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UROGENITAL

Diffusion-weighted MR imaging of uterine leiomyomas following uterine artery embolization

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Abstract

Purpose To test whether variations in apparent diffusion coefficient (ADC) values of uterine leiomyomas after uterine artery embolization (UAE) may correlate with outcome and assess the effects of UAE on leiomyomas and normal myometrium with magnetic resonance imaging (MRI).

Methods Data of 49 women who underwent pelvic MRI before and after UAE were retrospectively reviewed. Uterine and leiomyoma volumes, ADC values of leiomyomas, and normal myometrium were calculated before and after UAE.

Results By comparison with baseline ADC values, a significant drop in leiomyoma ADC was found at 6-month post-UAE (1.096×10^{-3} mm^2/s vs. 0.712×10^{-3} mm^2/s, respectively; $p < 0.0001$), but not at 48-h post-UAE. Leiomyoma devascularization was complete in 40/49 women (82 %) at 48 h and in 37/49 women (76 %) at 6 months. Volume reduction and leiomyoma ADC values at 6 months correlated with the degree of devascularization. There was a significant drop in myometrium ADC after UAE. Perfusion defect of the myometrium was observed at 48 h in 14/49 women (28.5 %) in association with higher degrees of leiomyoma devascularization.

Conclusion Six months after UAE, drop in leiomyoma ADC values and volume reduction correlate with the degree of leiomyoma devascularization. UAE affects the myometrium as evidenced by a drop in ADC values and initial myometrial perfusion defect.

Key Points

- *A drop in leiomyoma ADC values is observed 6 months after UAE.*
- *Drop in leiomyoma ADC value is associated with leiomyoma devascularizarion after UAE.*
- *MR 48 h post-UAE allows assessing leiomyoma devascularization.*
- *Myometrium perfusion defect occurs more often in women with a smaller uterus.*

Keywords Uterine artery embolization · Diffusion-weighted imaging · Magnetic resonance imaging · Leiomyomas · Myometrium ischemia

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Introduction

Uterine artery embolization (UAE) is a well-established treatment for symptomatic uterine leiomyomas that can be used alone or in combination with surgery [1–6]. Determination of the most appropriate therapeutic option requires an accurate evaluation that is currently best performed using magnetic resonance (MR) imaging [7]. In this regard, MR imaging is a reliable and reproducible technique for the initial assessment, multidisciplinary decisions, and follow-up after UAE of uterine leiomyomas [8–10].

Diffusion-weighted (DW) MR imaging with apparent diffusion coefficient (ADC) calculation provides functional

information on microscopic water molecule motions in tissue, which correlates with cellularity, water content, and microvascular perfusion [11–14]. DW-MR imaging has demonstrated utility in various areas including abdominal and pelvic imaging for the initial diagnosis and therapeutic evaluation of a wide range of pathologic conditions [15–21].

Recent publications have reported marked variations in signal intensity of uterine leiomyomas on DW-MR imaging after UAE along with a drop in ADC values. However, no studies were able to definitely demonstrate a correlation or association between variations in DW-MR imaging features and outcome [22–24].

The goal of our study was to test whether variations in ADC values of uterine leiomyomas after UAE may correlate with outcome and the role of an early MR examination including DW-MR imaging to assess the effects of UAE on leiomyomas and normal myometrium.

Materials and methods

Patients

The files of all consecutive women with symptomatic leiomyomas who were treated using UAE in our department between August 2008 and June 2012 inclusively and who had had three MRI examinations (before UAE, at 48 h post-UAE, and at 6 months post-UAE) including DW-MR imaging were retrospectively reviewed. This initial cohort consisted of 69 women. Among them, 20 women were excluded because they had combined treatment (that included UAE and surgery at the same time). The final cohort consisted of 49 women. They had a mean age of 41.4 years ± 5.4 years (SD) (range; 35-54 years). No women were menopausal or postmenopausal. Decision to perform UAE was taken during multidisciplinary meetings with the participation of gynaecologists, radiologists and interventional radiologists.

