

MRI Enhancement as A Predictor of Uterine Fibroid Volume Reduction after Embolism

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ABSTRACT

Aim of the Study: To evaluate the response of necrotic fibroids to UAE and to identify whether pre-UAE enhancement or other factors are predictors of fibroid shrinkage.

Materials and methods: This is a retrospective review of all women who underwent UAE for symptomatic fibroids from January 2013 till July 2017, who experienced a follow-up MRI 5-6 months after UAE were included. There were 54 fibroids (37 non-enhancing and 17 enhancing) among 24 women with a mean age of 56 (range 40-59) years. All fibroids were assessed for size, position, enhancement on subtraction images, and Apparent Diffusion Constant (ADC).

Results: Enhancing fibroids had an average decrease in diameter by $23 \pm 6\%$, not significantly different compared to that non-enhancing fibroids which decreased by $19 \pm 3\%$ ($p=0.491$). Multiple linear regression with percent change in fibroid diameter as the dependent variable and patient age, fibroid position, and pre-UAE fibroid diameter, enhancement, and ADC as independent variables, showed that ADC ($p<0.005$) and pre-UAE diameter ($p<0.005$) were the only significant independent variables.

Conclusion: Pre-UAE size and ADC, but not contrast enhancement, predicted fibroid diameter reduction. Enhancing and non-enhancing fibroids had similar size reduction after UAE. Non-enhancement should not be considered a contraindication to UAE.

Keywords: MRI, diffusivity, uterine artery embolization, fibroid.

INTRODUCTION

Uterine artery embolization (UAE) is an accepted alternative to surgery in the management of symptomatic patients with uterine fibroids. UAE has been accepted as a safe and effective alternative treatment for symptomatic fibroids firstly reported by Ravina in 1995⁽¹⁾. Uterine fibroids (also called leiomyoma or myoma) are one of the most common benign tumors which occur in about 40% of women by age 35 years⁽²⁾.

Although many of women with fibroids are asymptomatic, some of them have annoying symptoms. These symptoms include prolonged and heavy menstrual bleeding, pelvic pain, pelvic pressure, urinary frequency and reproductive dysfunction. The costs for annual health care for a woman with uterine fibroids are 3.2 times higher than a woman without fibroid in united stated⁽³⁾. However, the role of UAE in symptomatic women with a large fibroid burden is a subject to debate. In several small studies,

response to UAE was judged insufficient in patients with a large fibroid, >8 cm, with a higher rate of need for additional therapy after UAE⁽⁴⁾. In addition, there is general unspecified fear of an excessive effect after embolization in these patients due to rapid ischemia and necrosis. This fear is based on several early case reports describing rare but serious complications shortly after UAE for large fibroids, such as unbearable pain, infection, septic uterine necrosis, and lethal sepsis⁽⁵⁾.

The criteria for successful endovascular treatment are not universally accepted, although patient satisfaction and fibroid shrink are essential. Most symptoms (especially those that are bulk-related) are related to fibroid volume⁽⁶⁾. There have been several studies presenting a fibroid volume reduction rate of approximately 50–55% after embolization⁽⁷⁾.

Uterine-sparing, minimally invasive procedures are increasingly preferred over hysterectomy in the management of symptomatic

fibroids, and are typically performed without a prior tissue diagnosis.

Recent advances in MR technology, including higher magnetic field strengths, parallel imaging techniques, and phased-array receiver coils, have driven investigation of the role of diffusion-weighted imaging in differentiating benign fibroids from sarcomas⁽⁸⁾. As expected, the mean apparent diffusion coefficient value of sarcomas is lower than that of normal myometrium as a result of histopathological characteristics, such as hypercellularity, enlargement of nuclei, and hyperchromatism.

Takeuchi *et al.*⁽⁹⁾ reported an overlap between sarcomas and cellular leiomyomas when diffusion-weighted imaging is used alone⁽⁹⁾. A combination of T2-weighted MRI and 3-T diffusion-weighted imaging has been shown to greatly improve sensitivity and specificity⁽¹⁰⁾.

