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Arterial Embolization in Large Uterine Fibroids: A 4-Year Single Center Experience

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Abstract

Purpose: Current knowledge concerning the use of uterine artery embolization (UAE) in large uterine fibroids is limited with the majority of studies being limited to case reports. The present retrospective study aimed to investigate the impact of UAE on symptoms and tumor size in symptomatic women with at least one large uterine fibroid.

Methods: 39 patients undergoing UAE for symptomatic large uterine fibroids (>5cm) were consecutively enrolled in this study. All patients underwent a detailed physical examination and contrast-enhanced pelvic MRI at 3, 6 and 12 months after the procedure.

Results: Compared to baseline values (7.8 ± 2.4 cm), the mean diameter of the fibroids significantly reduced at 3rd (5.5 ± 1.7 cm), 6th (4.2 ± 1.3 cm) and 12th (3.1 ± 0.6 cm) months follow-up ($p<0.005$ for each compared to baseline) implying a 60 % reduction in tumor size at 12 months compared to baseline measurements. At the end of the 12 months follow-up, complete necrosis of the fibroid was achieved in 88%, complete symptom resolution was achieved in 92%, and >50 % reduction in fibroid diameter was acquired in 87 % of the participants.

Conclusion: Uterine artery embolization provides 60 % reduction in fibroid volume and a 92 % improvement in fibroid-related symptoms in patients with large fibroids at the end of 12 months follow-up.

Introduction

Uterine leiomyomas (also known as uterine fibroids) originate from smooth muscles and are the most frequently seen pelvic neoplasms in women. They are often asymptomatic; however pain, bulkiness and excessive menstrual bleeding may be seen when they do cause symptoms (1-3).Apart from these direct effects, patients with uterine fibroids may experience reproductive problems and complications in pregnancy (4). Due to the asymptomatic nature of the majority of fibroids, patients are often diagnosed incidentally; therefore, currently there is no hard data regarding their incidence and prevalence. Even so, data from recent studies in the United States indicate that fibroids are the cause for almost 30% of gynecologic hospitalizations and up to 60% of all hysterectomies are reportedly performed due to uterine fibroids (5, 6).

The classical approach to treatment of symptomatic uterine fibroids is performing hysterectomy and myomectomy which still remain as highly successful treatments. However, uterine artery embolization (UAE) has emerged to become another widely accepted treatment, in part due to the increasing popularity of minimally invasive procedures. Since the procedure's first implementation almost 2 decades ago, various studies have found UAE as a safe and effective treatment on par with the hysterectomy and myomectomy approach in terms of treatment success (7). However, uterine fibroids may reach extremely large size which may cause difficulties in the implementation of UAE. As such, current knowledge concerning the use of UAE in large uterine fibroids is lacking and mostly limited to case reports (8).

Therefore, the present prospective study aimed to investigate the impact of UAE on symptoms and tumor size in symptomatic women with at least one large uterine fibroid.

Methods

All pre- and postmenopausal women aged 18–60 years who underwent UAE at our institution from February 2014 to April 2018 were consecutively enrolled in this retrospective study.

All patients underwent a detailed physical examination and contrast-enhanced pelvic MRI for evaluation before the procedure (Fig.1a and 1b). All myomas are classified according to the FIGO (International Federation of Gynecology and Obstetrics) classification (Table 1).

Figure 1: Preoperative T1-weighted sagittal images obtained with MRI. Fig. 1a shows of a 8 x 7 cm uterine fibroid located at the corpus and Fig. 1b shows diffuse contrast enhancement of the mass.