All included women were treated with UAE alone. This retrospective study had institutional review board approval.

MR imaging

All women had MR imaging examinations before UAE (mean: 17 weeks, range:1-36 weeks), 48 h post-UAE and 6 months post-UAE. All women underwent MR imaging examination of the pelvis using a 1.5-T system (Magnetom Avanto®, Siemens Healthcare, Erlangen, Germany; running software Syngo MR VB17). All MR imaging examinations were performed with 18 receiver channels and using one anterior torso phased-array coil with six channels and two posterior spine clusters with three channels each, with the woman in supine position. All women had T2-weighted fast spin-echo (FSE) MR imaging in the transverse and sagittal planes, DW-MR imaging sequences using *b* values of 0, 500, and 1000 s/mm^2 in the sagittal plane and T1-weighted three-dimensional gradient-echo sequence (3D VIBE®) with fat suppression, in the transverse and sagittal planes, before and after intravenous administration of gadoterate meglumine (Dotarem®, Guerbet, Roissy-Charles de Gaulle, France) at a dose of 0.2 mL/kg. MR imaging parameters are reported in Table 1. The ADC value

Table 1 Imaging parameters for MR imaging

Parameters	Sequence		
Sequence name	T2-weighted FSE	DW	3D VIBE
TR (ms)	5510	3000	6.1
TE (ms)	141	91	2.75
Flip angle (°)	90	90, 180	15
Number of signal averages	1	4	1
Reconstruction matrix size	448x448	192 × 192	174 × 192
Section thickness (mm)	6	5	1.8
Intersection gap (mm)	1.2	0.5	0.36
Voxel size (mm^3)	0.7 × 0.7 × 6	2.1 × 2 × 5	1.5 × 1.5 × 1.8
Field of view (mm)	300	380	280
Echo train length	28	*N.A.*	*N.A.*
Echo spacing (ms)	10.9	0.85	*N.A.*
Echo-planar imaging factor	*N.A.*	131	*N.A.*
Number of sections acquired	20	20	80
Acquisition time (s)	100	95	24

Note. *N.A.* indicates not applicable. *FSE* indicates fast spin-echo. *DW* indicates diffusion-weighted MR imaging. *3D VIBE* indicates three-dimensional volume interpolated breath-hold imaging and was obtained with fat suppression.

was calculated using three b values ($b = 0$, 500, 1000 s/mm^2) with the implemented software (Syngo, Siemens Healthcare, Erlangen, Germany).

Uterine artery embolization protocol

Pelvic digital subtraction angiography was performed using a right-sided unifemoral approach with a 5-Fr cobra-shaped catheter (Cobra Radifocus®, Terumo Medical Corporation, Tokyo, Japan) and a hydrophilic 0.032-inch angled guidewire (Radifocus®, Terumo Medical Corporation). Left and right internal iliac artery angiography and selective study of the anterior division of the left and right iliac arteries was performed to localize the origin of the left and right uterine arteries as previously described [1, 25, 26]. Superselective catheterisation of uterine arteries was performed with a 2.7-Fr microcatheter (Progreat®, Terumo Medical Corporation, Tokyo, Japan).

Angiographic images obtained before UAE were carefully analyzed and presence of utero-ovarian anastomosis was carefully searched for [26]. UAE was performed with trisacryl microspheres (EmboSphere®, BioSphere Medical, Louvres, France) with a diameter of 500-700 μm and 700-900 μm using a free-flow technique under fluoroscopic guidance. The choice of microspheres diameter was made by the interventional radiologist during the procedure. Embolization was stopped when stasis or near stasis was observed in the ascending segment of the uterine artery. Microspheres with a calibre of 700-900 μm were used when the angiographic end-point was not reached in the case of large and multiple leiomyomas despite the injection of 6 to 8 mL of 500-700 μm microspheres in the uterine artery. Microspheres with a diameter of 700-900 μm were also used as first option when an utero-ovarian anastomosis was identified [27].

