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Uterine Artery Embolization for Symptomatic Uterine Fibroids: a Prospective Study on 102 Patients in Iran

Background/Objectives : To evaluate the safety, efficacy and complication rate of uterine artery embolization in symptomatic fibroid patients in Iran.

Patients and Methods: A hundred and two patients aged 20-48 years (mean age: 35.7 ± 6.4 years) with symptomatic fibroids entered the study from September 2001 to November 2004. The most common presenting symptom was increased menstrual bleeding, which occurred in 74.5% of all patients. Urinary symptoms occurred in 43%, and bulk-related symptoms were seen in 63.7 % of our patients.

We performed bilateral UAE (uterine artery embolization) using PVA (polyvinyl alcohol) particles (500-710 micron) and assessed the patients before UAE and at regular follow-ups at 1, 3, 6 and 12-month intervals by questionnaires / interviews and ultrasound. MRI without gadolinium (Gd-DTPA) injection was done before embolization and at 6 and 12 months after the procedure.

Results: By Friedman test, sequential follow-up (up to 12 months) showed that the vaginal bleeding severity significantly decreased ($p < 0.0001$), with menorrhagia resolving in 59.4% of patients at 1 month, and in 69% at 12 months. The mean uterus volume decreased $38.5 \pm 30\%$ after 12 months. The paired t-test showed that dominant fibroid volume changed from 273.7 ± 439.2 cm³ to 112.1 ± 141.6 cm³ at month 6 ($n=58$, $p=0.001$) and from 246.1 ± 314.5 cm³ to 70.1 ± 73.5 cm³ at month 12 ($n=41$, $p < 0.0001$). The initial size of the fibroids did not affect the success rate.

Conclusion: The study showed the high efficacy of UAE in controlling fibroid related symptoms, with only few complications.

Keywords: uterine artery embolization, fibroids, interventional radiology

Introduction

Uterine fibroids are benign tumors occurring in 20-50% of women in their reproductive age.^{1,2} They are the most frequent indication for hysterectomy at pre-menopausal age.² Fifty percent of fibroids are asymptomatic and require no treatment, but the rest may cause menorrhagia, dysmenorrhoea, dyspareunia, abdominal distension, pressure effects, pregnancy loss and infertility.²

Unfortunately all the primary treatments for fibroma, (including hysterectomy, myomectomy and hormonal therapy) have substantial disadvantages.^{3,4} Hysterectomy has the risks associated with major surgical procedures and eliminates fertility. Besides, the psychological aspects of uterine sacrifice are significant. Myomectomy also has similar risks, with approximately 20-25% recurrence of symptoms.³ Hormonal therapy is effective in the short term, and is associated with side-effects such as hot flashes, mood swings, insomnia and dyspareunia.⁴

Uterine artery embolization (UAE) as a primary therapy for fibroids was reported for the first time by Ravina in 1995.^{5,6} Larger studies then confirmed the safety and efficacy of this technique.⁶⁻¹⁰ The clinical success rate has been

reported at 80-94%.¹¹⁻¹⁴ The mean decrease in uterine volume varies from 35% to 48%, and fibroid size varies in the range of 45-78%.^{5, 7, 15}

Our university affiliated hospital is currently the main referring center that has been applying UAE for symptomatic fibroids since September 2001 in our country. In this study, we report our experience with the embolization of fibroids in a population of Middle-Eastern women and compare the outcome with the studies from western nations.

Patients and Methods

Patient Selection

Women who were referred to a university affiliated hospital for symptomatic uterine fibroid by gynecologist colleagues from September 2001 to November 2004 constituted the study population.

A total of 102 patients with a mean age of 35.7±6.4 (ranging 20-48 years) were evaluated in the study period.

Baseline patient demographic data is presented in Table 1.

The mean uterus volume was 552.6±649.5 cm³ (41.8 to 4656.7 cm³), and dominant fibroid size was 228.1±359.8 cm³ (1.8 to 2618.2 cm³) before the procedure.