Fig. 1a

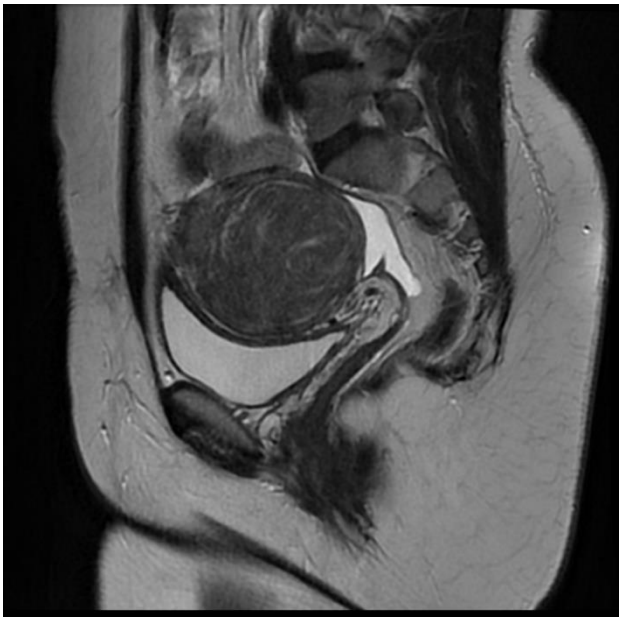


Fig. 1b

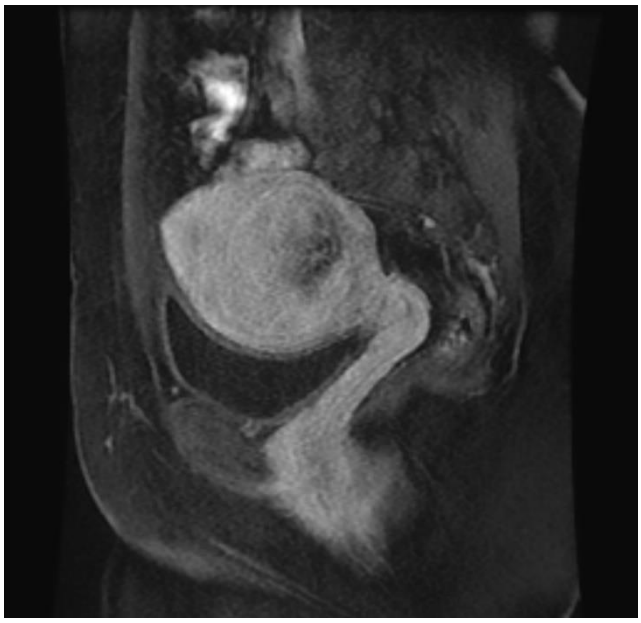


Table 1. FIGO classification

SM - Submucosal	0	Pedunculated intracavitary
	1	< 50% intramural
	2	≥ 50% intramural
O – Other	3	Contacts endometrium; 100% intramural
	4	Intramural
	5	Subserosal ≥ 50% intramural
	6	Subserosal < 50% intramural
	7	Subserosal pedunculated
	8	Other (specify e.g. cervical, parasitic)
Hybrid leiomyomas (impact both endometrium and serosa)	2-5	Submusocal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities, respectively.

Inclusion criteria were as follows: Having single or multiple fibroids (intramural or submucosal) with a diameter larger than 5 cm, and having at least one of the following symptoms: pelvic pain, abnormal uterine bleeding or mass effects. Patients with pelvic inflammatory disease, endometritis, subserosal fibroids, coagulation disorders and those with a history of contrast nephropathy were excluded from the study. Written informed consent was obtained from all patients. The study protocol was approved by the Institutional Ethics Committee and the study was conducted in accordance with the latest version of the Helsinki declaration.

All interventions were performed by the same interventional radiologist who had 5 years of individual experience with embolization procedures. Prior to interventions, all subjects received intravenous cefuroxime 1000 mg and midazolam 0.05mg/kg. A 6F introducer was inserted under local anesthesia to the right or left common femoral artery using the Seldinger technique. In order to evaluate vascular anatomy, a pelvic angiography was performed with a 5F pigtail catheter from aortoiliac segment. Following bilateral catheterization of the internal iliac arteries with 5F simmons-1 catheter, contrast enhancement of the fibroid was confirmed with an angiography. A 2.8 F microcatheter (Direxion HI-FL, Boston Scientific, MA, USA) selectively located at the ostium of the uterine artery with 0,018" micro guidewire (Transend-18, Boston Scientific, MA, USA). Under fluoroscopic guidance, the microcatheter was then advanced into the spiral artery that supplied the target lesion (Fig. 2a and 2b).