Image analysis

MR imaging examinations were evaluated by two radiologists on a picture archiving and communication system (PACS) viewing station (DirectView®, 11.3sp1 version, Carestream Health Inc., Rochester, NY, USA) using a standardized data collection form created for the study including all the information further described. The two radiologists worked independently for assessing inter-observer reproducibility. Reader 1 was a third-year radiology resident, and reader 2 was a radiologist with an experience of 6 years in pelvic MRI at the time of data analysis.

ADC value measurement of dominant leiomyoma, normal myometrium, and psoas muscle was obtained by placing a region of interest (ROI) on DW-MR images obtained with $b = 0$ s/mm^2 and were then transferred from the $b = 0$ images to the ADC maps by using the "copy-and-paste" function of the workstation.

ADC value of dominant leiomyoma was measured by each observer using circular ROIs that were manually drawn on DW-MR images obtained with $b = 0$ s/mm^2. ROIs were placed over the section encompassing as much as possible leiomyoma, but excluding the periphery of the leiomyoma to avoid possible partial volume effect. Cystic or necrotic parts of leiomyoma identified by high signal intensity on T2-weighted MR images and low signal intensity on T1-weighted MR images were excluded from the ROI. ADC values of the myometrium and psoas muscle were obtained with ROIs with a minimum size of 100 pixels. Parametric ADC map was generated with the integrated Syngo software using a mono-exponential model. All b values were used for ADC calculation. The resulting ADC was the ADC_{total}, which included perfusion and true diffusion effects [18].

A normalized ADC value of leiomyomas (ADC_N) was further calculated using the psoas muscle as a reference organ using the following formula $ADC_N = ADC_L/ADC_P$, where ADC_L represents the ADC of the leiomyoma and ADC_P the ADC of the psoas muscle.

Dominant leiomyoma volume was determined with the following formula: $A \times B \times C \times 0.52$, where A, B, and C represent the dimensions in the three planes assuming that the leiomyoma had an ellipsoid shape. Uterine volume was estimated using the same formula: $H \times T \times W \times 0.52$, where H represents the height, T the thickness, and W the width of the uterus. The second observer used a semi-automated segmentation method integrated in the PACS system on contrast-enhanced 3D VIBE MR images (LiveWire software, Carestream Health Inc., Rochester, NY, USA).

Devascularization of the dominant leiomyoma was visually graded semi-quantitatively on 3D VIBE MR images obtained 30, 60, 120, and 180 s after intravenous administration of gadolinium chelate at 48 h and 6 months after UAE and women were further divided into three different groups depending on the degree of leiomyoma devascularization [6, 28–30]. Group 1 consisted of women with complete (100 %) dominant leiomyoma devascularization (i.e., when there was only a peripheral rim of enhancement corresponding to normal myometrium, without internal enhancement of the leiomyoma) (Fig. 1). Group 2 consisted of women with almost complete (99-90 %) dominant leiomyoma devascularization (i.e., with persisting enhancement involving less than 10 % of the leiomyoma) (Fig. 2). Group 3 consisted of women with incomplete (89-0 %) dominant leiomyoma devascularization (i.e., with persistent contrast enhancement involving more than 10 % of the leiomyoma) (Fig. 3). Leiomyoma enhancement was evaluated on contrast-enhanced 3D VIBE MR images obtained at 30 and 60 s.

