



## ORIGINAL ARTICLE

# Assessment of Post Therapeutic Response of Uterine Artery Embolization for Treatment of Uterine Fibroids

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### Abstract

**Background:** Uterine fibroids are the most common benign gynecological tumors with an incidence rate reaching approximately 70% of women in their reproductive age and may cause serious complications in more than 50% of the patients, including vaginal bleeding, anemia, chronic pelvic pain, dyspareunia, infertility as well as secondary pressure manifestations. Uterine artery embolization (UAE) is an effective and widely used modality in managing uterine fibroids given that it is minimally invasive in managing the condition and its associated serious complications.

**Methods:** A retrospective assessment of 41 patients who underwent UAE in a 4-year period (2016-2020) was performed. The study evaluated the value of this new technique in the Kingdom of Bahrain, King Hamad University Hospital and included a follow up of its therapeutic response by monitoring the symptomatic status and confirmation by quantitative volumetric measurement by pre and post procedure multi parametric MRI.

**Results:** Post-embolization MRI fibroid findings revealed an overall volume reduction rate (VRR) of 19.3% with statistically significant reduction in all outcome variables. Complete resolution of symptoms was reported by 80% of the patients.

**Conclusion:** Uterine artery embolization is an effective treatment option for uterine fibroids.

**Keywords:** Interventional radiology; MRI; Uterine artery embolization; Uterine fibroids; Uterine bleeding.

### Introduction

Uterine fibroid/leiomyoma is the most common benign tumor affecting the uterine myometrium, with an incidence rate of more than 70% among

American and Caucasian females.<sup>1</sup> Anatomically, fibroids usually involve the uterine myometrium but may also involve the cervix (<5% of cases).<sup>2</sup>

According to location, fibroids are sub-divided

into sub-mucosal, intramural and sub-serosal. Sub-mucosal fibroids are located beneath the uterine mucosa and are immediately adjacent or protrude into the uterine cavity.<sup>3</sup> Intramural fibroids are located totally within the uterine wall. Sub-serosal fibroids are located beneath the uterine serosa and alter the contour of the outer surface of the uterus.<sup>4</sup>

A hysterectomy was considered for a long time the first line of treatment; however, lately concerns have been raised about the overuse of this procedure.<sup>5</sup>

Uterine artery embolization (UAE) is now a well-established uterine preserving and minimally invasive therapy for symptomatic fibroids, as it introduces strong evidence for safety and efficacy with low complications rates.<sup>6</sup> The procedure is performed by an interventional radiologist through administration of embolization materials [such as polyvinyl alcohol particles (PVA), PVA microspheres and trisacryl gelatine microspheres (TAGM)] to occlude the uterine arteries. This is done by introducing a catheter through the femoral artery till the uterine arteries are reached under fluoroscopic guidance and this leads to a significant reduction of blood flow that reaches the tumor, causing ischemia and necrosis of the fibroid cells.<sup>7</sup>

Magnetic resonance imaging (MRI) has been proven to be the most accurate and reliable imaging tool that is currently used to monitor fibroid changes after UAE.<sup>4</sup> Reduction of size in different planes and the entire volume of the target lesion are considered as indicative morphological signs of procedural success.<sup>3</sup>

The current study was conducted aiming to monitor volume reduction in fibroids (both quantitatively and qualitatively) following UAE.

## Materials & methods

### Patients

This retrospective study included all female patients over a period of four years who underwent UAE on presentation with uterine fibroids of variable size and numbers at the department of interventional radiology. The entire study was conducted at King Hamad University Hospital, Kingdom of Bahrain.

**Inclusion criteria:** All patients who were referred to the interventional Radiology Department and

underwent UAE over a period of 4 years from August 2016 until August 2020 from the Obstetrics and Gynecology Outpatient Clinics and Vascular Intervention Unit were included in the study.

**Exclusion criteria:** Patients found to be referred for treatment of uterine bleeding and those referred for treatment of adenomyosis were excluded.