Table 1. Baseline patient data (n=102)

Category	No.*	%
Marriage		
Married	57	56
Unmarried	45	44
Pregnancy		
No	57	56
Yes	45	44
Symptom History		
Menorrhagia	76	74.5
Without Impairment of Normal Activity	32	31.4
With Impairment of Normal Activity	44	43.1
Dysmenorrhea	67	65.7
Urinary	44	43
Bulk	65	63.8
Previous Treatment		
No	37	36
Hormonal Therapy	54	52.9
Myomectomy	6	6
Number of Fibroids		
Single	44	43.1
2-5	28	27.5
>5	28	27.5

*No: Number of patients

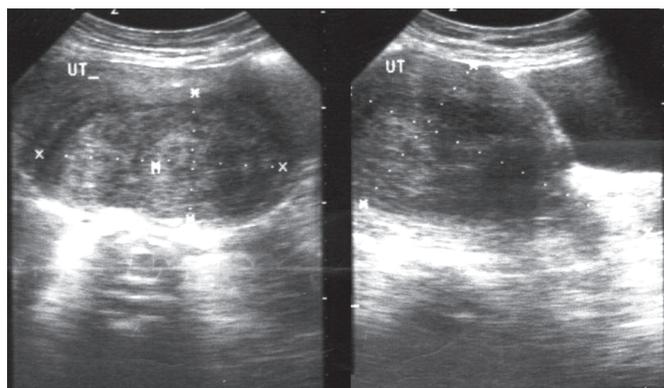


Fig 1. Preoperative trans-abdominal ultrasound images showing large intramural fibroids

Preprocedural Evaluations

Preprocedural evaluation included the following:

- Prior history, prepared by a general physician. In the questionnaire form, increased menstrual bleeding was defined as menstrual bleeding higher than prior, and heavy menstrual bleeding was defined as menstrual bleeding impairing normal activities.

- A gynecologic history and a physical examination including a pelvic examination, Papanicolaou test, and endometrial biopsy for women over the age of 40 were done.

- A radiologist's evaluation consisting of the results of the trans-abdominal ultrasound (Hitachi Eu 525) and MRI without gadolinium injection (1.5 T, Signa, GE, USA) included uterine size, dominant fibroid size, using the formula of a prolate ellipse (length × width × depth × 0.5233) and the state of the ovaries (Figure 1).

- Laboratory studies including a CBC (Complete Blood Count); serum levels of hemoglobin, Cr (Creatinine), and random FSH (Follicle-Stimulating Hormone);

- PT (Prothrombin Time); and PTT (Partial Thromboplastin Time).

We included patients who were symptomatic, were cooperative, had failed medical therapy and had refused hysterectomy (if indicated).

We excluded patients with acute renal failure (except patients under hemodialysis); acute vasculitis; pelvic inflammatory disease; endometrial inflammation; endometrial hyperplasia; carcinoma of cervix, uterus, or ovaries; tubal inflammation; endometriosis and adenomyosis; infarcted or infected fibroid; adenexal fibroid; bleeding diathesis; coagulopathies; pa-

tients who desired future pregnancy (except definite candidates for hysterectomy or patients who had been considered for myomectomy but hysterectomy was more likely), and patients who had other conditions that required surgery (such as uterine prolapse).

- An informed consent was obtained after informing the patient about the success rate and probable complications.

Embolization Procedure

Immediately before the procedure, all women were prophylactically treated with a single intravenous dose of Cefalotin (1 gm) and Gentamycin (80 mg).

All pelvic arteriography was performed by means of right groin approach, under conscious sedation with a 4F or 5F Cobra catheter without using microcatheters. The angiography device was a GE-DEX DSA with 1200 MA and 140 KVP. After the insertion of 4 or 5 Fr sheath, a catheter was placed in the abdominal aorta at the level of the renal arteries. Aortography was performed prior to pelvic arteriography by using a pigtail catheter. The catheter tip was positioned at or beyond the junction of the descending and horizontal portions of each uterine artery and embolization was performed using 500-710 μ m polyvinyl al-

cohol (PVA) particles (Contour, Boston Scientific, Boston, Mass, USA). PVA was injected into the uterine arteries until there was a complete cessation of blood flow (Figure 2).

After the procedure, the patients were admitted to an observation unit for post-procedural care, and pain was controlled with intramuscular or intravenous pethidine or morphine sulfate. All patients were discharged on the day of the procedure.

We followed each patient at 1, 3, 6, and 12 month intervals after discharge by questionnaires and/or interviews.