At the 48-h post-UAE MR examination, "myometrium ischemia" was searched for, and women were further categorized into two groups according to the presence or absence of this finding [31, 32]. Myometrium ischemia was defined as

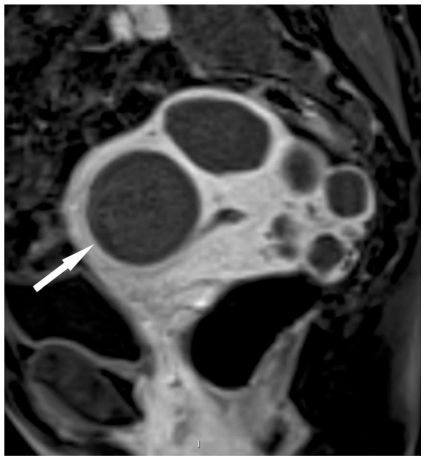

Fig. 1 48-year-old woman who had uterine artery embolization (UAE) for symptomatic uterine leiomyomas. Gadolinium chelate-enhanced, T1-weighted, three-dimensional gradient echo (3D-VIBE®) sequence in the sagittal plane shows complete (100 %) devascularization of the dominant leiomyoma (*arrow*) on the 48-h post-UAE MR imaging

perfusion defect of the myometrium in association with leiomyomas devascularization. This myometrium ischemia was considered significant when reaching junctional zone and/or exceeding the junctional zone on contrast-enhanced MR images obtained 60 s after intravenous administration of gadolinium chelate [31, 32]. Pre-UAE MR examinations were used to differentiate between post-UAE focal myometrium perfusion defects and intramural leiomyoma with complete devascularization.

The signal intensity of the dominant leiomyoma was evaluated on MR imaging examinations obtained before and 6 months post-UAE on T1- and T2-weighted MR images and dominant leiomyomas were further categorized into three types as follows [33]: Type 1 consisted of "typical leiomyomas" (i.e., with low signal intensity relative to the myometrium on T2-weighted MR images). Type 2 consisted of "degenerated leiomyomas" (i.e., with cystic or necrotic areas displaying high signal intensity on T2-weighted MR images with no enhancement on 3D VIBE images obtained after gadolinium-chelate administration). Type 3 consisted of "high cellularity leiomyomas" (i.e., with high signal intensity relative to the myometrium on T2-weighted MR images and intense enhancement on 3D VIBE images obtained after gadolinium-chelate administration).

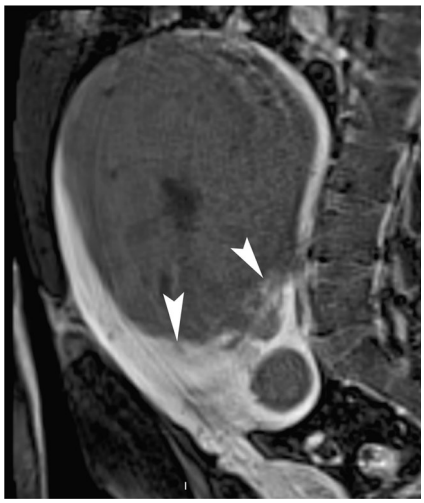

Fig. 2 35-year-old woman who had uterine artery embolization (UAE) for symptomatic uterine leiomyomas. Gadolinium chelate-enhanced 3D-VIBE® sequence in the sagittal plane shows almost complete (90-99 %) devascularization of the dominant leiomyoma on the 48-h post-UAE MR imaging with persisting enhancement of less than 10 % of the leiomyoma volume (*arrowheads*)

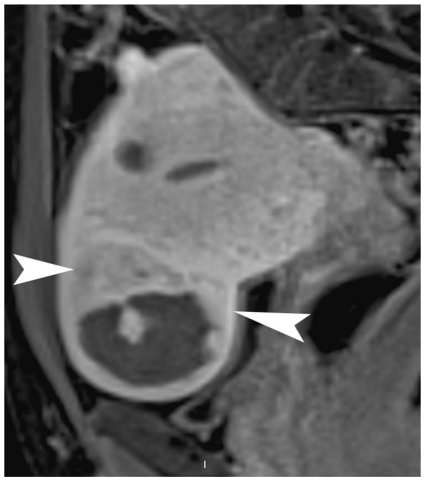

Fig. 3 38-year-old woman who had uterine artery embolization (UAE) for symptomatic uterine leiomyomas. Gadolinium chelate-enhanced 3D-VIBE® sequence in the sagittal plane shows incomplete (0-89 % devascularization of the dominant leiomyoma on the 48-h post-UAE MR imaging. There is a persisting enhancement of more than 10 % of the leiomyoma volume (*arrowheads*)

Statistical analysis

Statistical analysis was performed using software (SAS, version 9.2, SAS Institute, Cary, NC, USA; R, version 2.8, R Foundation, http://www.r-project.org/).