Figure 2: Fig. 2a and 2b shows contrast enhancement in bilateral uterine arteries following the administration of iv. contrast medium from a selective micro catheter.

Fig. 2a

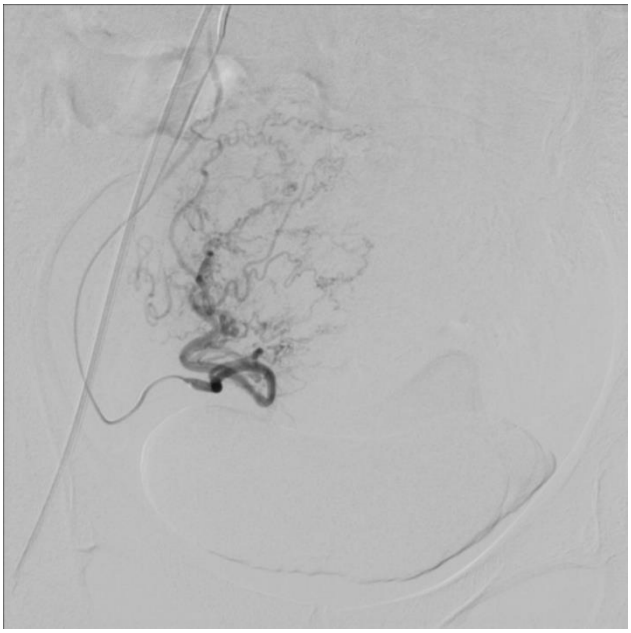
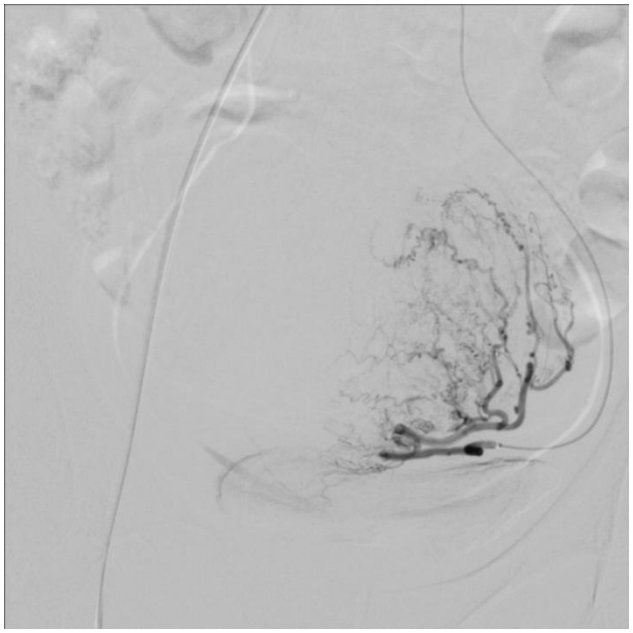


Fig. 2b



Then, biocompatible polyvinyl alcohol hydrogel compressible microspheres sized 500-700 microns (Bead Block, BTG, Beckenham, UK) were delivered to target area, which was followed by selective angiography to confirm that bilateral uterine arteries were occluded and the fibroid(s) did not show contrast enhancement. Finally, the sheath was removed and a vascular closure device (Exoseal, Cordis, USA) was used to obtain homeostasis.

