

## GENERAL GYNECOLOGY

# Uterine artery embolization vs hysterectomy in the treatment of symptomatic uterine fibroids: 5-year outcome from the randomized EMMY trial

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**OBJECTIVE:** The purpose of this study was to compare clinical outcome and health related quality of life (HRQOL) 5 years after uterine artery embolization (UAE) or hysterectomy in the treatment of menorrhagia caused by uterine fibroids.

**STUDY DESIGN:** Patients with symptomatic uterine fibroids who were eligible for hysterectomy were assigned randomly 1:1 to hysterectomy or UAE. Endpoints after 5 years were reintervention rates, menorrhagia, and HRQOL measures that were assessed by validated questionnaires.

**RESULTS:** Patients were assigned randomly to UAE (n = 88) or hysterectomy (n = 89). Five years after treatment 23 of 81 UAE patients

(28.4%) had undergone a hysterectomy because of insufficient improvement of complaints (24.7% after successful UAE). HRQOL measures improved significantly and remained stable until the 5-year follow-up evaluation, with no differences between the groups. UAE had a positive effect both on urinary and defecation function.

**CONCLUSION:** UAE is a well-established alternative to hysterectomy about which patients should be counseled.

**Key words:** fibroid tumor, hysterectomy, menorrhagia, uterine artery embolization

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Symptomatic uterine fibroids are disabling and are associated with significant morbidity that affects approximately 20-40% of women of childbearing age.<sup>1</sup> The most common symptom of uterine fibroids for which treatment is sought is heavy or prolonged menstrual bleeding, which may result in iron deficiency anemia.<sup>2</sup> When symptoms progress and pharmacotherapeutic options fail, surgical intervention may be necessary. During the last decade, uterine artery embolization (UAE) has been greeted as a minimally invasive treatment alterna-

tive for surgery in the reduction of symptoms of heavy menstrual bleedings caused by fibroids. Several randomized controlled trials compared UAE with hysterectomy and/or myomectomy and found similarly good results for both interventions up to 24 months of follow up.<sup>3-6</sup> Earlier, we reported on the 2-year results from the embolization vs hysterectomy (EMMY) trial and compared clinical results,<sup>7</sup> health-related quality of life (HRQOL) outcomes,<sup>8</sup> and menopausal symptoms<sup>9</sup> between UAE and hysterectomy. After 2 years the chance

to avoid a hysterectomy in the UAE group was 76.5% while menorrhagia and HRQOL improved significantly, similarly in both groups. Both UAE and hysterectomy affected ovarian reserve in women >45 years old. Based on these 2-year follow-up results, UAE was considered to be a good alternative to hysterectomy. Because fibroids may grow back, menorrhagia can recur, or other symptoms that warrant hysterectomy may emerge beyond the 2-years of follow-up period. Therefore, we observed our cohort until 5 years after treatment and investigated clinical and HRQOL results between UAE and hysterectomy as well as outcomes between baseline and 5-year follow-up in patients from the EMMY trial.

## MATERIALS AND METHODS

### Study design

The EMMY study is a multicenter, randomized controlled trial, that was conducted in The Netherlands. Patients who visited the gynecologic outpatient clinics were invited to participate if they (1) were premenopausal, (2) were diagnosed with uterine fibroids, (3) had

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**TABLE 1**  
**Baseline and procedural characteristics**

Variable	Uterine artery embolization (n = 88)	Hysterectomy (n = 89)
Age, y <sup>a</sup>	44.6 ± 4.8	45.4 ± 4.2
Body mass index, kg/m <sup>2a</sup>	26.7 ± 5.6	25.4 ± 4.0
Parity, n (%)		
0	30 (34.1)	20 (22.5)
≥1	58 (65.9)	69 (77.5)
Ethnicity, n (%)		
Black	24 (27.3)	20 (22.5)
White	54 (61.4)	57 (64.0)
Other	10 (11.4)	12 (13.5)
Marital status, n (%)		
Single	16 (18.2)	13 (14.8)
Married	55 (62.5)	54 (61.4)
Together but living apart	5 (5.7)	4 (4.5)
Divorced	12 (13.6)	15 (17.0)
Widow	0	2 (2.3)
Employment status, n (%)		
Employed	68 (77.3)	69 (78.4)
Unemployed	20 (22.7)	19 (21.6)
Smoking status, n (%)		
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, n (%)		
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
Previous treatment, n (%)		
None	11 (12.5)	15 (16.9)
Hormonal	59 (67.0)	59 (66.3)
Nonsteroidal antiinflammatory drugs/tranexamic acid	45 (51.1)	41 (46.1)
Iron supplement/blood transfusion	50 (56.8)	52 (58.4)
Surgical procedures	17 (19.3)	11 (12.4)

van der Kooij. UAE vs hysterectomy for uterine fibroids. *Am J Obstet Gynecol* 2010.

(continued)

menorrhagia, (4) had no other treatment options than a hysterectomy, and (5) had no desire for future pregnancy. After written informed consent was obtained, patients were allocated randomly (1:1) to UAE or hysterectomy. Randomiza-

tion was computer-based and stratified for participating hospitals. The study was approved by the Central Committee Involving Human Subjects ([www.ccmo.nl](http://www.ccmo.nl)) and by local ethics committees of participating hospitals.