Qualitative variables were expressed as raw numbers, proportions, and percentages. Quantitative variables were expressed as mean, median, first quartile (q1), third quartile (q3), standard deviation (SD), and range.

For inter-observer agreement, the mean difference, 95 % limits-of-agreement, and the intraclass correlation coefficient using the two-way random single measures method were calculated. Bland–Altman plots were used to determine whether the difference was influenced by the magnitude of the measurements [34, 35]. ADC values, uterine volumes, and dominant leiomyoma volumes obtained at different time points were compared using the paired Student's *t*-test when the variables were normally distributed. Normality of distribution was assessed using the Shapiro-Wilk test. Comparison of ADC values, dominant leiomyoma volumes and uterine

volumes between the three leiomyoma devascularization groups (1, 2, and 3) were made using the Kruskal-Wallis test. Correlation between volume reduction and ADC values obtained at 6 months post-UAE was searched for using the Pearson correlation test. A p value <0.05 was considered to indicate significance.

Results

Overall results

No women were excluded because of artefacts on MR imaging examinations. Mean volumes of the uterus and dominant leiomyoma, ADC and ADC_N values of dominant leiomyoma, myometrium ADC value for each reader and degree of dominant leiomyoma devascularization on MR imaging are reported in Table 2. At 6 months post-UAE, by comparison with the initial volumes, MR imaging examination showed significant drop in uterine volume for both readers (811 cm^3 vs. 561 cm^3, and 809 cm^3 vs. 546 cm^3, respectively; $p<0.00001$) and in dominant leiomyoma volume (177 cm^3 vs. 110 cm^3, and 180 cm^3 vs. 113 cm^3, respectively; $p<0.0001$), with an average volume reduction of 36 %±21 (SD) for uterine volume and 41 %±26 (SD) for dominant leiomyoma volume.

ADC and ADC_N values of dominant leiomyoma dropped significantly at 6 months post-UAE by comparison with pre-UAE ADC and pre-UAE ADC_N values for both readers (1.096×10^{-3} mm^2/s vs. 0.712×10^{-3} mm^2/s; $p<0.0001$, and 1.958×10^{-3} mm^2/s vs. 1.101×10^{-3} mm^2/s; $p=0.0001$, respectively) (Table 2) (Fig. 4). However, no differences were found between pre-UAE ADC and pre-UAE ADC_N values and those obtained at 48 h post-UAE for either readers. ADC values of the myometrium dropped significantly at 48 h and 6 months by comparison with pre-UAE ADC values for both readers ($p<0.0001$) (Table 2).

No correlations were found between the drop in ADC values in dominant leiomyomas and volume reduction of the uterus at 6 months post-UAE with the semi-automated method ($\rho=0.01$; $p=0.93$). Similarly, there was no correlation between the drop in ADC values of dominant leiomyomas and their volume reduction ($\rho=0.15$; $p=0.31$).

On T2-weighted MR images, no changes in signal intensity of dominant leiomyoma were observed on 48 h post-UAE images by comparison to pre-UAE findings in all women.

On T1-weighted MR images, all dominant leiomyomas showed high signal intensity at 48 h post-UAE that decreased at 6 months post-UAE.

Inter-observer agreement

Table 3 shows the interobserver agreement for measures of volumes and ADC between the two readers. Reader 1 measured volumes with the formula (H × T × W × 0.52) and reader 2 used the semi-automatic segmentation method. Volume measurements with the two methods demonstrated excellent reproducibility between the two techniques. The ICC for baseline and 6 months post-UAE measures was excellent ranging from 0.972 to 0.998, with the Bland–Altman plot showing narrow 95 % limits-of-agreement and almost all differences situated around 0 (Fig. 5). The Bland–Altman plot showing narrow 95 % limits-of-agreement and almost all differences situated around 0 (Fig. 6).

