

The Ontario Uterine Fibroid Embolization Trial. Part 2. Uterine fibroid reduction and symptom relief after uterine artery embolization for fibroids

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Objective: To evaluate fibroid uterine volume reduction, symptom relief, and patient satisfaction with uterine artery embolization (UAE) for symptomatic fibroids.

Design: Multicenter, prospective, single-arm clinical treatment trial.

Setting: Eight Ontario university and community hospitals.

Patient(s): Five hundred thirty-eight patients undergoing bilateral UAE.

Intervention(s): Bilateral UAE performed with polyvinyl alcohol particles sized 355–500 μm .

Main Outcome Measure(s): Three-month follow-up evaluations including fibroid uterine volume reductions, patient reported symptom improvement (7-point scale), symptom life-impact (10-point scale) reduction, and treatment satisfaction (6-point scale).

Result(s): Median uterine and dominant fibroid volume reductions were 35% and 42%, respectively. Significant improvements were reported for menorrhagia (83%), dysmenorrhea (77%), and urinary frequency/urgency (86%). Mean menstrual duration was significantly reduced after UAE (7.6 to 5.4 days). Improvements in menorrhagia were unrelated to pre-UAE uterine size or post-UAE uterine volume reduction. Amenorrhea occurring after the procedure was highly age dependent, ranging from 3% (1%–7%) in women under age 40 to 41% (26%–58%) in women age 50 or older. Median fibroid life-impact scores were significantly reduced after UAE (8.0 to 3.0). The majority (91%) expressed satisfaction with UAE treatment.

Conclusion(s): UAE reduced fibroid uterine volume and provided significant relief of menorrhagia that was unrelated to initial fibroid uterine size or volume reduction. Patient satisfaction with short-term UAE treatment outcomes was high. (Fertil Steril® 2003;79:120–7. ©2003 by American Society for Reproductive Medicine.)

Key Words: Uterine artery embolization, fibroids, leiomyoma, polyvinyl alcohol particles, menorrhagia, amenorrhea, treatment effectiveness, clinical study

Uterine artery embolization (UAE) is gaining in popularity as a minimally invasive therapeutic alternative to hysterectomy for patients with symptomatic fibroids. Early studies (1–10) have suggested that it is an effective treatment alternative for these patients. These reports have generally involved small patient numbers and are based on the experience at a single institution. To date, there have been few if any multicenter studies evaluating UAE in the treatment of symptomatic uterine fibroids.

The Ontario Uterine Fibroid Embolization (UFE) Trial is a multicenter prospective clinical study of UAE at eight Ontario hospitals. The overall objectives were to evaluate the technical success, safety, efficacy, and durability of this therapy. The objectives of this report were to evaluate the effects of UAE on fibroid/uterine volume reduction, symptomatic relief, and impact on life activity. Patient satisfaction with UAE treatment outcomes was also evaluated. This report is based on a 3-month ultrasound and telephone follow-up of 538 patients

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with symptomatic fibroids who underwent bilateral UAE at eight Ontario hospitals.

MATERIALS AND METHODS

Study Design

This multicenter clinical trial involved the prospective follow-up of women undergoing UAE for symptomatic fibroids. Treatment was provided by 11 interventional radiologists practicing at eight Ontario hospitals. Patients were eligible for the trial if they had ultrasound-documented fibroid(s), were symptomatic, and had been advised to have a hysterectomy. Symptoms included but were not restricted to menorrhagia, pelvic pain, or bulk-related symptoms (such as urinary urgency or frequency). Women with active pelvic inflammatory disease, renal insufficiency, undiagnosed pelvic mass, or pregnancy were ineligible. Approval for the Ontario UFE Trial was obtained from Institutional Review Boards at each center. Patients were prospectively followed by ultrasound exams and telephone interview at 2 weeks, 3 months, and 6 months, and follow-up was planned annually for 5 years.

Patient Characteristics

The patients were mainly white women (65%) and averaged 43 years of age (range, 19–56 years). Fifty percent were nulliparous, and 30% wished to retain their fertility. Symptoms included menorrhagia (17%), menorrhagia with pain (63%), pelvic pain (13%), or bulk/mass effects only (8%). A minority had previously undergone surgical treatment for their fibroids (14% myomectomy and 3% endometrial ablation).