### Procedures

UAE and hysterectomy were performed according to professional standards as described earlier (Table 1).<sup>7,8</sup> In the UAE group, 10 patients (12.3%) underwent unilateral UAE.<sup>7</sup>

**TABLE 1**  
**Baseline and procedural characteristics** (continued)

Variable	Uterine artery embolization (n = 88)	Hysterectomy (n = 89)
Symptoms, n (%)		
Menorrhagia	88 (100)	89 (100)
Dysmenorrhea	47 (53.4)	50 (56.2)
Pain (not during menstruation)	15 (17.0)	14 (15.7)
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, mo <sup>b</sup>	24 (3–250)	24 (4–240)
No. of fibroid tumors <sup>b</sup>	2 (1–20)	2 (1–9)
Uterine volume, cm <sup>3b</sup>	321 (31–3005)	313 (58–3617)
Fibroid volume: dominant fibroid, cm <sup>3b</sup>	59 (1–673)	87 (4–1641)
Type of embolization, n		
Target embolization		
Left uterine artery	65	—
Right uterine artery	59	—
Selective embolization		
Left uterine artery	8	—
Right uterine artery	12	—
Type of hysterectomy, n		
Abdominal hysterectomy	2	63
Vaginal hysterectomy	1	8
Vaginal hysterectomy with morcellator	1	1
LH with morcellator	—	2
LAVH	—	1

LAVH, laparoscopically assisted vaginal hysterectomy; LH, laparoscopic hysterectomy.  
 Derived, with permission, from Hehenkamp et al.<sup>8</sup>

<sup>a</sup> Data are given as mean ± SD; <sup>b</sup> Data are given as median (range).

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### Sample size and endpoints of the study

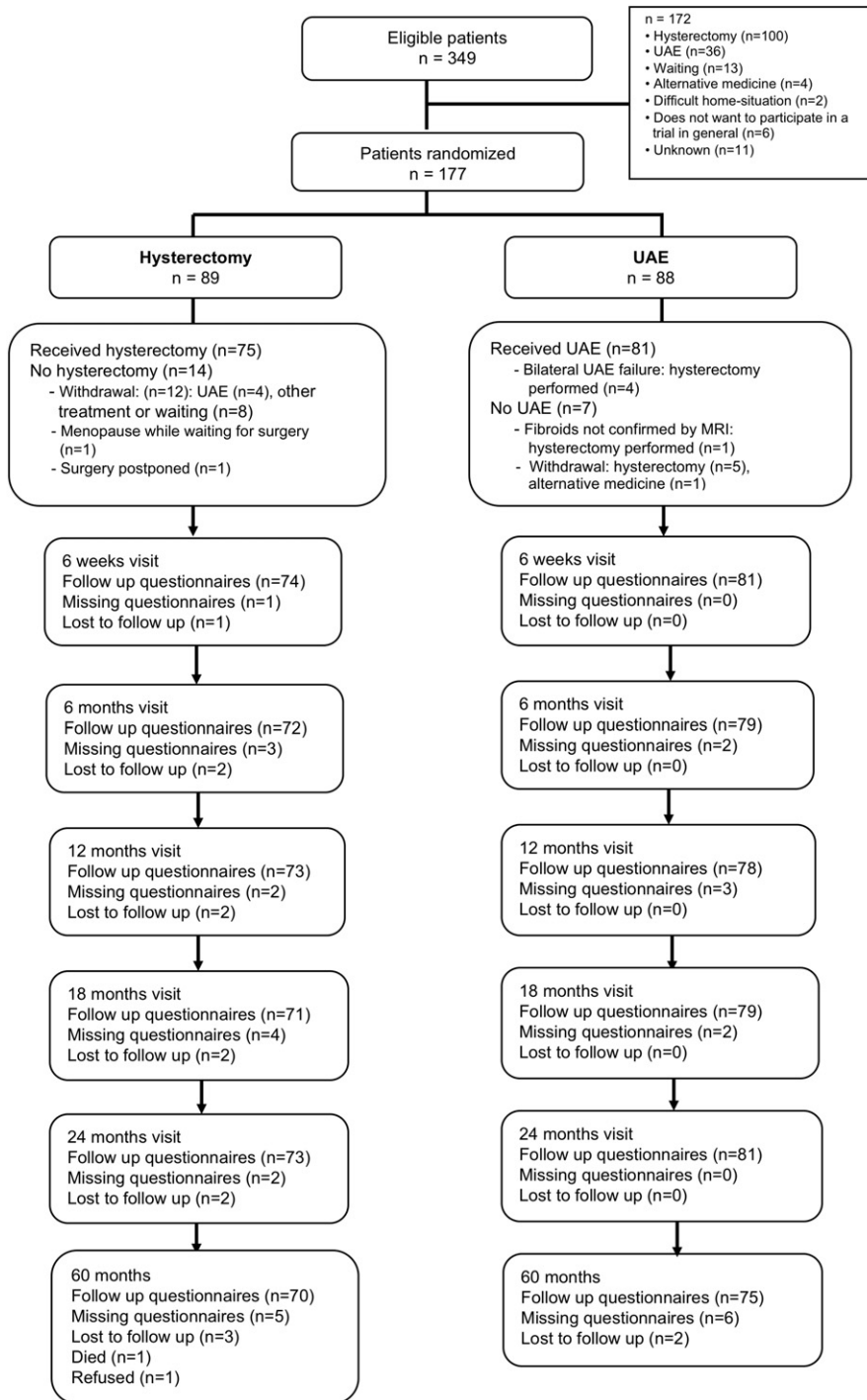
The sample size was based on the primary endpoint of the 2-year clinical study, the elimination of menorrhagia thus avoiding hysterectomy after UAE in at least 75% of the patients after 2 years.<sup>7</sup> To reject the null hypothesis that UAE and hysterectomy are not clinically equivalent, at least 2 × 60 (= 120) analyzable patients had to be included.<sup>7</sup> Endpoints after 5 years were reinterventions, menorrhagia, menopause and menopausal symptoms, quality of life, urinary and defecation function, and satisfaction with the received treatment.