The study was approved by the hospital Institutional Review Board.

Tele-consultation was performed for qualitative assessment of symptoms where participants were asked to evaluate their response on a Likert scale ranging from: “completely resolved”, “much improved”, “mild improvement”, “no improvement”.

### UAE procedure technique

The technique was done under general anesthesia, arterial puncture and access through the common femoral artery was carried out bilaterally to reach the uterine arteries using catheters. This was followed by digital subtraction angiography of the internal iliac artery for imaging, following which selective catheterization of both uterine arteries was carried out. Catheterization of the uterine artery was done using a 4F or 5F cobra catheter and co-axial micro-catheter. Use of micro-catheters combined with guide wire manipulation of the uterine artery was done to reduce the incidence of spasm of the uterine artery. Following this the contrast agent was injected to confirm the position of the catheter and verify the lack of collateral vessels supplying the ovaries as this can cause iatrogenic embolization of the pelvic organs. If the fibroid was found to be receiving blood supply from the ovarian artery, selective micro-catheter embolization of the fibroids was done.

### Post – procedural management

Follow-up by MRI was requested at 3-6 months' interval following the procedure. MRI was done on a 3.0 Tesla MRI machine (Siemens Medical Systems, Germany) supplied by a phased array torso surface coil.

Conventional non-contrast MRI sequences were obtained in axial, sagittal and coronal planes, with the following parameters: T1-weighted imaging using in-phase and out-phase (TR/TE=10/4.6 ms,

flip angle=15°, section thickness=7 mm, intersection gap=2 mm, and field of vision (FOV)=300–350 mm), T2-weighted imaging (TR/TE=1000/80 ms, flip angle=90°, section thickness=7 mm, intersection gap=2 mm, and FOV=300–350 mm); T2 fat-suppression (SPAIR) (TR/TE=1000/80 ms, flip angle=90°, section thickness=7 mm, intersection gap=2 mm, and FOV=300–350 mm); and diffusion-weighted imaging, including b values of 0, 200, and 1000 (TR/TE=1700/76 ms, section thickness=7 mm, intersection gap=2 mm, and FOV=300–350 mm).

MRI post contrast dynamic study was carried out in axial, sagittal and coronal planes. 3D fat-suppression T1-weighted images gradient echo sequences were obtained using the following parameters: TR/TE=4.6/2.3 ms, flip angle=15°, number of slices=130–140, section thickness=3 mm, intersection gap=1.5 mm, and FOV=300–350 mm. Unenhanced data set was first obtained before contrast injection. Injection of intravenous bolus of 0.1 mmol/kg body weight of Gadolinium-DTPA (Magnavist; Schering, Berlin, Germany) was started at a rate of 2 ml/s using an automatic injector.

**Imaging analysis:** The review of all pre and post-contrast MRI was performed on Medavis Unit workstation, utilizing the commercially available software (Medavis Medical Systems) by a clinical radiologist with more than 10 years of experience in cross-sectional MRI. Conventional MR images were assessed and the lesions were located and characterized in axial, sagittal and coronal planes according to their number, size and volume. T1 weighted images Pre and Post contrast series were reviewed for patterns of enhancement and heterogeneity. Overall volume reduction rate (VRR) was calculated as: (calculated volume pre–calculated volume post)/ calculated volume pre \* 100%.

## Data analysis

Collection, revision, coding, tabulation and analysis of data were done using the Statistical Package for Social Science (IBM SPSS) version 25. Presentation of Quantitative data as mean, standard deviations and ranges and presentation of categorical variables as number and percentages were done. **Chi-square test** was used in the comparison between two groups

with categorical data and **Fisher exact test** was used instead of the Chi-square test when the expected count in any cell was less than 5. Student t-test was used to determine the significant differences in the continuous scores. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the *p*-value was considered significant at the level of < 0.05 and highly significant at the level of < 0.01.