Uterine Artery Embolization

All women had a gynecological exam (performed by gynecologists) before UAE to exclude other causes for their symptoms. The procedure, risks, indications, and alternatives were explained to the patient in detail by the interventional radiologist, after which informed consent was obtained both for the procedure and the clinical trial. Preprocedural blood work included complete blood count (CBC), prothrombin time, partial thromboplastin time, and serum creatinine.

Bilateral UAE was accomplished in 97% (538/555) of cases. Unilateral UAE was performed in 14 patients, and UAE was unsuccessful in three cases because of difficulty catheterizing small or tortuous uterine arteries. Vascular access was obtained from a right common femoral arterial approach, and selective catheterization of the uterine arteries was carried out using four or five French catheters, with microcatheters used in 5% of cases.

The primary embolic agent used was polyvinyl alcohol particles (PVA) sized 355–500 μm (Contour; Target Therapeutics, Boston Scientific Corporation, Mississauga, Ontario; or Ivalon; Cook, Stouffville, Ontario, Canada). UAE

procedure time averaged 61 minutes, and the average amount of PVA used per procedure was 3.6 vials. Embolization proceeded until a standing column of contrast in the uterine artery was observed or contrast refluxed toward the uterine artery origin or into the internal iliac artery. Supplemental metal coils (Tornado; Target Therapeutics; and Gianturco; Cook) and absorbable gelatin sponge (Gelfoam; Pharmacia & Upjohn Inc., Mississauga, Ontario, Canada) were used by four interventional radiologists in 57% of the cases.

Follow-Up

Median follow-up was 8.2 months. Three-month telephone follow-up interviews were completed in 98% (526) of the 538 patients who underwent bilateral UAE. Pelvic ultrasound examinations were conducted at baseline and at 3 months post-UAE. Three-month follow-up ultrasound exams were available for 86% (464) of cases.

Ultrasound measurements were made by technicians using standardized measurement techniques and structured data collection forms. Transabdominal sonography was carried out using a 3.5–5.0 MHz curved array transducer, with transvaginal sonography added in some cases. The uterus was measured in three dimensions, longitudinal (D1), anterior-posterior (D2), and transverse (D3). Uterine and dominant (largest) fibroid volumes were calculated using the formula $(0.5233 \times D1 \times D2 \times D3)$ for an ellipsoid shape (11). The number of fibroids (1–4 and ≥ 5) was recorded, with the largest selected as the dominant or marker fibroid. The location of the dominant fibroid was indicated, and note was made of other pelvic pathology.

In the 3-month telephone interview, patients were asked to assess changes in their symptoms using a 7-point verbal scale as follows: much worse, moderately worse, slightly worse, unchanged, slightly improved, moderately improved, or much improved. Symptoms included dysmenorrhea, menorrhagia, mass or pressure effects, and urinary urgency/frequency. Specific questions about menstruation included: if menstruation had resumed; average duration of flow before and after UAE; and menstrual pad use on the heaviest day of flow before and after UAE. Menopausal women ($n = 15$) and women receiving GnRH-a injections after UAE ($n = 13$) were not included in the calculations for changes in menstrual bleeding and pain.

The overall impact of fibroid-related symptoms on usual or everyday activities after UAE (life-impact scale) was also rated on a 10-point numerical rating scale, where 1 was minimal interference and 10 was complete interference with their daily activities. Patient satisfaction with UAE was assessed at 3 months in two different ways: as their willingness to undergo another UAE if necessary and as their overall satisfaction rating with UAE. Satisfaction rating included a 6-point verbal scale: greatly dissatisfied, moderately dissatisfied, mildly dissatisfied, mildly satisfied, moderately satisfied, or greatly satisfied.

Statistical Analysis

Descriptive statistics including median, means, and 95% confidence intervals (CIs) were calculated for dominant fibroid and uterine volumes at baseline and at 3 months post-UAE. Percentage volume change was calculated as the difference between volume at 3 months post-UAE and volume at baseline. The relationship between mean percentage fibroid and uterine volume reductions and respective baseline volumes (quartiles) were tested by one-way analysis of variance.