Subgroup analysis

Response to UAE according to the degree of devascularization At 48 h post-UAE, MR imaging examination showed complete dominant leiomyoma devascularization in 40/49 women (82 %), almost complete in 2/49 women (4 %), and incomplete in 7/49 women (14 %). Table 4 shows ADC and ADC_N values, uterine and dominant leiomyoma volumes, and volume variation according to the degree of devascularization at 48 h post-UAE for reader 1.

At 6 months post-UAE, dominant leiomyoma devascularization was complete in 37/49 women (76 %), almost complete in 3/49 women (6 %), and incomplete in 9/49 women (18 %). Table 5 shows ADC and ADC_N values, uterine and dominant leiomyoma volumes, and volume variation according to the degree of devascularization at 6 months post-UAE for reader 1.

A significant association was found between uterine volume reduction at 6 months post-UAE and the degree of dominant leiomyoma devascularization at 48 h ($p=0.008$) and 6 months ($p=0.0056$) post-UAE (Tables 4 and 5). Significant differences in ADC and ADC_N values of dominant leiomyoma were observed at 48 h and 6 months post-UAE between the three groups of women based on the degree of devascularization.

Myometrium ischemia

At 48 h post-UAE, myometrium perfusion defect indicating "myometrium ischemia" was observed in 14/49 women (28.5 %), whereas 35/49 women (71.5 %) had complete myometrium enhancement (Fig. 7) (Table 6). A significantly smaller initial uterine volume was observed in this subset of women with myometrium ischemia by comparison with those who did not show this finding (481 cm^3 vs. 943 cm^3, respectively; $p=0.04$).

At 6 months post-UAE, complete devascularization of dominant leiomyoma was observed in 14/14 women (100 %) with myometrium ischemia and in 23/35 women (66 %) without myometrium ischemia ($p=0.01$). However, no significant differences in uterine volume reduction were found between these two groups of women ($p=0.07$). In the

Table 2 Variables in 49 women with leiomyomas treated by UAE on three different MR examinations