### Study measures

Patients received questionnaires at baseline and at fixed intervals for 2 years after treatment.<sup>8</sup> In addition, for logistic reasons, all patients received 1 questionnaire in the autumn of 2007, at a median follow up period of approximately 5 years after primary treatment, which resulted in a variable follow-up evaluation in both groups. In tables and figures, the median of 5 years is depicted as a fixed point in time for both treatment arms, despite this variation within the group. All questionnaires were identical, except for the 5-year questionnaire, which was a condensed version without the High-

Pictorial Chart, Euro-Quality of Life-5, Health Utilities Index Mark 3, sexual activity, and body image questionnaires to optimize the response rate.<sup>10–15</sup> The following subjects were evaluated in the 5-year questionnaire: additional interventions between 2- and 5-year follow up evaluation (in case of nonrespondents, the patients' general practitioners were contacted by telephone to check for any additional procedures), menstrual characteristics (intensity and regularity since UAE or no complaints because of menopause; only in the UAE group), and several HRQOL measures that were assessed by validated questionnaires.

**FIGURE 1**  
**Trial profile**



Profile represents the flow of patients through the trial.

MRI, magnetic resonance imaging; UAE, uterine artery embolization.

van der Kooy. UAE vs hysterectomy for uterine fibroids. *Am J Obstet Gynecol* 2010.

Menopausal symptoms were queried by the Kupperman score as modified by Wiklund et al.<sup>16</sup> Scores may range from 0–51; higher scores represent more seri-

ous menopausal symptoms. In addition we inquired whether patients believed themselves to be in or beyond menopause. Generic HRQOL was assessed by

the Medical Outcome Study Short Form 36 (SF-36).<sup>17,18</sup> The SF-36 can be divided into the physical component summary score (PCS) and the mental component summary score (MCS).<sup>19</sup> Scores may range from 0–100 (100 indicates the optimal score) and were validated for the Dutch population. The Urogenital Distress Inventory (UDI)<sup>20,21</sup> was used to investigate urinary symptoms. UDI scores range from 0–100; higher scores indicate worse functioning. For defecation complaints, the Defecation Distress Inventory (DDI) was used,<sup>22</sup> with scores ranging from 0–100; higher scores are less favorable. Patients were asked to rate the overall quality of their urinary and stool function as “very good,” “good,” “fairly good,” “not good or bad,” “fairly bad,” “bad,” or “very bad.” Furthermore, the use of pads for urinary incontinence or of laxatives was registered. Patients were asked to indicate how satisfied they were with the received treatment: “very satisfied,” “satisfied,” “fairly satisfied,” “not satisfied or unsatisfied,” “fairly unsatisfied,” “unsatisfied,” or “very unsatisfied.” We also inquired whether patients would recommend the primary treatment to a friend. Finally, we asked women whether they would indeed have chosen the assigned treatment again if they had had the opportunity to do so.

### Statistical analysis

Analyses were done with SPSS statistical software (version 16.0; SPSS Inc, Chicago, IL). Study outcomes were analyzed according to original treatment assignment (intention to treat). Reinterventions were also analyzed according to per-protocol analysis. A Kaplan-Meier curve was constructed to show the distribution of the secondary hysterectomies over time. Differences in categorical data were compared with  $\chi^2$  test or Fisher's exact tests, if appropriate. The Student *t* test (or Mann-Whitney test, when applicable) assessed differences in numeric data. A probability value of  $< .05$  was considered statistically significant. Predictors for failure (secondary hysterectomy) were tested by logistic regression analysis. In this analysis, baseline characteristics (Appendix) were included for