Differences in mean duration of menses before and after UAE were analyzed using the Student's paired *t*-test. Differences in median menstrual pad counts (use on the heaviest menstrual day) before and after UAE were tested by the Wilcoxon signed rank test. Trends in clinically significant menorrhagia improvement (proportion with moderate or better improvement) and baseline uterine volume or percentage uterine volume reductions ($\leq 20\%$, 21%–30%, 31%–50%, $>50\%$) were tested by the binomial trend test. Trends in amenorrhea (occurrence 3 months post-UAE) with patient age (<40 , 40–44, 45–49, ≥ 50 years) were also tested by the binomial trend test. Change in median symptom life-impact scores before and after UAE were analyzed using the Wilcoxon signed rank test. The relationships between clinically significant menorrhagia improvement and percentage uterine volume reduction to changes in life-impact score (<1 , 1–3, 4–6, 7–10) were measured by trend tests.

Associations between patient satisfaction (and menorrhagia improvement) with uterine volume reduction and change in life-impact score (<1 , 1–3, 4–6, 7–10) were tested by the binomial trend test. Associations between patient satisfaction and menorrhagia improvement were tested by the χ^2 test. All tests were two sided, and a *P*-value $\leq .05$ was considered statistically significant. CIs and binominal trend tests were performed using StatXact software (Cytel Software, Cambridge, MA). All other analyses were performed with SPSS, version 10.1 (SPSS Inc., Chicago, IL).

RESULTS

Fibroid Uterine Volume Reduction

Uterine and dominant fibroid mean and median volumes at baseline and at 3 months post-UAE are outlined in Table 1. Most women had multiple uterine fibroids with the majority of dominant fibroids intramural in location. Median and mean percentage (3 months post-UAE) volume reductions for the dominant fibroid were 42% and 33% (95% CI; 28%–38%). Median and mean percentage uterine volume reduction was 35% and 27% (95% CI; 23%–32%).

Larger fibroids were more likely ($P < .0001$) to have a greater percentage volume reduction after UAE (Table 2). The mean percentage volume reduction in larger fibroids ($>400 \text{ cm}^3$) was twice that of their smaller ($\leq 200 \text{ cm}^3$) counterparts (49% vs. 23%). The degree of uterine volume

TABLE 1

Ultrasound imaging at baseline and 3 months after uterine artery embolization (UAE).

	N (%)
Fibroid no.	
1	150 (30)
2–4	220 (44)
≥ 5	133 (26)
Dominant fibroid location	
Intramural	285 (60)
Intramural (+subserosal or submucosal)	63 (13)
Subserosal	92 (19)
Submucosal	33 (7)
Dominant fibroid	
Baseline	
Mean volume cm^3 (SD)	308 (380)
Median volume cm^3	178
Three months post-UAE	
Mean volume cm^3 (SD)	170 (215)
Median volume cm^3	105
Median % change	42
Mean % change (95% CI)	33 (28–38)
Uterus	
Baseline	
Mean volume cm^3 (SD)	704 (586)
Median volume cm^3	555
Three months post-UAE	
Mean volume cm^3 (SD)	428 (322)
Median volume cm^3	331
Median % change	35
Mean % change (95% CI)	27 (23–32)

Note: Volumes are in units of cm^3 .

CI = confidence interval.

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reduction after UAE was also significantly ($P < .0001$) related to its baseline size. Large uteri at baseline ($\geq 1,000 \text{ cm}^3$) had a mean reduction of 44% (95% CI; 40%–49%) compared with 11% (95% CI; 2%–20%) in smaller uteri ($\leq 500 \text{ cm}^3$).

Symptom Relief

Women reported significant improvements in all symptoms at 3 months post-UAE (Table 3). Improvements in menorrhagia were reported by 83% (95% CI; 80%–87%), in dysmenorrhea by 77% (95% CI; 72%–82%), in bulk/size by 84% (95% CI; 80%–87%), and in urinary urgency/frequency by 86% (95% CI; 82%–90%). A small percentage of women reported no changes or a worsening of symptoms for menstrual bleeding, dysmenorrhea, bulk, or urinary urgency/frequency.

Among women whose menstruation returned after undergoing UAE, the mean duration of menstrual flow, at 3 months post-UAE, was significantly reduced from 7.6 days to 5.4 days ($P < .001$). Before UAE, 30% had reported menstrual durations of longer than 7 days. After UAE, this

TABLE 2

Effect of pre-UAE fibroid uterine volume on post-UAE volume reduction.

