 436.1 mL, respectively; $P < .001$). Total admission time was significantly ($P < .001$) shorter in the UAE group (mean 2.0 days; SD 2.1; range 0-13 days) than in the hysterectomy group (mean 5.1 days; SD 1.3; range 2-8 days).

Complications during hospital stay

Table IV lists complications occurring during and after the procedures.

Intraprocedural complications were uncommon in both groups. In the UAE group, 7 minor complications occurred: 5 postpuncture hematomas, 1 blood clot in the gluteal artery, which resolved spontaneously, and 1 case of nausea during the procedure. In the hysterectomy group, 2 minor complications occurred: 1 allergic reaction to an anesthetic agent and 1 small tear in the rectus muscle.

During hospital stay febrile morbidity was significantly less common in the UAE group (4.9%) than after hysterectomy (20.0%; $P = .006$; RR 0.25; 95%CI 0.09-0.72). Postintervention fever occurred less frequently in patients who received antibiotics for both the hysterectomy (16.4% vs 50.0%; $P = .046$; RR 0.33; 95%CI 0.14-0.79) and UAE group (3.4% vs 5.8%; $P = .99$ (FE); RR 0.60; 95%CI 0.07-5.49).

Hematomas occurred significantly more frequently after UAE, while the hysterectomy group experienced more urinary tract infections and urinary retention. No patients in the UAE group required a blood transfusion, compared with 10 patients (13.3%) in the hysterectomy group. The minor complication rates were 22.2% (95%CI 13.7-32.8) in the UAE group and 30.7% (95%CI 20.5-42.4) in the hysterectomy group (RR 0.72; 95%CI 0.43-1.23; $P = .23$). Major complications were rare and concerned 2 cases of pulmonary embolisms, 1 in each group. The major complication rate was 1.2% (95%CI 0.03-7.2) and 1.3% (95%CI 0.03-7.2) for UAE and hysterectomy respectively (RR 0.93; 95%CI 0.06-14.54; $P = .99$). Both minor and major complication rates did not differ significantly between the 2 groups.

Follow-up

Table V describes the unscheduled visits within the first 6 weeks after discharge. In the UAE group, 30 patients (37.0% with a total of 46 visits) consulted a physician, mainly for pain and/or fever. In the hysterectomy group, 19 patients (25.3% with a total of 24 visits) consulted a physician after discharge for various reasons. This difference was not significant (RR 1.45; 95%CI 0.90-2.37, $P = .12$).

Readmissions (Table VI) were significantly more common in the UAE group: 9 patients versus 0 patients in the hysterectomy group ($P = .0032$). In the UAE

Table II Baseline characteristics: symptoms, previous treatment and uterus/fibroid characteristics

	UAE (n = 88) No. (%)	Hysterectomy (n = 89) No. (%)
Previous treatment		
None	11 (12.5)	15 (16.9)
Hormonal	59 (67.0)	59 (66.3)
Nonsteroidal anti-inflammatory drugs/tranexaminacid	45 (51.1)	41 (46.1)
Iron-supplement/blood transfusion	50 (56.8)	52 (58.4)
Surgical procedures*	17 (19.3)	11 (12.4)
Hysteroscopic myomectomy	6 (6.8)	8 (9.0)
Laparoscopic myomectomy	0 (0)	3 (3.4)
Laparotomic myomectomy	7 (8.0)	2 (2.2)
Hysteroscopic endometrium resection	3 (3.4)	1(1.1)
Curettage	3 (3.4)	0 (0)
Symptoms		
Menorrhagia	88 (100)	89 (100)
Dysmenorrhea	47 (53.4)	50 (56.2)
Pain (not during menstruation)	15 (17.0)	14 (15.7)
Urinary symptoms	13 (14.8)	20 (22.5)
Defecation problems	5 (5.7)	5 (5.6)
Anemia	43 (48.9)	42 (47.2)
Pressure symptoms	23 (26.1)	25 (28.1)
Other symptoms	6 (6.8)	11 (12.4)
Duration of symptoms (m)		
Median (range)	24 (3-250)	24 (4-240)
Duration of menstruation (d)		
Total days (median, range)	7 (4-28)	8 (3-42)
Heavy days (median, range)	3 (1-28)	4 (1-21)
Number of fibroids†		
1	35 (39.8)	25 (28.1)
2	13 (14.8)	16 (18.0)
3	17 (19.3)	25 (25.8)
>3	18 (20.5)	14 (15.7)
Median (range)	2 (1-20)	2 (1-9)
Uterine volume (cm^3)‡,‖		
0-250	33 (37.9)	26 (32.5)
251-500	26 (29.9)	30 (37.5)
501-1000	19 (21.8)	16 (20.0)
>1000	9 (10.3)	8 (10.0)
Median (range)	321 (31-3005)	313 (58-3617)
Fibroid volume (dominant fibroid, cm^3)§,¶		
0-100	55 (63.2)	41 (52.6)
101-200	14 (16.1)	20 (25.6)
201-400	11 (12.6)	12 (15.4)
>400	7 (8.9)	5 (6.4)
Median (range)	59 (1-673)	87 (4-1641)