All patients underwent a detailed physical examination and contrast-enhanced pelvic MRI at 3, 6 and 12 months after the procedure (Fig. 3a and 3b). The participants were also assessed for fibroid-related symptoms at each follow-up visit. Complete necrosis, symptom resolution and >50 % reduction in tumor size were defined as the major outcome measures of the study

Figure 3: T1-weighted sagittal images obtained with MRI at postoperative 6 months: Fig. 3a shows the reduction in fibroid size to 2x1.5cm and Fig.3b shows the necrosis at the residual fibroid and lack of contrast enhancement .

Fig. 3a

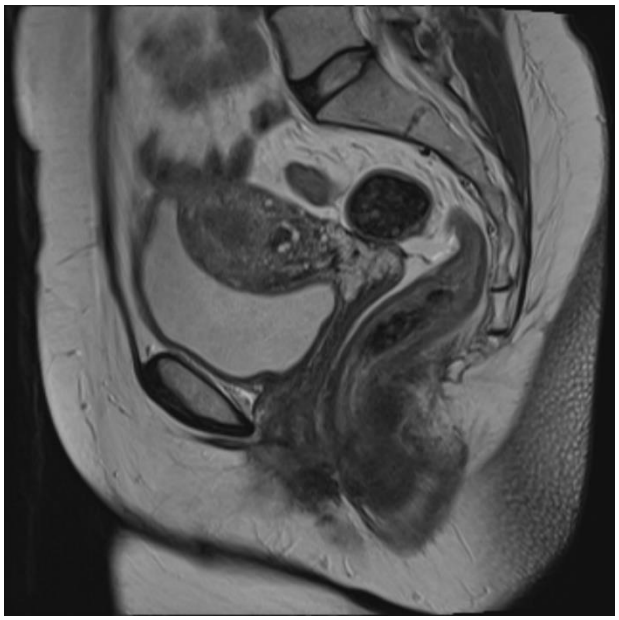
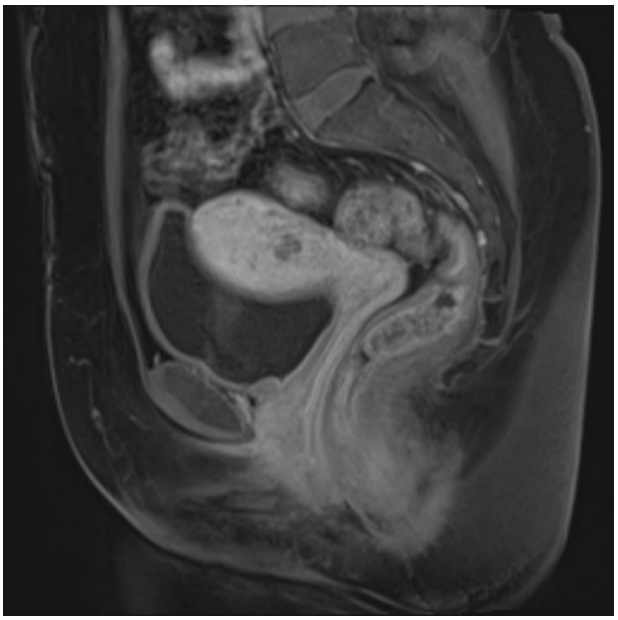


Fig. 3b



Data were analyzed using the IBM Statistical Package for Social Sciences v20 (SPSS Inc., Chicago, IL, USA). The distribution of quantitative data was checked using the Kolmogorov-Smirnov test. Parametric tests were applied to evaluate data with normal distribution and non-parametric tests were applied to data with non-normal distribution. The Paired samples t-test was used to compare continuous baseline and the follow-up data. Categorical variables were analyzed using the Pearson chi-square test. A p-value ≤ 0.05 was assumed to demonstrate statistical significance.

Results

A total of 40 patients with a fibroid >5cm in diameter were enrolled in this study. One patient was lost to follow-up and was excluded from all analyses; therefore, complete data were available for 39 patients (mean age 41.2 ± 9 years). Of all participants, 53.8% were premenopausaland 41% had a history of myomectomy. The FIGO classification data of the fibroids scheduled for UAE are listed in table (Table 2).