Pre-UAE dominant fibroid volume (cm ³)	Dominant fibroid volume reduction 3 months post-UAE		
	N	Median (%)	Mean (%) (95% CI)
≤200	249	38	23 (15–32)
201–400	76	40	38 (31–46)
>400	123	50	49 (44–54)

Uterine volume reduction 3 months post-UAE			
Pre-UAE uterine volume (cm ³)	N	Median (%)	Mean (%) (95% CI)
≤500	192	24	11 (2–20)
501–1,000	147	39	38 (34–42)
>1,000	97	43	44 (40–49)

Note: UAE = uterine artery embolization.

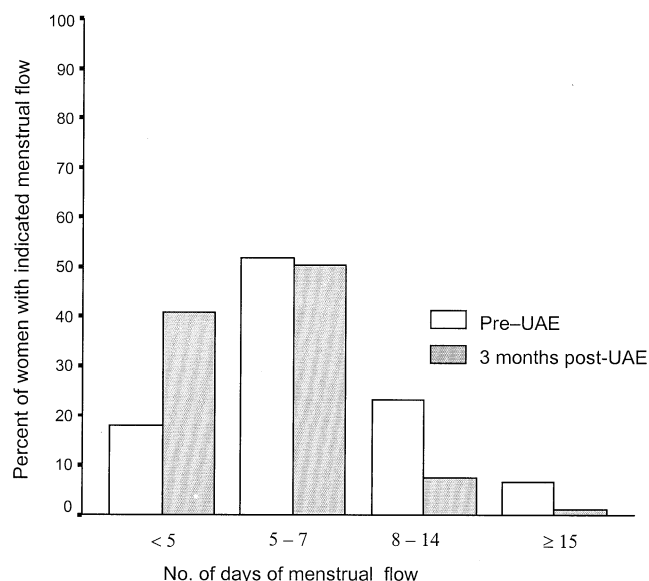
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decreased to 9% (Fig. 1). Median pad count for the day of heaviest menstrual flow was also significantly reduced from 9 to 4 ($P < .0001$).

Menstruation had not resumed in 8% (95% CI; 6%–11%) at 3 months post-UAE and in 4% at 6 months post-UAE

FIGURE 1

Fibroid UAE effects on menstrual duration. Mean duration menstrual flow: pre-UAE = 7.6 days; 3 months post-UAE = 5.4 days ($P < .001$).



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TABLE 3

Symptom improvement 3 months after uterine artery embolization.

	N (%)
Menorrhagia (n = 429)	
Improved	358 (83)
Much	249
Moderate	67
Slight	42
Unchanged	43 (10)
Worse	28 (7)
Slight	11
Moderate	9
Much	8
Dysmenorrhea (n = 322)	
Improved	249 (77)
Much	170
Moderate	34
Slight	45
Unchanged	43 (13)
Worse	30 (9)
Slight	16
Moderate	7
Much	7
Bulk (n = 464)	
Improved	388 (84)
Much	160
Moderate	111
Slight	117
Unchanged	72 (16)
Worse	4 (0.9)
Slight	3
Moderate	1
Urinary urgency/frequency (n = 306)	
Improved	263 (86)
Resolved	54
Much	109
Moderate	46
Slight	54
Unchanged	41 (13)
Worse	2 (0.7)
Slight	1
Moderate	1

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(Table 4). Amenorrhea after UAE was highly age dependent ($P < .0001$) and more frequently observed in older patients. The rate ranged from 3% (95% CI; 1%–7%) in women under age 40 to 41% (95% CI; 26%–58%) in women age 50 or older.

Relationship of Improvements in Menses to Uterine/Fibroid Volume Reduction

Improvements in menorrhagia were not related to pre-UAE uterine volume ($P = .08$) or to the amount of post-UAE uterine volume reduction ($P = .11$). Similar levels of menstrual improvements were noted in patients with large ($>1,000$ cm³) uteri, regardless of whether they had low

TABLE 4

Resumption of menses after uterine artery embolization (UAE).

Age group ^a	Resumed by 3 months post-UAE	Not resumed by 3 months post-UAE	Not resumed by 3 or 6 months post-UAE	Total
<40	159 (97)	5 (3)	3 (2)	164
40–44	134 (95)	7 (5)	2 (1)	141
45–49	137 (91)	13 (9)	6 (4)	150
≥50	23 (59)	16 (41)	10 (26)	39
Total	453 (92)	41 (8)	21 (4)	

Note: Data are represented as N (%).