Number of fibroids and uterine/fibroid volume were calculated by ultrasound unless stated otherwise. Data were available for all or all but 1 patient, unless stated otherwise. Logistic regression analysis did not reveal baseline characteristics that could predict randomization outcome.

* The surgical treatments do not add up because some patients had several treatments.

† UAE missing: 5, hysterectomy missing: 11.

‡ UAE missing: 1, hysterectomy missing: 9.

§ UAE missing: 1, hysterectomy missing: 11.

‖ MRI measurements were used in 5 patients.

¶ 1 patient in the UAE group because of missing ultrasound data.

group, 7 of the 9 (77.8%) readmissions occurred within the first week after discharge from the hospital. Patients were readmitted for pain (22.2%), fever (22.2%), or a combination of both (44.4%). One patient (11.1%) was readmitted for expulsion of a necrotic fibroid. Hysteroscopic removal was attempted, but failed because of cervical dilation which interfered with uterine dilatation. Antibiotics were administered intravenously and the

Table III Procedural characteristics

	UAE (n = 81) No.	Hysterectomy (n = 75) No.
Type of UAE		
Target embolization*		
Left uterine artery	65	–
Right uterine artery	59	–
Selective embolization*		
Left uterine artery	8	–
Right uterine artery	12	–
Type of hysterectomy	**(n = 4)**	
Abdominal hysterectomy	**(2)**	63
Pfannenstiel incision	**(1)**	50
Median incision	**(1)**	13
Vaginal hysterectomy	**(1)**	8
Vaginal hysterectomy with morcellator	**(1)**	1
LH with morcellator	–	2
LAVH	–	1
Cervix		
Conservation of cervix	**(2)**	22
Other procedures		
Removal of hydrosalpinx	–	1
Adhesiolysis	**(1)**	–
Salpingo-oophorectomy		
Unilateral	**(1)**	2
Bilateral	–	1
Anesthesia		
Local	71	–
Epidural	9	1
Spinal	1 **(+1)**	3
General anesthesia	**(2)**	52
General and epidural	**(1)**	17
General and spinal	–	2
Duration of procedure (min)		
Mean (SD)	79 (30.5)†; **(109 (59.2))**	95.4 (30,9)†
Median (range)	75 (30-165); **(90 (60-195))**	90 (45-175)
Blood loss (mL)		
Mean (SD)	30.9 (23.8)‡; **(1000 (823.6))**	436.1 (474.5)‡
Median (range)	20 (5-150); **(850 (300-2000))**	300 (10-2500)
Antibiotics		
Antibiotics administered	29 (35.8%); **(4 (100.0%))**	67 (89.3%)

Abbreviations: *LAVH*, Laparoscopic-assisted vaginal hysterectomy; *LH*, laparoscopic hysterectomy. Characteristics of hysterectomies performed after bilaterally failed embolizations are presented in **(bold)** in the UAE column.

* For successful procedures.

† $P = .007$, compared with hysterectomy group.

‡ $P < .001$, compared with hysterectomy group.

patient stayed in the hospital until fever and pain had subsided. The mean admission time for UAE increased from 2.0 to 2.5 days (SD 2.7; range 0-16 days) as a result of readmissions, but remained significantly shorter compared with hysterectomy ($P < .001$).

Complications and symptoms between discharge from the hospital and the first routine visit at 6 weeks are shown in Table IV. UAE patients complained of vaginal discharge in 21.0% compared with 8.0% of the hysterectomy patients ($P = .022$). A percentage (14.8%) of UAE patients experienced vaginal loss of fibroid tissue. Hot flashes were present in 19.8% (UAE) and 20.0% (hysterectomy) of patients. Four cases of pain and/or fever that required readmission were classified as minor complications because the definition of major complications which we used (as described in the methods section) did not apply here.