	Baseline	48-h post-UAE	6-month post-UAE	*p* values	
				Pre-UAE vs. 48 h	Pre-UAE vs. 6 months
Uterine volume (reader 1)					
Mean ± SD	811 ± 1106	N.M.	561 ± 947	N.A.	**<0.001**
Range	[145-7589]	N.M.	[58-6511]		
Median [q1-q3]	593 [381-772]	N.M.	349 [205-506]		
Uterus volume (reader 2)					
Mean ± SD	809 ± 929	N.M.	546 ± 706	N.A.	**<0.001**
Range	[165-6309]	N.M.	[66-4628]		
Median [q1-q3]	591 [425-882]	N.M.	374 [230-528]		
Dominant leiomyoma volume (reader 1)					
Mean ± SD	177 ± 291	N.M.	110 ± 216	N.A.	**<0.001**
Range	[6-1783]	N.M.	[1-1374]		
Median [q1-q3]	64 [36-204]	N.M.	42 [10-121]		
Dominant leiomyoma volume (reader 2)					
Mean ± SD	180 ± 300	N.M.	113 ± 219	N.A.	**<0.001**
Range	[6-1909]	N.M.	[2-1404]		
Median [q1-q3]	71 [41-201]	N.M.	41 [14-124]		
Myometrium ADC (reader 1)					
Mean ± SD	1.840 ± 0.197	1.570 ± 0.209	1.626 ± 0.181	**<0.001**	**<0.001**
Range	[1.504-2.232]	[1.124-1.990]	[1.368-2.064]		
Median	1.874	1.571	1.618		
[q1-q3]	[1.696-1.950]	[1.418-1.725]	[1.489-1.716]		
Myometrium ADC (reader 2)					
Mean ± SD	1.786 ± 0.216	1.566 ± 0.233	1.605 ± 0.194	**<0.001**	**<0.001**
Range	[1.353-2.426]	[1.142-2.043]	[1.285-2.108]		
Median	1.766	1.595	1.573		
[q1-q3]	[1.620-1.916]	[1.391-1.707]	[1.478-1.702]		
Dominant leiomyoma ADC (reader 1)					
Mean ± SD	1.096 ± 0.212	1.051 ± 0.174	0.712 ± 0.375	0.199	**<0.001**
Range	[0.642-1.634]	[0.737-1.550]	[0.172-1.522]		
Median	1.087	1.046	0.703		
[q1-q3]	[0.980-1.252]	[0.931-1.163]	[0.393-0.986]		
Dominant leiomyoma ADC (reader 2)					
Mean ± SD	1.113 ± 0.241	1.059 ± 0.183	0.751 ± 0.389	0.159	**<0.001**
Range	[0.513-1.711]	[0.770-1.517]	[0.172-1.522]		
Median	1.107	1.024	0.748		
[q1-q3]	[1.004-1.253]	[0.926-1.143]	[0.397-1.067]		
Normalized ADC (reader 1)					
Mean ± SD	1.958 ± 1.355	1.752 ± 0.793	1.101 ± 0.602	0.154	**0.001**
Range	[0.989-9.962]	[0.945-5.211]	[0.246-2.591]		
Median	1.754	1.504	0.912		
[q1-q3]	[1.272-2.084]	[1.190-2.009]	[0.690-1.503]		
Normalized ADC (reader 2)					
Mean ± SD	2.108 ± 1.751	1.776 ± 0.733	1.181 ± 0.619	0.114	**0.001**
Range	[0.833-12.641]	[0.981-4.495]	[0.302-2.870]		
Median	1.667	1.497	1.135		
[q1-q3]	[1.375-2.220]	[1.280-2.310]	[0.665-1.568]		
Dominant leiomyoma devascularization					
100 %	N.A.	40	37		
90-90 %	N.A.	2	3		
0-8 9 %	N.A.	7	9		

Note. *SD* indicates standard deviation. *N.M.* indicates not measured. *N.A.* indicates not applicable. Uterine and dominant leiomyoma volume are expressed in cm^3. Normal myometrium and dominant leiomyoma ADC is expressed in $\times 10^{-3}$ mm^2/s. Statistical analysis were performed using a paired Student's *t*-test

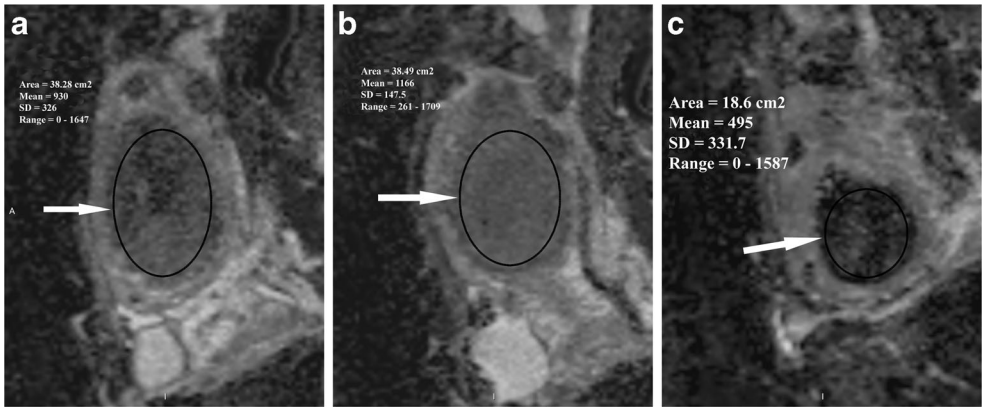

Fig. 4 41-year-old woman who underwent uterine artery embolization (UAE) for symptomatic leiomyomas. ADC maps in the sagittal plane were obtained before UAE (**a**), at 48 h (**b**), and 6 months (**c**) after UAE. There is a drop in dominant leiomyoma (*arrows*) ADC value on the 6-month MR examination compared to baseline (0.495×10^{-3} mm^2/s vs. 0.93×10^{-3} mm^2/s) without major modification at 48 h (1.166×10^{-3} mm^2/s)