The purpose of the present study was to determine the response of necrotic fibroids to UAE and to identify whether pre-UAE enhancement or other factors are predictors of fibroid shrinkage

MATERIALS AND METHODS

This is a retrospective review of all women who underwent UAE for symptomatic fibroids between January 2012 and July 2017 with follow-up MRI at 5-6 months after the procedure, identified through a search of the departmental picture archiving and communication system. Mean follow-up period was 7.1 months. A total of 54 fibroids (37 non-enhancing and 17 enhancing) were analyzed in 24 patients ranging between 40-59 years of age with a mean age of 56 years. Fibroids analyzed ranged in size from 1.2-20.1 cm with a mean diameter of 6.4 cm. We should also mention that other ninety-one patients underwent UAE during this period, but did not have follow up imaging and were therefore excluded.

Uterine artery embolization

UAE was performed and procedures were performed with monitored anesthesia care. Access was obtained via the right common femoral artery, using a 5-Fr. introducer sheath (Cordis, Miami Lakes, FL); the anterior division of the internal iliac artery on each side was selected with a 5-French guiding Cobra catheter (Angiodynamics, Latham, NY). A 2.8-French ProGreatmicrocatheter (Terumo Interventional Systems, Somerset, NJ) was then directed into each uterine artery.

Embolization was carried out with 400-700-micron Embospheres (BioSphere Medical, Rockland, MA) until antegrade flow stasis. In addition to that, a completion peri-renal aortogram was done in order to root out ovarian artery supply to the uterus. Furthermore, all Patients were committed for at least one night of observation.

Image analysis

T1- and T2-weighted MR images were done within 1.5 months before UAE and at 5-6 months after UAE with and without gadolinium contrast enhancement.

For each fibroid, pre- and post-UAE size was determined by measuring the widest diameter on T2-weighted imaging. All fibroids measuring at least 2 cm were assessed for each patient. Fibroids were classified by position as either submucosal, intramural, or subserosal. T1-weighted signal intensity of each fibroid was recorded on dynamic contrast-enhanced subtraction MRI by placing a circular Region of Interest (ROI) over the axial or coronal slice with the largest cross-sectional area. Additionally, fibroids were characterized as non-enhancing or enhancing by subjective comparison of the fibroid to the myometrium on post-contrast images. Apparent Diffusion Constant (ADC) was determined for each pre-UAE fibroid with a corresponding ROI.

Statistical analysis

Statistical analysis was performed using Graph Pad Prism 6⁽¹¹⁾. Comparisons were made using paired Student's *t*-tests⁽¹²⁾ when variables were normally distributed and Mann-Whitney tests when variables were not normally distributed. A $p < 0.05$ was considered to be statistically significant. Percent fibroid enhancement pre-UAE was calculated by dividing the fibroid signal intensity by myometrial signal intensity on contrast-enhanced T1W imaging. Multiple linear regression was used to determine if fibroid enhancement, ADC value, fibroid size, fibroid location (intramural, subserosal, submucosal), and patient age were independent predictors of fibroid shrinkage after UAE. Data is presented as mean \pm standard error of the mean.

The study was done after approval of ethical board of King Abdulaziz university.

RESULTS

A total of 54 fibroids were assessed, 33 (61.1%) of which were intramural. ADC was, on average $697.6 \pm 54.7 \times 11^{-5}$ mm²/s.

Mean diameter was 54.8 ± 4.1 mm before UAE, and 42.0 ± 3.2 mm after UAE. Mean enhancement on subtraction MRI was 128.4 ± 16.1 SI before UAE and 3.7 ± 0.3 SI after UAE (Table 1).