Laboratory studies after the procedure consisted of CBC, FSH, Cr and Hb, which were all performed after each follow-up. Follow-up imaging studies were transabdominal ultrasound at 1, 3, 6 and 12 months postprocedure. An MRI was performed at 6 or 12 months after the procedure. The MRI protocol was sagittal, coronal and axial T2-weighted imaging.

Complications that occurred after discharge were recorded through the patient's medical history.

Volume measurements were obtained for the uterus and fibroids in all patients at 1, 3, 6, and 12 months after the procedure.

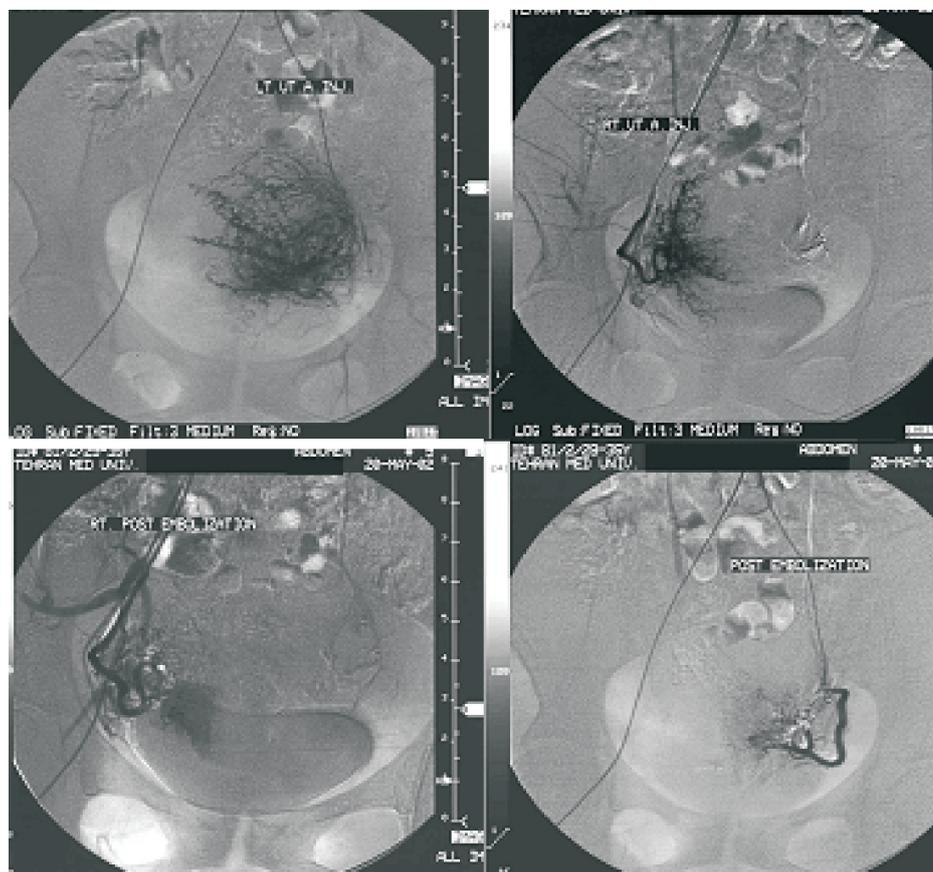


Fig 2. Pre- and post-embolization angiograms of both uterine arteries.

Table 2. Patient's symptom improvement 1, 3,6,12 months after UAE

Symptom		1month	3months	6months	12months
Improvement in Menstrual Bleeding	Complete resolution (%)	55	62.5	76.8	65.3
	Improvement (%)	21.1	18	10	12.2
	No change (%)	8.8	14	4.3	8.2
	Worst (%)	2.9	4.2	5.8	6.1
	Transient Amenorrhea (%)	5.9	1.4	2.9	8.2
Improvement in Urinary Symptom	Complete Improvement (%)	58.3	61	68.7	84
	Relative Improvement (%)	22.2	19.4	18.7	8
Improvement in Bulk related Symptoms	Complete Improvement (%)	50	66.7	82	84.3
	Relative Improvement (%)	25	14.5	11.4	6.2

Statistical Analysis

We used SPSS version 11.5 for the statistical analysis. In addition to descriptive statistics, we used the paired t-test, repeated measure ANOVA and Friedman test. Type I statistical error was set at 0.05.