^a Patients who were menopausal (n = 15) or receiving GnRH 1 day post-UAE (n = 13) were not included in this analysis.

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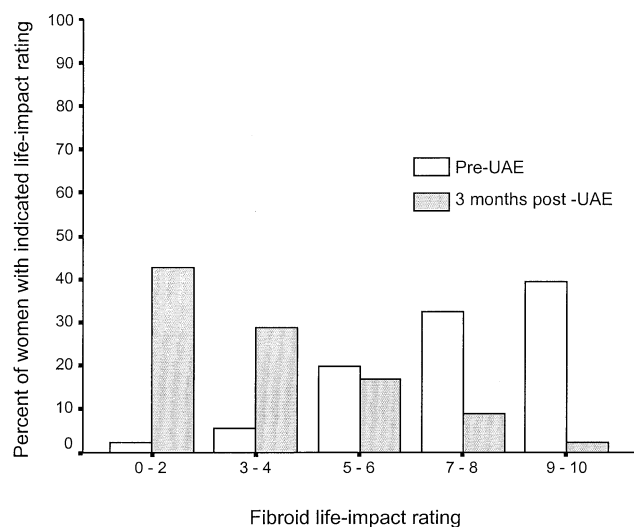
(<30%) or high (>50%) uterine volume reductions (73% vs. 76%).

Reduction in Fibroid Symptom Life-Impact

The overall life-impact scores (representing the interference of symptoms with everyday or usual activities) were markedly improved after UAE (Fig. 2). The median life-impact score was significantly lower at 3 months post-UAE (8.0 vs. 3.0; $P < .001$). Before UAE, 72% reported impact scores of 7–10 (high interference with daily activities). After UAE this decreased to 11%. Decreases in life-impact scores were strongly associated with improvements in menstrual

FIGURE 2

Fibroid symptom life-impact scores pre- and post-UAE. Median fibroid symptom life-impact score: pre-UAE = 8.0; 3 months post-UAE = 3.0 ($P < .001$).



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bleeding ($P < .0001$) but not with reductions in uterine volume ($P = .90$).

Patient Satisfaction with UAE

The majority of patients (91%; 95% CI; 89%–94%) were satisfied with UAE at 3 months post-UAE. Strong dissatisfaction (moderate or greater) was reported by only 7% (32 of 487). Although 85% (414 of 487) of the patients were willing to undergo repeat UAE if it became necessary, 19% (93 of 487) reported that they would only conditionally undergo another procedure. For many of these women, reservations were expressed about postprocedural pain. Patient satisfaction was highly associated with the degree of improvement in menses ($P < .0001$) as well as the improvement in fibroid life-impact scores (Fig. 3; $P < .001$).

DISCUSSION

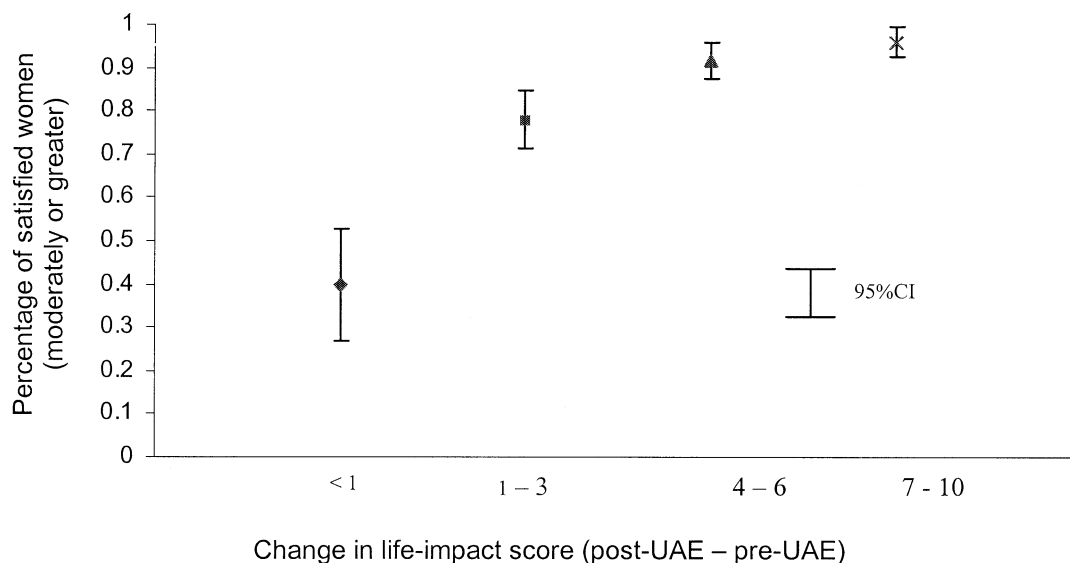
One of the major objectives of this study was to evaluate the efficacy of UAE in reducing uterine fibroids and related symptoms. The design of the Ontario UFE Trial has several strengths. Its size makes it the largest group of UAE patients reported thus far. UAE was also evaluated using the practices of a varied group of interventional radiologists in diverse practice settings. These factors, as well as the minimal exclusion criteria, may also permit a broader applicability of the study results. Other studies have tended to exclude younger women. In the Ontario UFE Trial, women desiring future fertility were not refused UAE (but were informed of the uncertain effects on fertility).