## Results

The current study retrospectively reviewed data of 41 patients, of mean age  $40.90 \pm 9.55$  years, whose socio-demographic data is illustrated in Table 1.

**Table 1:** Socio-demographic data of patients:

	No. (%)
<b>Nationality</b>	
Bahraini	34 (82.9%)
Non-Bahraini	6 (14.7%)
<b>Marital Status</b>	
Single	15 (36.5%)
Married	20 (48.7%)
Divorced	3 (7.3%)
Widowed	2 (4.8%)
<b>Family History</b>	
Positive	16 (39.0 %)
Negative	24 (58.5 %)
<b>Previous Surgery</b>	
Yes	17 (41.4%)
No	23 (56.1%)

Seventeen (42.5%) of the included patients had a single fibroid, 6 (15%) of them had 2 fibroids, 4 (10%) of them had 3 fibroids and 13 (32.5%) of them had more than 3 fibroids. A mean VRR of  $61.14 \pm 12.6$  was found. Their pre- and post-embolization findings are shown in table 2.

**Table 2:** Pre- and post- embolization MRI fibroid findings:

	Pre-op (Mean± SD)	Post-op (Mean± SD)
<b>AP diameter (mm)</b>	72.45± 22.28	49.36 ± 31.66
<b>TR diameter (mm)</b>	72.91±29.99	47.63 ± 32.97
<b>CC diameter (mm)</b>	79.27±33.22	48.90 ± 33.12
<b>volume (CC)</b>	296.18±295.29	128.70 ± 152.83
<b>VRR</b>	61.14±12.6	

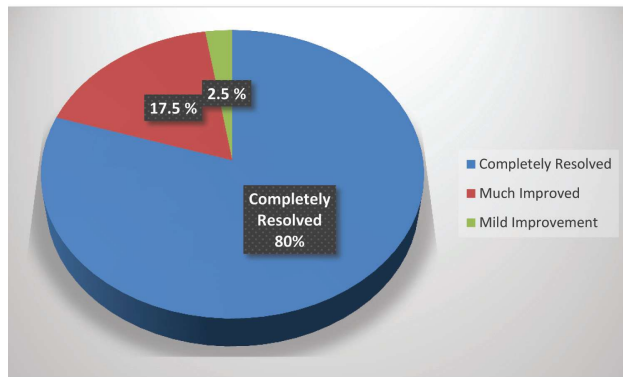
AP, Antero-posterior; TR, Transverse; CC, Cranio-caudal

Post-embolization MRI fibroid findings revealed an overall VRR of 19.3% with statistically significant reduction in all outcome variables (Table 3).

**Table 3:** Post-embolization MRI fibroid findings:

	Mean Difference	P value
AP Diameter (post-op – pre-op)	-23.09 (18.00)	0.002
TR diameter (post-op – pre-op)	-25.27 (11.02)	<0.001
CC diameter (post-op – pre-op)	-30.36 (13.05)	<0.001
volume CC (post-op – pre-op)	-167.60 (145.29)	0.003

Tele-consultation for monitoring of patients' symptom status revealed that 32 (80%) of the cases reported that their condition had "completely resolved", 7 (17.5%) of them reported that their condition had "much improved" and 1 (2.5%) of them reported that she had "mild improvement" (figure 1).



**Figure -1:** A diagram illustrating the symptoms status as reported by the patients.

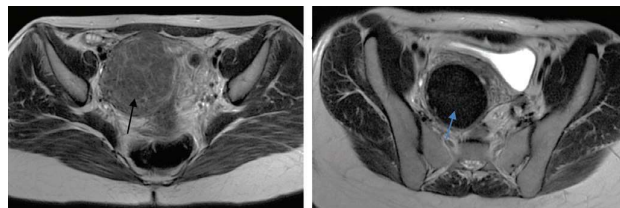
## Discussion

Uterine fibroids (myomas or leiomyomas) are the most common benign tumors among women.<sup>8</sup> Uterine fibroids are benign, monoclonal tumors of the smooth muscle cells found in the uterus.<sup>9</sup> Despite the fact that their cause is still unknown, there is considerable evidence that estrogens and progestogens proliferate tumor growth as the fibroids rarely appear before menarche and regress after menopause.<sup>10</sup>