Three patients (3.7%) in the UAE group had major complications: pneumonia in a patient with a history of recurrent pneumonia caused by asthmatic disease (n = 1); reintervention because of an incomplete fibroid expulsion (n = 1); and septicemia (n = 1). One patient (1.3%) in the hysterectomy group was diagnosed with a vesicovaginal fistula, which was surgically repaired beyond the 6 weeks' follow-up period (not reported in Table VI).

The minor complication rate in the first 6 weeks after discharge was significantly higher in the UAE group than in the hysterectomy group: 58.0% (95%CI 46.5-68.9) and 40.0% (95%CI 28.9-52.0), respectively (RR 1.45; 95%CI 1.04-2.02; $P = .024$). The major complication rate in the first 6 weeks after discharge was 3.7% (95%CI 0.8-10.4) and 1.3% (95%CI 0.03-7.2) for UAE and hysterectomy, respectively (RR 2.78; 95%CI 0.30-26.13; $P = .62$), and did not differ significantly.

The overall minor complication rate (ie, from the procedure until the 6-week routine visit) was 64.2% (95%CI 52.8-74.6) (52 patients) in the UAE group compared with 56.0% (95%CI 44.1-67.4) (42 patients) in the hysterectomy group (RR 1.12; 95%CI 0.87-1.46; $P = .38$). The overall major complication rate was 4.9% (95%CI 1.4-12.2) (4 patients) in the UAE group compared with 2.7% (95%CI 0.3-9.3) (2 patients) in the hysterectomy group (RR 1.85; 95%CI 0.35-9.82; $P = .68$). Both findings were not statistically significant. Also, when only abdominal hysterectomies were compared with UAE, overall major and minor complication rates did not differ significantly ($P = .28$ and $P = .70$). The difference in hospitalization time remained statistically significant ($P < .001$). Radiologists' experience with UAE was not associated with the technical failure rate. Less experienced hospitals were not associated with higher complication or readmission rates.

Comment

Present knowledge on UAE derives from numerous uncontrolled case series and only 1 small pre-consent

Table IV Complications until the first scheduled visit (6 weeks after the procedure)

	Hospital stay			6 weeks after discharge		
	UAE[a] (n = 81)	Hyst. (n = 75)	Relative risk	UAE[b] (n = 81)	Hyst. (n = 75)	Relative risk
Complication	n	n	RR (95%CI)	n	n	RR (95%CI)
General						
Nausea	52	42	1.15 (0.89-1.48)	25	11	2.10 (1.11-3.97)[c]
Pain	72	71	0.94 (0.85-1.03)	57	52	1.01 (0.83-1.25)
Febrile morbidity (>38.5°C)	4	15	0.25 (0.09-0.71)	17	8	1.97 (0.90-4.29)
Minor complications						
Vaginal discharge	–	–	–	17	6	2.62 (1.09-6.30)[d]
Pain requiring readmission	–	–	–	2	–	N/A
Pain/fever requiring readmission	–	–	–	2	–	N/A
Fibroid expulsion not requiring reintervention	–	–	–	12	–	N/A
Hematoma	13	4	3.01 (1.03-8.82)[e]	3	2	1.39 (0.24-8.08)
Wound abscess	1[f]	0		0	1	·
Woundbleeding	1	1	0.93 (0.06-14.54)	–	–	–
Wound dehiscence	0	0		0	1	·
Urinary tract infection	0	3	·	5[g]	2	2.31 (0.46-11.57)
Urinary retention	0	3	·	1	1	0.93 (0.06-14.54)
Urinary incontinence	–	–	–	6	4	1.39 (0.41-4.73)
Endometritis	0	–	N/A	2	–	N/A
Hot flashes	–	–	–	16	15	0.99 (0.53-1.86)
Anemia requiring transfusion	0	10	·	–	–	–
Hypertension	7[h]	1	6.48 (0.82-51.45)	0	1	·
Hypotension	0	2	·	–	–	–
Other	1[i]	2[j]	0.46 (0.04-5.00)	2[k]	1[l]	–
Total	23 (in 18 patients)	26 (in 23 patients)	0.72 (0.43-1.23) *P* = .23	68 (in 47 patients)	34 (in 30 patients)	1.45 (1.04-2.02) *P* = .024
Major complications						
Pneumonia	0	0	·	1	0	·
Ileus	0	0	·	0	0	·
Thrombosis	0	0	·	0	0	·
Vesicovaginal fistula	–	–	–	0	1	·
Pulmonary embolism	1	1	0.93 (0.06-14.54)	0	0	·
Intra-abdominal infection	0	0	·	0	0	·
Sepsis	0	0	·	1[m]	0	·
Fibroid expulsion requiring re-intervention	0	0	·	1[n]	0	·
Death	0	0	·	0	0	
Total	1 (in 1 patient)	1 (in 1 patient)	0.93 (0.06-14.54) *P* = .99	3 (in 3 patients)	1 (in 1 patient)	2.78 (0.30-26.13) *P* = .62