TABLE 2

## Reinterventions in UAE and hysterectomy group until 2 and 5 years after initial treatment

Primary intervention	Secondary intervention	Reason for intervention	Time since primary intervention, mo
UAE			
1	Abdominal hysterectomy	Bilateral failure UAE	<1
2	Abdominal hysterectomy	Bilateral failure UAE	<1
3-1	Abdominal hysterectomy	Bilateral failure UAE	<1
3-2	Laparoscopic reconstruction surgery	Incisional hernia	9
4	Vaginal hysterectomy with morcellation	Bilateral failure UAE	<1
5-1	Failed attempt to hysteroscopically remove fibroid	Persistent abdominal pain/myoma nascens	1
5-2	Hysteroscopic myoma resection converted to vaginal hysterectomy	Menorrhagia	20
6	Manual resection fibroid	Discharge, fever, persistent abdominal pain/myoma nascens	2
7	Abdominal hysterectomy	Menorrhagia, persistent abdominal pain	5
8	Abdominal hysterectomy	Menorrhagia	6
9	Abdominal hysterectomy	Menorrhagia, persistent abdominal pain, bulk complaints	7
10	Abdominal hysterectomy	Menorrhagia	7
11	Abdominal hysterectomy	Persistent abdominal pain, irregular menstruation	10
12	Vaginal hysterectomy	Menorrhagia, persistent abdominal pain, dyspareunia	12
13-1	Diagnostic hysteroscopy with curettage	Postmenstrual blood loss	12
13-2	Abdominal hysterectomy	Irregular cycle, pain, bulk complaints	13
14	Abdominal hysterectomy	Menorrhagia, bulk complaints	13
15	Abdominal hysterectomy	Menorrhagia	13
16	Laparoscopic-assisted vaginal hysterectomy	Menorrhagia	15
17	Abdominal hysterectomy	Menorrhagia	17
18	Vaginal hysterectomy	Menorrhagia	17
19	Abdominal hysterectomy	Menorrhagia	20
20	Abdominal hysterectomy	Menorrhagia	24
21	Laparoscopic myomectomy	Menorrhagia	25
22	Abdominal hysterectomy	Menorrhagia	36
23	Curettage	Menorrhagia	37
24	Abdominal hysterectomy	Menorrhagia	44
25	Endometrium ablation	Menorrhagia	47
26	Hysteroscopic polypectomy	Menorrhagia	48
27	Abdominal hysterectomy	Menorrhagia	48
28	Abdominal hysterectomy	Menorrhagia	63

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(continued)

TABLE 2

## Reinterventions in UAE and hysterectomy group until 2 and 5 years after initial treatment (continued)

Primary intervention	Secondary intervention	Reason for intervention	Time since primary intervention, mo
Hysterectomy			
1-1	Adhesiolysis by laparotomy	Persistent abdominal pain	4
1-2	Bilateral adnextirpation	Persistent abdominal pain	11
2	Fistula repair with Latzko technique	Vesicovaginal fistula	7
3	Reconstruction surgery	Incisional hernia	9
4	Adhesiolysis and cystectomy by laparotomy	Persistent abdominal pain	23
5	Diagnostic laparoscopy	Persistent abdominal pain	24
6	Ovariectomy	Persistent abdominal pain	38
7	Suburethral sling procedure	Stress incontinence	50
8	Reconstruction surgery	Cosmetic	54

UAE, uterine artery embolization.

Derived, with permission, from Volkers et al.<sup>7</sup>

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multiple regression analysis whenever univariate analysis revealed probability values of  $< .1$ . In the multiple regression analysis, a probability value of  $< .05$  was considered statistically significant. Repeated measurements analysis was used to evaluate longitudinal differences in MCS, PCS, DDI, UDI, and Wiklund scores between treatment strategies with time as repeated factor. Self-reported quality of urinary and stool function at follow-up evaluation was compared with baseline and yielded 1 of 3 possible answers: worse, the same, or better. Logistic regression analysis was performed to test the impact of improvement in SF-36 MCS and PCS on satisfaction at 5 years ("very satisfied" and "satisfied" vs "moderately satisfied" and "very unsatisfied"). To evaluate the impact of baseline variables (Appendix) on the change in MCS, PCS, UDI and DDI at 5 years compared with baseline, multiple linear regression analysis was performed for those variables that yielded probability values of  $< .1$  in the univariate analysis. Nonresponders were not included in the analyses.

## RESULTS

### Patients

Patients were enrolled between March 2002 and February 2004. In the hysterectomy group, 75 women received the al-

located treatment vs 81 in the UAE group. Table 1 lists the baseline characteristics of the participating patients, which include myoma characteristics; all characteristics were not significantly different. Figure 1 shows the flow of patients through the trial: 93% of the mailed 5-year questionnaires were returned, with a median follow-up period of 59 months, ranging from 47-73 months (UAE: median, 60 months [range, 49-73 months]; hysterectomy: median, 58 months [range, 47-71 months]). The median age of all patients when responding to the 5-year questionnaire was 50 years, ranging from 39-63 years (UAE: median, 49 years [range, 39-63 years]; hysterectomy: median, 49 years [range, 40-59 years]).

### Clinical outcome

#### Reinterventions

In addition to the 19 secondary hysterectomies (23.5%) that were performed in the UAE group in the first 2 years,<sup>7</sup> another 4 hysterectomies were required between 2 and 5 years, all because of insufficient improvement of bleeding complaints (Table 2). This adds up to a total of 23 secondary hysterectomies after a median follow up of 5 years (28.4%). Distribution over time is presented in Figure 2. Per protocol analysis showed that, after a technically successful UAE, 19 of 77 patients underwent a sec-

ondary hysterectomy (24.7%). Of the 10 women who underwent unilateral UAE, 3 women underwent a hysterectomy, all within the first 2 years of follow up. Multiple regression analysis of failures within 5 years revealed only a higher body mass index to be associated with failed UAE (odds ratio, 1.12; 95% confidence interval [CI], 1.02-1.24;  $P = .02$ ). All additional interventions that were performed after UAE, including hysterectomies, are listed in Table 2. Twelve women in the UAE group used medication (tranexamic acid/oral contraception/levonorgestrel intrauterine device) to remedy still symptomatic menorrhagia (Table 3). After 5 years 8 of 75 of the women (10.7%) in the hysterectomy group needed reintervention (Table 2).