Table 2: comparison between diameters and enhancement of pre-UAE and post-UAE

	Before UAE	After UAE
Mean diameter	54.8 ± 4.1	42.0 ± 3.2
Mean enhancement	128.4 ± 16.1 SI	3.7 ± 0.3 SI

Overall, fibroids decreased in diameter by $20 \pm 3\%$. Seventeen of which were non-enhancing. These fibroids decreased in diameter by $23 \pm 6\%$, whereas enhancing fibroids decreased by $19 \pm 3\%$ ($p=0.49$), (Table 2).

Table 2: Mean enhancement % for enhancing and non-enhancing fibroids

	Enhancing	Non-enhancing	P Value
Number of fibroids	37	17	p=0.49
Mean enhancement	$18 \pm 8\%$	$22 \pm 9\%$	

Next, multiple linear regression with percent change in fibroid diameter as the dependent variable and patient age, fibroid location (subserosal, submucosal or intramural) and pre-UAE fibroid diameter, enhancement and ADC as independent variables was performed. In a nutshell, only ADC ($p<0.05$) and pre-UAE diameter ($p<0.05$) were significant independent variables; smaller diameter and higher ADC were associated with greater decreases in size.

To elucidate, fibroids with a pre-UAE diameter greater than the median (47.9 mm) decreased in diameter by 16% whereas fibroids with a pre-UAE diameter less than the median decreased in diameter by 24% ($p=0.05$). In contrast, pre-UAE enhancement was not an independent predictor of post-UAE size diminution ($p=0.33$).

DISCUSSION

UAE is, at present, gaining acceptance as an alternative to hysterectomy or myomectomy in symptomatic women with uterine fibroids. Many

women appreciate the results that can be obtained with UAE: improvement or elimination of symptoms and reduction of uterine size, with maintenance of the uterus and preservation of fertility. In many studies the good long-term results and low complication rates of this treatment have been reported⁽¹³⁾. Despite these overall satisfying results, in the subgroup of patients with a large fibroid burden, a higher rate of serious ischemic, necrotic, and infectious complications is ascribed, based on several anecdotal reports⁽¹⁴⁾.

Our study adds to this literature by showing that non-enhancing and presumably necrotic fibroids respond to UAE, despite their relative avascularity. Therefore, women with necrotic fibroids should not be excluded from treatment. Though one may assume that embolization should be more effective for fibroids of greater vascularity, fibroids have particularly abnormal angiogenesis and vascularization patterns that are not completely understood. The avascular and hypoxic environment of fibroids is paradoxically associated with more pro-angiogenic factors⁽⁵⁾.

Our findings also suggest that ADC is an independent predictor of fibroid shrinkage. Fibroids with higher ADC values pre-UAE demonstrated greater shrinkage, which has been reported in other retrospective and prospective investigations⁽¹⁶⁾. It is unclear what the degree of diffusion restriction of water molecules signifies, but ADC provides some information about the molecular and/or cellular composition of masses including fibroids, and it may be useful in pre-UAE patient selection. We also found that smaller fibroid size predicted greater reduction after UAE, which is in contrast to other studies that showed either no correlation between fibroid size and volume reduction, or better response in larger fibroids⁽¹⁷⁾.

LIMITATION OF THE STUDY

- A single-center retrospective study
- The length of follow-up is also limited due to the practice of obtaining MRI imaging 6 months after embolization without the need for longer-term imaging.
- Primary marker of UAE response is restricted to fibroid size instead of clinical outcomes due to limited data availability in our medical database

CONCLUSION

We can conclude that Non-enhancing fibroids have a significant response to UAE, precisely in terms of size reduction. Moreover, MRI characteristics such as ADC values can better predict response to UAE. Particularly for women who either do not desire surgery or want to preserve fertility, UAE may be the best option and it is important not to withhold therapy without clear evidence of its inefficacy, in the setting of non-enhancement. These results suggest that physicians should reconsider excluding women with non-enhancing fibroids, as these patients may also benefit from embolization.

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