Table 2. Demographic features of the study population

	n=39
Complete necrosis	34 (88%)
Complete symptom resolution, n (%)	36 (92 %)
>50 % size reduction, n (%)	34 (87 %)
New lesion during follow-up, n (%)	2 (5%)
Undergone myomectomy, n (%)	3 (8 %)
Development of menopause symptoms, n (%)	5 (13 %)

Compared to baseline values (7.8 ± 2.4 cm), the mean diameter of the fibroids significantly reduced at 3^{rd} (5.5 ± 1.7 cm), 6^{th} (4.2 ± 1.3 cm) and 12^{th} (3.1 ± 0.6 cm) month follow-up studies ($p<0.005$ for each compared to baseline). A 60% reduction in tumor size was determined at 12 months compared to baseline measurements (Fig. 1). In addition, pelvic pain and menometrorrhagia also decreased significantly within three months of UAE and continued to resolve during the follow-up. However, a significant improvement in mass symptoms was not observed until the 6^{th} month. At the 12^{th} month, nearly all symptoms associated with the mass effect were resolved (Table 3).

Table 3. Follow-up data

	n=39
Age, years	41.2 ± 9
Premenopausal, n (%)	21 (53.8 %)
FIGO Class, n (%)	
2	16 (41 %)
3	8 (20.5 %)
4	5 (12.8 %)
2-5	9 (23 %)
3-5	1 (2.6 %)
Submucosal, n (%)	25 (64 %)
Intramural, n (%)	14 (36 %)
Previous myectomy, n (%)	16 (41 %)

[a]: $p<0.05$ between baseline and three months

[b]: $p<0.05$ between baseline and six months

[c]: $p<0.05$ between baseline and 12 months

At the end of 12 months of follow-up, complete necrosis of the fibroid was achieved in 88%, complete symptom resolution was achieved in 92%, and >50 % reduction in fibroid diameter was acquired in 87 % of the participants. In 5% of patients, a new lesion was found to have developed during the follow-up. Among all patients, 8% were scheduled for myomectomy due to clinical failure (Table 4).

Table 4. Major outcomes

	Baseline	**Postoperative 3 months**	**Postoperative 6 months**	**Postoperative 12 months**
Fibroid diameter, cm	7.8 ± 2.4 **[a, b, c]**	5.5 ± 1.7	4.2 ± 1.3	3.1 ± 0.6
Menometrorrhagia, n (%)	34 (87%) **[a, b, c]**	12 (30%)	3 (7%)	0 (0%)
Pelvic pain, n (%)	36 (92%) **[a, b, c]**	17 (43%)	9 (23 %)	2 (5%)
Mass symptoms, n (%)	20 (51%)**[b, c]**	14 (36%)	8 (20%)	1 (3%)

The most prevalent complication observed in our study group following the procedure was the post-embolic syndrome (pelvic pain, fever, malaise, and leukocytosis) which was encountered in 18 (46 %) of the participants. Majority of the patients (14 subjects, 77%) facing post-embolic syndrome had a large fibroid > 7 cm. Symptom recovery was obtained within 8 hours of the administration of the analgesic and antipyretic agents (Dexketoprofen 50 mg iv. and Paracetamol 10000 mg iv.). Also, ovarian dysfunction occurred in one patient (2.5 %) due to the miss of the embolization target. Uterine infection was not observed in any of the subjects.

Discussion

Our results demonstrate that UAE provides a significant reduction in the diameter of the tumor in women with large fibroids, as evidenced by a 12-month follow-up. The present study also shows that UAU leads to almost-complete improvements in fibroid-related symptoms including menometrorrhagia, pelvic pain, and mass symptoms by 6 months after the procedure. At the end of follow-up, complete symptom resolution was achieved in 92% of patients and complete necrosis of large fibroids was accomplished in 88% of the study population.