#### Bleeding characteristics

Table 3 shows various bleeding characteristics of the UAE group. On average menorrhagia decreased over time. After 5 years, 67 of 81 women (82.7%) were either symptom-free ( $n = 58$ ) or reported great ( $n = 4$ ) or moderate ( $n = 5$ ) improvement. Of the 58 women who still had their uterus after 5 years, 44 women (75.9%) were symptom free or reported great or moderate improvement; 8 women (13.8%) reported their menstrual bleeding to be unchanged, compared with baseline. In this group, 10 women reported

## FIGURE 2

## Kaplan-Meier curve for preservation of the uterus after UAE

Curve represents preservation of the uterus after UAE. *Censored* means that a patient was lost to follow up and had not undergone a hysterectomy before the last follow-up moment.

UAE, uterine artery embolization.

van der Kooij. UAE vs hysterectomy for uterine fibroids. *Am J Obstet Gynecol* 2010.

not experiencing menorrhagia anymore because of menopause.

### Menopause

Patients were asked the question: do you feel that you are in or beyond menopause? In the UAE group 34.6% of the women and in the hysterectomy group 47.1% of the women answered “yes,” which is significantly different ( $P = .03$ ). The mean Wiklund score for menopausal symptoms of both treatments is plotted over time in Figure 3. Within group analysis revealed a significant increase in the hysterectomy group from baseline to 5 years ( $P = .04$ ). The UAE group did not show a significant increase ( $P = .43$ ). Repeated measurements analysis showed no differences between the groups after 5 years.

### Quality of life outcomes

#### Generic HRQOL

Figure 4, A and B, display mental health and physical health scores throughout the study period for both groups. Results to the 2-year follow-up evaluation were described earlier.<sup>8</sup> Repeated measurement analysis shows no differences between the groups during the 5-year follow-up period for both the MCS and PCS scores. Table 4 shows the differences in PCS and MCS between and within groups over time. Within-group analysis in the hysterectomy group revealed significantly worse physical health after 5 years compared with 2 years ( $P = .01$ ), although mental health remained stable ( $P = .34$ ). Within the UAE group, no differences over time were noted

(MCS,  $P = .36$ ; PCS,  $P = .18$ ). In the multivariate analysis, none of the baseline variables was associated with improvement of SF-36 MCS scores at 5 years. The increase in SF-36 PCS score after 5 years was influenced positively by a hemoglobin level that was  $<12.0$  g/dL at baseline ( $\beta = 8.50$ ; 95% CI, 3.28–13.6;  $P = .002$ ) and age ( $\beta = -0.51$  per year; 95% CI,  $-0.87$  to  $-0.15$ ;  $P = .006$ ): having a low hemoglobin level at baseline resulted in more improvement in PCS; older women had less improvement in PCS scores at 5 years.

#### Urinary and defecation function

Figure 4, C, depicts urinary function (UDI). Repeated measurements analysis showed no differences between the groups after 5 years. After 6 months, the

**TABLE 3**  
Menstruation changes to 5 years after UAE (intention to treat)

Variable, n (%)	60 mo (n = 81)
<b>Menorrhagia</b>	
Symptom free <sup>a</sup>	58 (71.6)
Great improvement	4 (4.9)
Moderate improvement	5 (6.2)
Unchanged	8 (9.9)
Worse	0
<b>Additional treatment for menorrhagia</b>	
Tranexamic acid	2 (2.5)
Oral contraception	3 (3.7)
Levonorgestrel intrauterine device	7 (8.6)
<b>Amenorrhea</b>	
Because of hysterectomy	23 (28.4)
Because of self-reported menopause	10 (12.3)

UAE, uterine artery embolization.

<sup>a</sup> Includes 23 hysterectomies.

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UDI score stabilized in both groups at a continuously significant higher level compared with baseline until 5 years after treatment without any significant differences between groups (Table 4). Defecation function (DDI) is shown in Figure 4, D. In the UAE group, a persistent significant improvement from 6 months onward was found. In the hysterectomy group, no significant changes were demonstrated compared with baseline. After 5 years, repeated measurements analysis showed the UAE group to

have significantly better defecation function than the hysterectomy group. A smaller number of fibroid tumors was associated with improved UDI scores after 5 years ( $\beta = -3.87$ ; 95% CI,  $-6.29$  to  $-1.44$ ;  $P = .02$ ); the intended treatment (embolization) was associated with improvement of the DDI score after 5 years ( $\beta = -12.65$ ; 95% CI,  $-22.08$  to  $-3.22$ ;  $P = .01$ ). For the variables UAE and time, a significant interaction effect was shown in the repeated measurements on DDI scores. Urinary incontinence was present at baseline in 18.5% of UAE patients vs 14.7% of hysterectomy patients ( $P = .52$ ). After 5 years, urinary incontinence was reported by 27.2% of UAE patients vs 22.7% of hysterectomy patients ( $P = .31$ ). After 5 years, most patients in both groups reported a similar or improved quality of urinary or defecation function compared with baseline (UAE, 70.4% and 67.9%; hysterectomy, 77.3% and 61.3%), without significant differences between groups ( $P = .20$  and  $.61$ , respectively). The use of laxatives decreased over time in the UAE group only (from 9.7% at baseline to 1.3% at 2 years).<sup>8</sup> However, after 5 years, an increased use of laxatives was found (13.3%). In the hysterectomy group, this

proportion was stable at 5.8%, with an increase after 5 years to 8.7%. After 5 years, 17.3% of women in the UAE group and 10.0% of women in the hysterectomy group used incontinence pads ( $P = .23$ ).