Results

Bilateral selective uterine artery catheterization and embolization was technically successful in 91 patients (89.5%). At the beginning of our experience, 11 patients underwent unilateral embolization due to technical difficulties.

The most common complication was vomiting, which occurred in 52 patients (51%). Approximately 37 patients (36.3%) were treated with pethidine and 5 patients (4.9%) with morphine sulfate for pain relief. Low grade fever was detected in 32 patients (31.4%).

All of our patients were discharged the same day.

Mean days for returning to normal activity were 7±5.2 days.

Follow-ups were carried out for 76 patients at one month, for 72 patients at three months, for 69 patients at six months, and for 49 patients at twelve months.

Improvement in menstrual bleeding after 6 months was 86.8% (Table 2). By the Friedman test, during a sequential follow-up of up to 12 months, vaginal bleeding severity decreased significantly (n=30, p<0.0001).

Urinary symptom improvements were seen in 87.5% after 6 months. Improvements in the bulk-related symptoms were seen in 93.4% after 6 months.

Using the paired t-test, mean uterus volume changed significantly from 559.5±787.1 cm³ to 368.3±329.6 cm³ in 6 months (n=60, p=0.015), and from 561.8±446.8 cm³ to 367.8±375.2 cm³ in 12

months (n= 42, p=0.003). Also, using the paired t-test, mean fibroid volume decreased significantly from 273.7±439.2 cm³ to 112.1±139.1 cm³ in 6 months (n= 58, p=0.001) and from 246.1±314.5 cm³ to 70.1±73.5cm³ in 12 month (n= 41, p=0.0001). Thus, over a 6 month follow-up, the mean size of the uterus decreased by 29±31.7%, and after 12 months, decreased by 38.4±30.1%.

Uterine fibroids underwent shrinkage of 50.3±35.8% after 6 months and 64.4±22.7% after 12 months (Figure 3).

Arbitrarily we categorized the patients in two groups according to the size of fibroid, less than or equal to 50 cm³ and greater than 50 cm³. Then we compared relative reduction of fibroid size in these two groups. The mean relative reduction in the first group was 66.1% and in the second group was 64.5% (p=0.95). In addition, the improvement in bleeding scale was similar in these two groups after one year (p= 0.86). Similarly, we considered two other cut-off points of primary fibroid size of 70 and 100 cm³, and

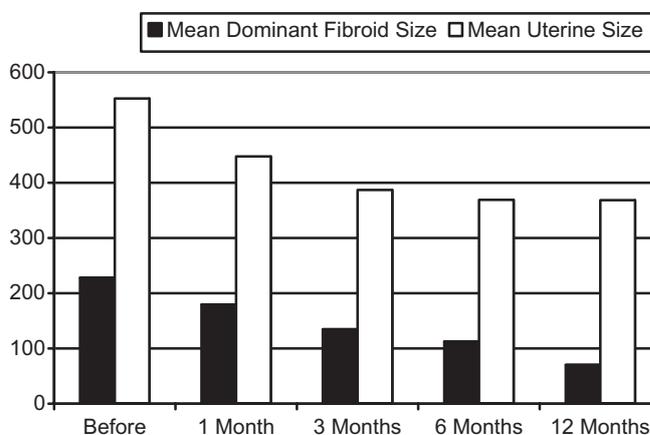


Fig 3. Mean uterine and fibroid size before and 1, 3, 6, and 12 months after UAE (cm³)

a similar analysis was done between patients with primary fibroid size less and greater than the cut-off points. The same results were reached again ($P>0.2$) (Table 3).

Partial or complete expulsions of fibroids were observed in 14 patients (between 2 to 7 months after procedure). The expulsion rate according to anatomical site was 13.3% in the group in which the dominant fibroid had no relation with the submucosal region, and 18.2% in the group in which the fibroid somehow extended to the submucosal region ($P=0.39$); however we found complete expulsion only in two patients, in which both fibroids were submucosal.

Discussion

The average reduction in the volume of the fibroid and the mean uterine size comply well with many other reports. ($p=0.93$)^{5, 7-9, 11, 12}

Menorrhagia in Georgetown's 200 patients showed improvement in 87% at month 3 and 89% at month 6.¹³ Similar results were reported by Hutchins and Worthington -Kirsch;¹⁶ in their report, menstrual improvement occurred in 85% after 6 months, which supports our results (Table-2). ($p=0.4$)

Improvement of urinary symptoms by UAE was approximately 87% after six months, and improvement of bulk-related symptoms was 93 %; very similar to other reports.^{13,16} The results from the published series and those of our patients are similar in the degree of symptom improvement, but fibroid shrinkage after UAE shows much better results in our patients than many other reports.