The traditional hysterectomy and myomectomy approach is still being utilized in the treatment of uterine leiomyomas with significant success. However, the paradigm shift towards less invasive techniques in

gynecologic surgery led to the introduction of procedures such as UAE(9, 10). During the course of 2 decades following the introduction of the UAE procedure, many studies ranging from small case series to large-scale investigations have approved the safety and efficacy of UAE in the treatment of uterine fibroids. As a consequence of the increasing popularity of this procedure, various guidelines addressing the procedural and patient-based characteristics of UAE have been published (11-13). With this interest, the number of UAE procedures have increased to around 25.000 procedures yearly(14).

There have been a number of prospective, randomized trials investigating the role of UAE in uterine fibroids since the first report published by Ravina et al. in1995(15). The multicenter, prospective Ontario Uterine Fibroid Embolization Trial showed a 42% reduction in dominant fibroid volume and improvements in symptoms such as menorrhagia, dysmenorrhea, and urinary frequency, as early as 3 months after the procedure (16). Additionally, one of the first prospective multicenter trials performed to evaluate UAE efficacy; the Fibroid Registry for Outcomes Data study which included 2112 patients with long-term follow-up, demonstrated significant improvements in symptoms and quality of life of patients at 6 months to 3 years of follow-up(17). The UAE procedure is now seen as a safe and effective approach to uterine fibroid treatment, as later small and large studies have confirmed that UAE provides long-term symptom regression and increases the quality of life of patients(18, 19).

Published registry data have also shown that the two groups which gain the most benefit from UAE are those who have relatively smaller leiomyomas and those presenting with abnormal uterine bleeding (14).However, Smeets et al., in their study comprised of 71 women undergoing UAE for large fibroids (42 patients with >10 cm diameter), reported that the outcomes and complications in their group of patients were similar to that of studies comprised of patients with smaller fibroids (20).In a more recent study, which compared the outcome of UAE in large fibroids among patients who had or had not received pre-treatment with gonadotropin-releasing hormone (GnRH) agonists, it was found that fibroid size was reduced by around 35% in those who did not receive GnRH agonists. Although the reduction was significantly higher in those who received GnRH (56.5%), the study also reported that 39 of the total 40 patients had had complete necrosis of their predominant large fibroid, indicating that the procedure was effective in such cases(21).

Despite the studies on this topic providing largely positive feedback, there still exists some controversy in regard to the use of UAE in patients with large fibroids. Our results, which confirm previous data showing the high success rate of the UAE procedure in both reducing tumor size and improving fibroid-related symptoms, are indicative that UAE implementation in such large fibroids would indeed be beneficial to patients; especially when we consider that the quality improvement guidelines for UAE use in fibroids states that a 50% reduction in fibroid volume, an 88-92% reduction in bulk symptoms and a 90% improvement in menometrorrhagia are expected following the UAE procedure (12). Results of the present study show that UAE might provide a success rate higher than these expected values even in large uterine fibroids. We suggest that the presence of a large fibroid should not directly be a cause to discourage the use of UAE, since UAE had been shown time and time again to provide a reduction in tumor size and also patients' symptoms, independent of the baseline fibroid size. However, at this point it is crucial to remind physicians that, with UAE, mass effect complaints require a longer time to subside. Furthermore, patients with urgent problems due to mass effects or other symptoms (such as intestinal obstructions or excessive bleeding) should be evaluated on a case-by-case basis and the patient's specific requirements and safety should be given foremost priority when considering approach.

A weakness of the present study is the relatively small sample size; however, the number of patients included in the study were limited by the inclusion/exclusion criteria and also the fact that only patients with large fibroids were included. Also, the lack of a second treatment arm including patients that underwent surgical treatment could have enhanced the value of our results.

The UAE procedure was shown to provide 60% reduction in fibroid volume, and 92% improvement in fibroid related symptoms in patients with large fibroids, at the end of 12 months of follow-up. Our results suggest that clinicians should be more open-minded about utilizing UAE in patients with large fibroids, especially in cases where patients do not present with emergency situation and elective approach is possible.

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