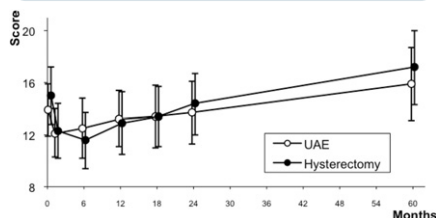
### Satisfaction

After 5 years, most patients were (very) satisfied about the received treatment (ie, 85.3% of women in the UAE vs 88.6% of women in the hysterectomy group ( $P = .37$ ; Table 5). Logistic regression analysis showed none of the variables to be associated with satisfaction levels at 5 years after treatment. In the hysterectomy group, 62 of 70 women (88.6%) would advise a friend to have a hysterectomy. In the UAE group, 61 of 79 women (77.2%) would recommend UAE to their friends ( $P = .07$ ). Most women expressed a preference for the actual received treatment (56/79 women [70.8%] from the UAE group preferred UAE; 44/70 women [62.9%] from the hysterectomy group preferred hysterectomy;  $P = .10$ ).

### COMMENT

This article describes the results of a large, long-term, randomized trial that compared UAE with hysterectomy in the treatment of menorrhagia in the presence of uterine fibroids. After a median of 5 years, 23 hysterectomies (28.4%) were performed in the UAE group, all because of uncontrolled menorrhagia. The success rate of 71.6% (or 76.5% after a technically successful UAE procedure) is comparable to prospective uncontrolled single arm UAE studies<sup>23,24</sup> but lower than those reported in retrospective studies.<sup>25-27</sup> This may be explained by the fact that our patients could participate only in the EMMY study when severe bleeding complaints were present, while other treatment options had failed. In contrast to other studies, all our patients had a classic indication for hysterectomy and were indeed willing to undergo surgery. Because 82.6% (19/23) of the secondary hysterectomies in this study occurred within 2 years after UAE, not undergoing a hysterectomy in the first 2 years after UAE might be a predictor for being long-term hysterectomy

**FIGURE 3**  
Wiklund score



The graph represents the Wiklund score for menopausal symptoms until 5 years of follow up. Scores range from 0–51; the higher scores represent more serious menopausal symptoms.

UAE, uterine artery embolization.

van der Kooij. UAE vs hysterectomy for uterine fibroids. *Am J Obstet Gynecol* 2010.

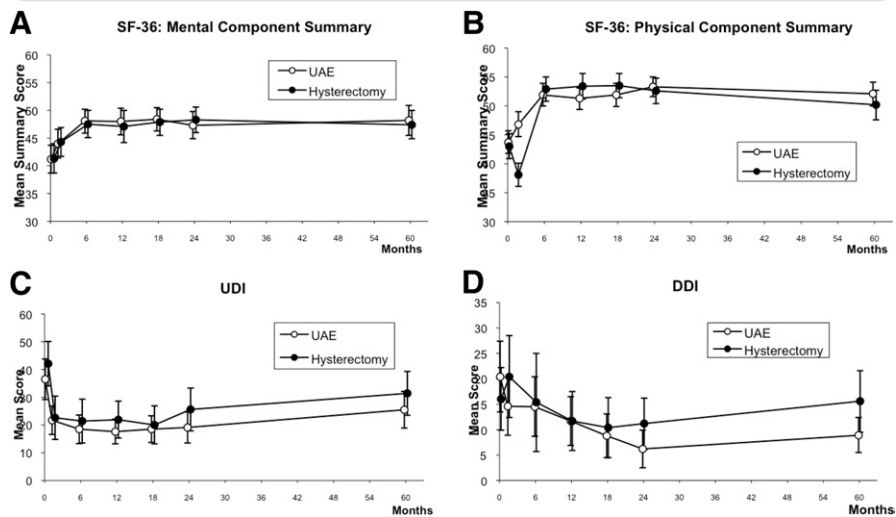


free. This corresponds with other data.<sup>23</sup> Some studies have pointed out that failure rates are likely to increase whenever bilateral embolization cannot be performed.<sup>25,28</sup> In our study, 10 women underwent unilateral UAE. Three of them eventually underwent hysterectomy, all within the 2-year follow-up period. This percentage (3/10) of secondary hysterectomies is more or less the same as in bilateral embolization in this study group, which does not underline the higher percentage of failure in unilateral embolization. Our finding that a high body mass index at baseline is a predictor for failure of UAE is a new finding that might be of importance when a patient is being counseled for UAE. However, the risk for obese patients to undergo surgery is extensive also. The gynecologist should balance the risks and benefits of both options with the individual patient.