N/A, Not applicable.

[a] The UAE group comprises both failed and successful embolizations.

[b] Complications of patients with hysterectomies after failed embolizations are described for the 6 weeks after discharge after their hysterectomy procedure.

[c] *P* = .016.

[d] *P* = .022.

[e] *P* = .03.

[f] Occurred in a hysterectomy performed after bilaterally failed UAE.

[g] Complication led to a readmission in 3 patients.

[h] Including 1 patient that was admitted to the medium care unit for extreme hypertension.

[i] Spontaneous blood clot in gluteal artery during procedure.

[j] Small tear of *m. rectus abdominis* during surgery, allergic reaction to anesthetic agent during surgery.

[k] Gout attack, liquor spill after epidural anesthesia.

[l] Headache after epidural anesthesia.

[m] Complication led to readmission in 1 patient.

[n] Readmission, attempt to remove necrotic fibroid hysteroscopically, which only partly succeeded.

Table V Unscheduled visits after discharge until first routine visit (6 weeks after procedure)

Contact	Symptom(s)	UAE (n = 81) Number of contacts	Hysterectomy (n = 76) Number of contacts
General physician	Pain	3	3
	Fever	5	0
	Vaginal bleeding	0	3
	Groin hematoma	1	0
	Constipation	0	2
	Blood pressure issues	1	2
	Other	3*	4†
	Total	13 (in 10 patients)	14 (in 12 patients)
Gynecologist	Fever	4	0
	Fever and pain	7	0
	Fever and vaginal bleeding	0	1
	Pain	12	2
	Pain and vaginal discharge	2	1
	Pain and vaginal bleeding	3	0
	Vaginal bleeding	0	3
	Vaginal discharge	2	0
	Wound dehiscence	0	2‡
	Other	0	1§
	Total	30 (in 22 patients)	10 (in 8 patients)
Lung specialist	Fever, dyspnea: pneumonia	3	0
	Total	3 (in 1 patient)	0
	Total number of visits	45	24
	Total number of patients	30‖	19

* Checking hemoglobin level; gout attack; sensitive breast.
† Coughing, dizzy, and constipation; stomach pain; urge incontinence complaints; vaginal itch.
‡ Same patient.
§ Severe hair loss.
‖ RR 1.45 (95%CI 0.90-2.37; $P = .12$), compared with number of patients in the hysterectomy group.

randomized trial of moderate quality.[17] According to the National Institute of Clinical Excellence (NICE), the limitations of the available literature only allow tentative conclusions about the safety and efficacy of UAE,[18] especially since highly selected patient inclusion and high loss to follow-up bias the results. NICE strongly recommends the initiation of randomized controlled trials, which is exactly what we did here.

We deliberately chose to compare UAE with hysterectomy, not with myomectomy,[19] for several reasons. First, hysterectomy is the standard procedure of choice to eliminate all fibroid-related complaints. In our view, myomectomy should be preserved for those women with symptomatic uterine fibroids with a strong desire for future pregnancy. Because UAE is considered to be contraindicated for women desiring pregnancy, a randomized comparison with myomectomy might even be considered unethical at this stage.[20] In the absence of randomized data, we judged it more ethical to perform a study at the other end of the clinical spectrum, ie, in women facing hysterectomy as the last resort for their fibroid-related complaints. Although hysterectomy is an absolute cure for menorrhagia, possible sequalae, eg, incontinence, vaginal vault prolapse, risk for premature ovarian failure, long recovery, high costs, and the desire of some patients to preserve their uterus, justify serious consideration of alternative therapies such as UAE. The procedural success rate (88.9%) was comparable to the results of the aforementioned small semi-randomized trial, but lower than the success rates reported in most other studies, thereby illustrating the necessity of randomized data collection.[17]