Although for patients with a desire for future pregnancy we only included patients who were candidates for extensive myomectomy or hysterectomy, the average age of our patients was lower than many other studies.^{1, 3, 16}

Our technical success rate was slightly lower than other studies. This might be due to by the unilateral uterine artery embolization in 11 patients at the beginning of our experience. It shows that the failure rate has a linear correlation with the experience of the radiologist.

No serious complication occurred after UAE in our patients. We did not have any mortality in our patients. The major adverse effect following UAE was pain, which was controlled by pethidine or morphine sulfate. It is therefore important to forewarn women about the pain they will experience, and which will probably last for several days.

Several reports have described the relationship between improvement in menorrhagia and primary tumor size. Katsumori et al. reported that improvement in menorrhagia was unrelated to initial uterine size.¹⁷

Spies et al. reported that bleeding outcome demonstrated a trend toward improvement with smaller baseline uterine and fibroid volumes.¹⁸ In our study, the improvement in menorrhagia at one year after embolization had no association with the primary size of fibroids. Our study confirms that clinical success after bilateral uterine artery embolization is not related to the size of the fibroid. However, we did not perform embolization in patients with fibroids larger than 2618 cm³.

Katsumori demonstrated that there was no statistical difference between fibroid volume reduction rate in two groups of patients with fibroids smaller and larger than 10 cm.¹⁷ Spies et al. reported that smaller baseline fibroid size is more likely to result in a positive imaging outcome.¹⁸

In our study, similar to Katsumori, there was no statistical difference between baseline fibroid volume and reduction in fibroid size after one year.

UAE has several potential advantages over hysterec-

Table 3. Association of the primary size of fibroid with relative reduction of fibroid volume and decrease in bleeding scale after one year:

Primary Fibroid Volume (Cm ³)	Fibroid Volume (%)			Bleeding Scale	
	Mean relative reduction (%)	n	P-Value	Mean reduction	P-Value
<50	66.1 ± 19.7	6	0.95	1.4 ± 1.2	0.86
>50	64.5 ± 23.5	33		1.3 ± 1.4	
<70	65 ± 15.9	9	0.88	1.6 ± 1.1	0.18
>70	65.7 ± 24.6	30		1.1 ± 1.4	
<100	61.2 ± 21.9	15	0.46	1.4 ± 1.3	0.51
>100	66.3 ± 23.5	24		1.1 ± 1.4	

tomy, myomectomy and hormonal suppression. Unlike myomectomy or hysterectomy, UAE involves virtually no complications of major surgery.³

Recovery time is several weeks shorter than with hysterectomy or open myomectomy (7 days versus 6 weeks).³ Early menopause-like symptoms, which are often seen with GnRH therapy are rarely induced as a result of UAE.

UAE has the advantages of allowing preservation of uterine function (i.e., normal menses and even pregnancy). In addition, the patients do not suffer the psychological problems of uterine sacrifice.

The procedure is well tolerated by patients. A clinical advantage is that if UAE fails, the full range of other options for treatment of fibroma will be still available. And if necessary, surgery will be easier and safer because of the preoperative embolization. Hysterectomies have higher facility costs than UAE because of longer hospital stay, procedure duration and recovery time. One of the disadvantages associated with UAE is that it is currently somewhat difficult for women to learn about the procedure or its accessibility in their area. Some gynecologists may be unfamiliar with it or may counsel the patients to stay with the tried and trusted surgical procedures.

According to our results, we can conclude that UAE is a safe and effective method in treatment of uterine fibroids. This conclusion has been approved in other reports too.^{4-6, 16}

However, there are a number of additional questions that require further studies. For example, the long-term effects on ovarian function and future fertility are yet to be determined. Successful pregnancy after this procedure has been reported^{6, 8}, but as of yet, the pregnancy rate cannot be calculated because it is not known how many patients treated with UAE have attempted to become pregnant. It is likely that a large multi-centric long-term study will be required to answer these questions.

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