Control of bleeding of women in the UAE group who still had their uterus after 5 years in our study was 75.9%. Although failure was defined strictly as a secondary hysterectomy, 12 patients in the UAE group still needed to use medication to remedy menorrhagia, and 8 of them showed no improvement of menorrhagia; these women are potential candidates for reintervention. For this reason, we will approach them after another 5 years to establish the definitive long-term failure rate of UAE in this trial. Evidently even a hysterectomy does not guarantee an intervention-free life; in our study, 10.7% of patients in the hysterectomy group needed a reintervention, most of them because of complications caused by the hysterectomy (adhesiolysis, a vesicovaginal fistula, or reconstruction surgery). Some studies even demonstrate that women after a hysterectomy are at higher risk for pelvic floor repair,<sup>29</sup> which underlines the reintervention risk after a hysterectomy to be present. However, this could not be found in our study; the UDI did not show a difference in complaints between the UAE and the hysterectomy group. Ovarian failure after UAE is a well-recognized complication that may result from inadvertent embolization of uterovaginal collateral vessels.<sup>30,31</sup> Earlier we showed both UAE and hysterectomy to

FIGURE 4

Graphs show scores until 5 years of follow-up evaluation



**A**, Short Form 36 (*SF-36*): Mental Component Summary: scores range from 0–100 (higher scores mean a better mental quality of life); **B**, Short Form 36 (*SF-36*): Physical Component Summary; scores range from 0–100 (higher scores mean a better physical quality of life); **C**, Urogenital Distress Inventory (*UDI*): scores range from 0–100 (higher scores indicate worse functioning); **D**, Defecation Distress Inventory (*DDI*): scores range from 0–100 (higher scores indicate worse functioning).

UAE, uterine artery embolization.

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affect ovarian reserve.<sup>9</sup> As a consequence, especially those women >45 years old seem to be at higher risk than women without UAE/hysterectomy for becoming menopausal after both interventions. In our 5-year analysis, however, in the hysterectomy group, a higher percentage of patients reported subjectively to believe that they were beyond menopause than in the UAE group. This might be explained by the absence of objective symptoms (ie, menstrual periods) in women who had a hysterectomy and therefore might be biased, although it can provide an indication. The Wiklund score (evaluating the menopausal symptoms instead of bleeding) did not show a difference in menopause between both groups after 5 years. Comparing HRQOL, we showed that the main increase in HRQOL occurred in the first months after treatment<sup>8</sup> and remained stable for 5 years without showing differences between the groups. Hemoglobin level <12.0 g/dL and age at baseline were predictive of PCS increase; worse physical condition at baseline (low hemoglobin level and being older) predicted a higher increase in phys-

ical condition after 5 years. Apparently, these patients had the most to gain in the long-term. Higher age at baseline that predicted a worse physical condition probably reflects the normal decline in physical function that comes with age. For clinical practice, this substantiates that the best indication for treatment is heavy symptoms at baseline. Evident differences between the 2 groups in urinary function were not observed during the 5-year follow-up period; both groups showed a comparable improvement. A positive effect of hysterectomy on urinary function has been described before;<sup>32</sup> the positive effect of UAE on urinary function, however, is a new finding. Defecation function only improved in the UAE group. After 5 years, this group had a significantly better defecation function than the hysterectomy group, which did not show an increase or a decrease in defecation function. The positive effect of UAE on defecation function is another new finding that has not been described before. The increasing use of laxatives in the UAE group from 1.3–13.3% is a very contradictory finding. The possible effect of adhesion formation to the colon

**TABLE 4**  
**Quality of life change scores until 5 years after UAE and hysterectomy**

Variable	12-mo change score <sup>7</sup>			24-mo change score <sup>7</sup>			60-mo change score					
	UAE (n = 81)	Hysterectomy (n = 75)	Change score difference (95% CI)	P value	UAE (n = 81)	Hysterectomy (n = 75)	Change score difference (95% CI)	P value	UAE (n = 81)	Hysterectomy (n = 75)	Change score difference (95% CI)	P value
Short Form 36: Mental Component Summary	6.3 <sup>a</sup>	7.67 <sup>a</sup>	1.34 (-2.63 to 5.32)	.505	5.80 <sup>a</sup>	7.26 <sup>a</sup>	1.47 (-2.78 to 5.71)	.496	6.31 <sup>a</sup>	6.87 <sup>a</sup>	-0.56 (-5.07 to 3.95)	.806
Short Form 36: Physical Component Summary	7.32 <sup>a</sup>	10.13 <sup>a</sup>	2.81 (-0.59 to 6.21)	.104	9.42 <sup>a</sup>	9.32 <sup>a</sup>	-0.10 (-2.98 to 2.79)	.948	8.47 <sup>a</sup>	7.20 <sup>a</sup>	1.26 (-2.16 to 4.70)	.468
Urogenital Distress Inventory	-17.16 <sup>a</sup>	-17.88 <sup>a</sup>	-0.72 (-9.74 to 8.30)	.875	-17.03 <sup>a</sup>	-14.66 <sup>a</sup>	2.37 (-8.13 to 12.87)	.656	-10.70 <sup>a</sup>	-8.41 <sup>a</sup>	-2.29 (-13.45 to 8.87)	.686
Defecation Distress Inventory	-5.90 <sup>a</sup>	-4.99	0.91 (-6.55 to 8.36)	.810	-14.42 <sup>a</sup>	-5.39	9.03 (-0.82 to 18.88)	.072	-12.72 <sup>a</sup>	0.01	-12.73 (-22.31 to 3.15)	.010 <sup>a</sup>

CI, confidence interval; UAE, uterine artery embolization.