The technical failure rate (5.3%) was higher than the 0.5% to 2.5% reported in large case series,[2,3,5,21] but similar to the technical failure rate of 5.0% reported in the only semi-randomized trial,[17] because of several possible reasons. First, our study is a mix of both academic and nonteaching hospitals, whereas UAE in the reported case series was mostly performed in highly specialized single-centers, decreasing the generalizability of those results.[22] However, in our study, experience of the interventional radiologist was not associated with outcome. Moreover, one series performed a second embolization attempt after initial technical failure, which obviously improves technical success rates.[4] Generally, results from randomized controlled trials can

Table VI Readmissions after UAE until first routine visit (6 weeks after the procedure)

Reason for readmission	n	Course	Days after discharge	Length of stay
Fever	1	Antibiotics administered, urine and cervix cultures positive for *Streptococcus*	4	3
	1	Antibiotics administered for urinary tract infection	4	4
Fever and pain	1	Analgesics and antibiotics administered for urinary tract infection	3	5
	2	Analgesics and antibiotics administered, no definite diagnosis	3	2
			3	4
Pain	2	Analgesics administered	1	1
			4	1
Septicemia	1	MRI scan revealed an infectious process cranial in the uterus, which drained itself vaginally. Antibiotics and analgesics administered	51	11
Myoma nascens	1	Failed attempt to hysteroscopically remove necrotic tissue due to cervix dilation. Antibiotics and analgesics administered.	23	6

No hysterectomy patients were readmitted to the hospital.

substantially differ from those in case series because of publication bias and patient selection criteria.[23,24]

Mean hospital stay was significantly shorter for UAE than for hysterectomy. Mean hospital stay for UAE was longer than in some studies, but in our experience most patients need more care.[25,26] Therefore, we would not recommend performing UAE as an outpatient procedure. Surprisingly, the number of unscheduled visits was higher in the UAE group. Readmission rates after UAE within the first 6 weeks (11.1%) were higher compared with other reports (2.9%-5.0%), although the reasons for readmission were similar.[17,27] The experimental status of the UAE procedure could be the reason why physicians were more inclined to see patients and readmit them more quickly. Most readmissions in our study occurred within the first week after discharge (77.8%), underlining the need for adequate follow-up during this period. None of our hysterectomy patients were readmitted within the first 6 weeks, while Pinto et al found a readmission rate of 5.0% after hysterectomy.[17] Because most hysterectomy patients were still in the hospital when most readmissions in the UAE group occurred, the comparison is not completely fair: if UAE patients would stay in the hospital as long as hysterectomy patients, only 2 readmissions would have occurred.

Overall major and minor complication rates in both groups were comparable, but minor complications in the period between discharge and the first 6 weeks' visit were significantly higher in the UAE group. Our study, therefore, cannot support the suggestion made by others[28] that UAE has a lower complication rate than hysterectomy, again stressing the need for randomized studies. A detailed comparison of complication rates with other studies is hampered by the fact that various studies apply different classification systems for reporting complications. Major complications were rare in our study. Although many series reported emergency hysterectomy rates up to 1.3% within the first weeks after UAE, no such procedures occurred in our patients.[3,4,21,27]

There are several limitations to our study. First, 21 (11.9%) patients withdrew from the study after randomization before treatment. Their baseline characteristics, however, did not differ from those being treated. Second, given the low major complication rates, our study size was too small to detect any difference in major complication rates, and definite conclusions, therefore, cannot be drawn. In contrast, we did find differences in minor complication rates and length of hospital stay, so lack of power was not an issue here. We used no objective criteria for menorrhagia but relied on subjective appreciations of our patients. By doing so, the generalizability of our findings is probably enhanced: included patients represent those seen in daily practice where the decision to perform a hysterectomy is not based on objective measurements (eg, pictorial charts) either. We could not find any differences in major complication rates between UAE and hysterectomy. Unsuccessful UAE procedures, however, seem to occur more often than previously reported. Hospital stay is significantly shorter for UAE. The higher minor complication rate after discharge in the UAE group, as well as the readmission rates and unscheduled visits,

emphasize the necessity for careful follow-up and clear instructions to the patient. Although the study results are supportive for UAE, the question as to whether UAE is a good alternative for hysterectomy depends on the balance of efficacy, costs, and quality of life, and still remains to be answered.

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