Therapeutic options to treat uterine fibroids include medical therapy, surgical interventions and UAE.<sup>11</sup> UAE is usually performed by an interventional radiologist and has been reported to be an effective

and safe method for treatment of fibroids.<sup>12, 13</sup> The goal of therapy in UAE is to relieve symptoms and symptom improvement from fibroid tumor therapy is consistent with tumor regression. A retrospective review of 84 fibroids treated over one year showed an average decrease in size of 60% among the patients. Sub-mucosally located fibroids showed greatest shrinkage, while sub-serosally located fibroids showed the least.<sup>5</sup>

The utility of MRI for pre- and post-UAE procedural evaluation is well documented and provides a reliable method to assess the size and location of fibroids pre-treatment as well as to visualize UAE outcomes. Fibroid infarction percentage on MRI has been shown to predict clinical outcome and early UAE treatment failure is often due to incomplete fibroid infarction.<sup>14</sup> (Figure 2)



**Figure -2:** On the left side (black arrow) axial T2 WI before treatment shows large right lateral wall intra-mural uterine fibroid and at the right side (blue arrow) axial T2 WI after treatment shows regression of size with infarction and total tissue necrosis of the target fibroid.

This study was conducted to monitor volume reduction in fibroids (both quantitatively and qualitatively) following UAE.

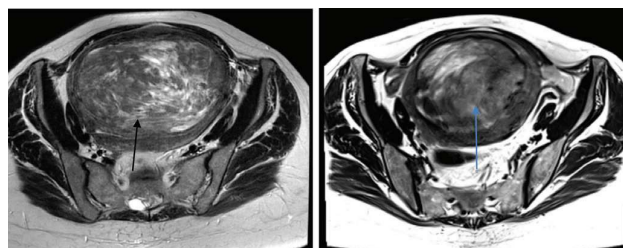
The current study included 41 patients whose mean age was  $40.90 \pm 9.55$  years which is lower when compared to a previous study which included 24 women with an average age of 52 years and the difference could be attributed to different inclusion criteria as their study included patients meeting the stages of reproductive age group criteria for menopause.<sup>15</sup> The incidence of uterine fibroids is known to increase with age through the reproductive years and decline in the postmenopausal years.<sup>16</sup> A study with randomly selected women between 35 to 49 years, who were screened by self-report, medical record and sonography revealed that the incidence of uterine fibroids by age 35 was 60%

among African-American women, increasing to > 80% by age 50, whereas Caucasian women showed an incidence of 40% by age 35 and almost 70% by age 50.<sup>17</sup>

The current study revealed that 36.5% of the patients were unmarried, 48.7% of them were married, 7.3% of them were divorced and 4.8% of them were widowed. The relationship between marital status and uterine fibroids is multi-faceted. Fibroids have been found to be associated with deep dyspareunia. However, the association may not be causal but may reflect shared etiology and/or pathologic pathways.<sup>18</sup> On the other hand, it is also biologically plausible that stress can lead to fibroids as a result of fluctuations in estrogen and progesterone hormone levels, both important in fibroid development, caused by stress activation of the hypothalamic pituitary adrenal axis and the subsequent release of cortisol, a stress hormone.<sup>19</sup>

The current study revealed that family history was positive in 39% of the included patients, this finding is relatively higher than results of *Vikhlyeva et al* in which it was 24%.<sup>20</sup>