Derived, with permission, from Volkers et al.<sup>7</sup>

<sup>a</sup> Indicates a statistically significant ( $P < .05$ ) change from baseline in the within-group analysis.

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described after UAE might explain this.<sup>33</sup> Additionally, the subjective change in overall quality of defecation, compared with baseline, was not reported to be different between both groups, which makes the huge difference in (the objective) DDI after 5 years difficult to ground. From 2 years onward, in both groups, a mild but significant deterioration in urinary and defecation function was found, which probably can be ascribed to the effect of increasing age on the prevalence of pelvic floor dysfunction.<sup>34</sup> The number of fibroid tumors appeared to be the only predictor for UDI improvement, which probably is explained by the mechanical effect of enlarged fibroid uteri. Satisfaction, treatment preference (for the received treatment), and recommendation of the received treatment to a friend were all similarly good in both groups without differences between them, which confirms earlier findings.<sup>35</sup> These findings support that patients perceive both treatment alternatives as acceptable options. Despite the accumulating beneficial evidence from randomized trials, the implementation of UAE as an alternative to hysterectomy in gynecologic practice is relatively slow. In Europe, it is estimated that <5% (Cardiovascular and Interventional Radiological Society of Europe survey 2008, unpublished data) potential UAE candidates are being offered this alternative, and most women who undergo UAE seem to be those who discovered this alternative to surgery through the Internet. In conclusion, UAE is a proven valuable treatment alternative for surgery in women with symptomatic uterine fibroids. In view of the currently available evidence, the time is ripe to counsel all women who are candidates for hysterectomy for their symptomatic uterine fibroids on the possibility of UAE. In 5 years, in 71.6% of all women who underwent UAE, a hysterectomy was avoided, and there was no difference in HRQOL between groups. Besides this, one has to keep in mind that there might be a chance that, instead of a hysterectomy, a less invasive intervention or the use of medication may be needed, which is reflected in the number of patients who reported their menorrhagia complaints as unchanged compared with baseline. However, because these women chose not to have a second-

**TABLE 5**  
**Satisfaction until 5 years after UAE and hysterectomy**

Variable	12 mo <sup>7</sup>			24 mo <sup>7</sup>			60 mo		
	UAE (n = 81)	Hysterectomy (n = 75)	P value	UAE (n = 81)	Hysterectomy (n = 75)	P value	UAE (n = 81)	Hysterectomy (n = 75)	P value
Very satisfied	29	48	.001	34	45	.020	37	42	.13
Satisfied	21	14		29	16		27	20	
Moderately satisfied	18	3		11	5		4	4	
Not satisfied nor unsatisfied	5	3		2	3		1	3	
Moderately unsatisfied	3	1		3	0		3	0	
Unsatisfied	1	1		1	1		3	1	
Very unsatisfied	1	0		0	3		0	0	

UAE, uterine artery embolization.

Derived, with permission, from Volkers et al.<sup>7</sup>

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ary hysterectomy so far, the chance would only increase that they would continue not to request one in the future. The mean age of our patient group is 50 years now, and menopause is looming. Of course, this is not a certainty and can be certified only by observation of this patient group until menopause. ■

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## APPENDIX

Predictors for failure	Effect of baseline variables on HRQOL
Age (continuous)	Age (continuous)
Ethnicity (white as reference category)	Ethnicity (white as reference category)
Body mass index (continuous)	Body mass index (continuous)
Parous (yes/no)	Parous (yes/no)
Smoking (yes/no)	Smoking (yes/no)
Comorbidity (yes/no)	Comorbidity (yes/no)
Previous surgical treatment (yes/no)	Previous surgical treatment (yes/no)
Previous hormonal treatment (yes/no)	Any previous treatment (yes/no)
Duration of menorrhagia symptoms (> or <1 y)	Duration of menorrhagia symptoms (continuously)
Hemoglobin level (continuous)	Previous iron-substitution therapy/blood transfusion (yes/no)
Anemia (yes/no)	Anemia before treatment (yes/no)
No. of fibroid tumors (continuous)	No. of fibroid tumors (continuous)
Uterine volume (continuous)	Uterine volume (continuous)
Dominant fibroid volume (continuous)	Intended treatment (UAE/hysterectomy)
Location of dominant fibroid (submucosal, subserosal, intramural, not classified)	Educational level (intermediate level or higher vs lower level)
Flow in dominant fibroid using ultrasound (hypovascular, isovascular, or hypovascular)	Married (yes/no)
T2 signal intensity on magnetic resonance imaging (hyperintens, isointens, hypointens, mixed)	Paid work (yes/no)
Radiologist's experience	Baseline SF-36 MCS (continuously, not on MCS change outcome)
Concomitant adenomyosis	Baseline SF-36 PCS (continuously, not on PCS change outcome)

HRQOL, health related quality of life; MCS, Mental Component Summary; PCS, Physical Component Summary; SF-36, Short Form 36; UAE, uterine artery embolization.

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