The volume reduction in the fibroid uterus seen in our study at early follow-up after UAE was similar to that reported by others, ranging from 20% to 55% for the fibroid (1–3, 6–8, 10) and from 13% to 46% for the uterus (1, 3, 4, 6, 8). The response of patients to UAE in our trial with respect to their volume reduction, however, was highly variable. Some patients experienced a rapid response to UAE with dramatic reductions in uterine volume seen at this early point of follow-up. Others experienced slower and less dramatic reductions and in some cases negligible volume reductions. We also found that post-UAE reduction varied directly with uterine fibroid size at baseline with a larger percentage of volume reductions occurring in patients with larger baseline volumes. This may only represent volume changes that would be proportional to the greater volumes of larger masses or it may be that larger fibroids are more susceptible to UAE. Larger fibroids may have a greater vulnerability to vascular disruption presumably because they have a greater vascular supply than smaller fibroids.

Based on our study, large fibroid/uterine size did not seem to be a contraindication for UAE. In fact, patients with large fibroids had similar symptomatic responses (with respect to menorrhagia) to their counterparts with smaller fibroids. However, patients with large uteri in excess of 1,000 cm³ that had marked reductions of 50% in size still had consid-

FIGURE 3

Relationship of patient satisfaction with UAE treatment to changes in their fibroid symptom life-impact score after UAE.



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erable mass. A time course for fibroid reduction after UAE has not been determined, but other studies have shown continued reduction in the fibroid uterus 6 months and beyond (3, 8). For large uteri, measurements at 6 months or at 1 year may better reflect fibroid uterine response and eventual shrinkage after UAE.

The major indication among women requesting UAE was for menorrhagia, with most patients reporting significant improvement in this symptom after UAE. These data suggest that the efficacy of UAE in the treatment of fibroid-related menorrhagia is independent of fibroid uterine volume as well as postembolization volume reduction. Significant improvements in menorrhagia still occurred in patients with very large uteri ($\geq 1,000 \text{ cm}^3$) and even in those with minimal volume reductions of less than 30%. Previous studies (12–16) have established that UAE is effective in reducing menorrhagia or hemorrhage in the absence of fibroids and is in keeping with vascular interruption as the primary mechanism of action for fibroid-related menorrhagia.

The high rate of women’s satisfaction with UAE in our study was directly related to their improvements in menorrhagia and to the reduced impact on their lives. Menorrhagia, however, did not improve in approximately 20%. Others (1, 3, 4, 6, 10) have reported failure rates ranging from 4% (1) to 21% (10). Several reasons could account for the failure of UAE in fibroid-related uterine bleeding. Unrecognized malignancy was a cause for treatment failure in two of our patients who underwent hysterectomies for uterine leiomyosarcomas. One patient had bulk symptoms, and the other

presented with menorrhagia; both were unaffected by UAE. Progressive enlargement of the “uterine fibroid” with persistent and worsening pain in both cases served as a clue to the underlying diagnosis. However, uterine leiomyosarcomas in patients treated for uterine fibroids are rare (<1%) and would not be a commonly expected cause of failure (17, 18).