Post-embolization MRI fibroid findings in the current study revealed a mean VRR of  $61.14 \pm 12.6$  with an overall VRR of 19.3 % with statistically significant reduction in all outcome variables (figure-3). Complete vanishing of the target fibroids was also noted in two cases with total remission of the presenting symptoms ( figure - 4 ). These findings are in line with those of *Chrisman et al.* as they reported significant reduction of both mean uterine volume and mean dominant uterine fibroid volume following UAE.<sup>15</sup> Similarly, *Korashi et al.* reported that MRI showed highly significant reduction in uterine as well as dominant fibroid volumes post-UAE.<sup>21</sup>



**Figure -3:** On the left side axial (black arrow) T2 WI before treatment shows large intra-uterine sub-mucosal fibroid and at the right side (blue arrow)

axial T2 WI after treatment shows regression of size and increased tissue necrosis of the target fibroid.



**Figure-4:** On the left side (black arrow) sagittal T2 WI before treatment shows large uterine cervix sub-mucosal fibroid surrounded by uterine bleeding and at the right side (blue arrow) axial T2 WI after treatment shows complete resolution of the target fibroid.

The current study revealed also that 80% of patients reported that they had “completely resolved”, 17.5% of them reported that they had “much improved” and 2.5% of them reported that they had “mild improvement”. It was reported that for women with ideal procedure selection characteristics, a high symptom control rate, procedure satisfaction rate and self-reported quality of life rate can be achieved for up to 10 years after treatment. Furthermore , about 90% of women would experience a reduction in bulk symptoms and more than 90% could expect elimination of abnormal uterine bleeding following UAE.<sup>22</sup> Findings of the current study are in line with those published by *Smith et al.* as they utilized a validated , fibroid specific , symptom severity and health-related quality of life (HRQOL) questionnaire that was mailed to 80 women who had undergone UAE and reported that women who undergo UAE have a significant decrease in symptom severity and increase in HRQOL, associated with high levels of satisfaction with the procedure.<sup>23</sup> However, these findings are slightly different from those published by *Chrisman et al.* as they reported that clinical success (defined as a qualitative reduction in bulk symptoms) was achieved in 92% of their patients following UAE and the difference between results might be explained by the different baseline criteria and symptom severity in the included patients as well as by the different methods and time-points for assessment of improvement.<sup>15</sup> The findings regarding the VRR also differ from those published

by *Toor et al.*<sup>3</sup> They reported clinical failure and poor results in volume reduction of UAE especially in large sub-serosal pedunculated fibroids which is seen in this study. Meanwhile *Kim et al* reported poor therapeutic response and poor volume reduction results in cervical leiomyomas due to poor vascularity which is incidentally contrasting to this study in two patients, one of them in the follow up MRI showed entirely infarcted and completely resolved cervical fibroid (figure-4).<sup>2</sup>

Regarding the long term complications of UAE, a five year follow up study by *Yoon et al.* indicated a higher risk of reintervention following UAE due to the presence of viable non-dominant leiomyoma.<sup>24</sup> A previous study by *Mukherjee et al.* indicated that the most common complaint following embolization was pelvic pain that could be managed conservatively.<sup>25</sup> *Ghiaroni et al.* in their study indicated a potential negative effect of UAE on reducing the ovarian function, especially in older patients in which menopause can occur earlier than expected.<sup>26</sup> A randomized trial by *de Bruijn et al.* indicated that in long-term follow-up (median of 11 years), secondary hysterectomy was required in 35% of patients who underwent UAE.<sup>27</sup>

There are several limitations in this study. It is retrospective and comprises of a small sample size thus not all outcome possibilities could have occurred. Long-term complications including effect on fertility in reproductive age group patients were not included due to fall outs in clinical follow up due to novel Coronavirus 2019 (COVID-19) outbreak and limitation of access to the out-patients' clinic for all elective cases for a long period. No biochemical assessment of hormonal impact following UAE was performed and hence the long-term effect on ovarian function and menopausal state are unknown.

## Conclusion

UAE should be considered as an effective treatment option for uterine fibroids.

## Conflicts of Interest

The authors declare that they have no competing interests.

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