Other diagnostic errors could be either misdiagnosis of fibroids or the underdiagnosis of another concomitant benign uterine pathology. Misdiagnosis of adenomyosis is a concern because it commonly occurs in conjunction with fibroids (19) and may present in a similar manner to fibroids (20). Reports on UAE in patients with adenomyosis have been contradictory, with some authors suggesting that this entity could account for some cases of treatment failure (1, 21) and others advocating the use of UAE to manage menorrhagia secondary to adenomyosis (22, 23) or to adenomyosis with fibroids (24, 25). Magnetic resonance imaging (MRI) is known to be more effective than ultrasound in the diagnosis of benign uterine pathology (26–28), and the fact that patients in our study did not undergo an MRI represents a limitation of the study.

Alternate or supplemental uterine vascular supply is another potential cause of treatment failure. Several studies have documented supplemental vascular supply to the uterus most commonly involving the ovarian arteries (29, 30). In at least one report, an enlarged bilateral ovarian artery supplying the upper portion of the uterus after UAE was cited as a reason for treatment failure (31). We did not routinely catheterize the ovarian arteries or search for supplemental ves-

sels. Another potential cause for treatment failure would be underembolization, which results in insufficient disruption of vascular supply to the uterus. Because angiographic endpoints are subjective, this can always be a potential source of treatment failure. Re-embolization in this case may result in a better outcome.

Amenorrhea post-UAE, both transient and permanent, has been reported in several studies (1–3, 7, 32–34) ranging from 2% to 15%. Goodwin et al. (1) reported permanent amenorrhea in 1 out of 57 premenopausal women (2%) after UAE. Spies et al. (3) reported amenorrhea at 3-month follow-up in 11 out of 181 patients (6%) that turned out to be temporary in 7 and permanent in 4. Pelage et al. (7) reported amenorrhea in 6 of 76 patients (8%), 4 of which turned out to be permanent. Chrisman et al. (32) reported the highest amenorrhea incidence (15%; 10/65). In 9 of these patients, biochemical and clinical findings were consistent with ovarian failure and presumed menopause. All of the amenorrheic patients in that study, however, were over age 45 (43%; 9/21). Spies et al. (33) studied ovarian function after UAE with serial FSH in 63 patients and found age-related increases in FSH levels. Although none of these patients developed postembolization amenorrhea, women older than age 45 were found to have a 15% chance of increased basal FSH (>20 U/L) into the perimenopausal range.

Although our 8% amenorrhea rate after UAE was similar to reports in other studies, we found it to be highly age dependent. We noted the incidence to gradually rise with age with a sharp increase (from 9% to 41%) between age groups 45–49 and 50 or older. Several explanations are possible for this trend. Amenorrhea may occur more commonly in older women because they are more sensitive to disruptions in vascular supply. It may also have occurred as a natural consequence of aging, effect of embolization, or a combination of these factors.

UAE could produce amenorrhea in several ways. Transient amenorrhea may have occurred simply as the result of a decreased uterine vascularity. The ovarian arteries have been shown in some cases to communicate directly with the uterine arteries via several potential anastomoses (29), and inadvertent occlusion of ovarian vessels could produce temporary or permanent ovarian dysfunction. The effects of fluoroscopy-associated radiation on the ovaries cannot be ignored, although this has not been studied in detail.

Whether amenorrhea is viewed as a complication or a successful outcome of UAE is dependent on the patient's treatment objective. For older women or those not desiring further fertility, amenorrhea may be seen as an intended consequence of therapy. Amenorrhea rates are often reported as measures of treatment success after ablation therapies for menorrhagia (35–37). However, in younger women or those desiring to maintain their fertility, amenorrhea or premature menopause would be a significant complication.

Although we found that amenorrhea after UAE was an infrequent occurrence in younger women, it is a significant potential complication and should be carefully discussed with them before UAE. The risk of premature menopause was not appreciated by us at the onset of the trial, and unfortunately we did not take hormonal measurements in our study. To better evaluate this risk, hormonal measurements before and after UAE should be taken in future trials to determine short-term and longer-term UAE effects on ovarian function.

In our study group, UAE reduced fibroid uterine volumes and produced significant symptomatic relief, particularly for patients with menorrhagia. Patient satisfaction with short-term treatment outcomes after UAE was very high. Satisfaction was highly associated with improvements in menstrual bleeding and with a summary score that measured the overall life-impact of fibroid symptomatology on women's lives. Ongoing follow-up, however, is needed to evaluate the long-term efficacy of this therapy.

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