14 women with myometrium ischemia at 48 h post-UAE, a lower myometrium ADC value was found by comparison with those without myometrium ischemia (1.38×10^{-3} mm^2/s vs. 1.646×10^{-3} mm^2/s, respectively; $p = 0.0001$).

Discussion

In our study we have investigated how post-UAE changes in ADC values of dominant leiomyomas may correlate with imaging outcome estimated by the degree of devascularization and uterine and dominant leiomyoma volume reduction. We found a significant drop in mean ADC value of dominant leiomyoma at 6 months post-UAE, but not at 48 h post-UAE. This result is consistent with those of others obtained with a more limited sample size [22–24]. We observed that the drop in ADC value of dominant leiomyoma was significantly associated with the degree of dominant leiomyoma devascularization at 48 h and 6 months post-UAE. We found in our study, similar to other studies, that long-term results and volume reduction depends mainly on post-UAE devascularization degree [28–30, 36]. Thus, a decrease in ADC value of dominant leiomyoma at 6 months post-UAE by comparison with pre-UAE ADC value is significantly

Table 3 Inter-observer agreement for volume and ADC measurement of leiomyomas between two independent readers*

	Mean difference	95 % limits of agreement	ICC† (95 % CI)
Volumes (cm^3)			
Baseline uterine volume	35.7 ± 98.0	-156 to 228	0.988 (0.979–0.993)
6 months post-UAE uterine volume	18.8 ± 49.1	-77.5 to 115.0	0.972 (0.950–0.984)
Baseline dominant leiomyoma volume	3.4 ± 35.1	-65.4 to 72.2	0.997 (0.994–0.998)
6 months post-UAE dominant leiomyoma volume	0.4 ± 15.4	-29.8 to 30.6	0.998 (0.996–0.999)
ADC values ($\times 10^{-3}$ mm^2/s)			
Baseline myometrium ADC	-0.036 ± 0.150	-0.330 to 0.258	0.719 (0.502–0.842)
48-h post-UAE myometrium ADC	-0.004 ± 0.152	-0.302 to 0.294	0.869 (0.767–0.926)
6-month post-UAE myometrium ADC	-0.020 ± 0.128	-0.271 to 0.230	0.868 (0.768–0.926)
Baseline dominant leiomyoma ADC	0.016 ± 0.069	-0.120 to 0.153	0.975 (0.956–0.986)
48-h post-UAE dominant leiomyoma ADC	0.008 ± 0.072	-0.132 to 0.149	0.958 (0.926–0.976)
6-month post-UAE dominant leiomyoma ADC	0.039 ± 0.104	-0.164 to 0.242	0.977 (0.957–0.987)
Baseline normalized ADC	0.143 ± 0.585	-1.004 to 1.289	0.959 (0.928–0.977)
48-h post-UAE normalized ADC	0.024 ± 0.360	-0.682 to 0.729	0.942 (0.897–0.967)
6-month post-UAE normalized ADC	0.080 ± 0.251	-0.411 to 0.571	0.953 (0.913–0.974)

Notes. *Reader 1 measured volumes (V) with the following formula V = H × T × W × 0.52 and Reader 2 used the semi-automated segmentation method. † *ICC* indicates intraclass correlation coefficient calculated according to the "two-way random single measures" method (ICC = 1.0–0.81 indicates excellent agreement; 0.80–0.61 good; 0.60–0.41 moderate; 0.40–0.21 fair; and 0.20–0.00 poor agreement). Uterine and dominant leiomyoma volume differences are expressed in cm^3. ADC is expressed in $\times 10^{-3}$ mm^2/s.

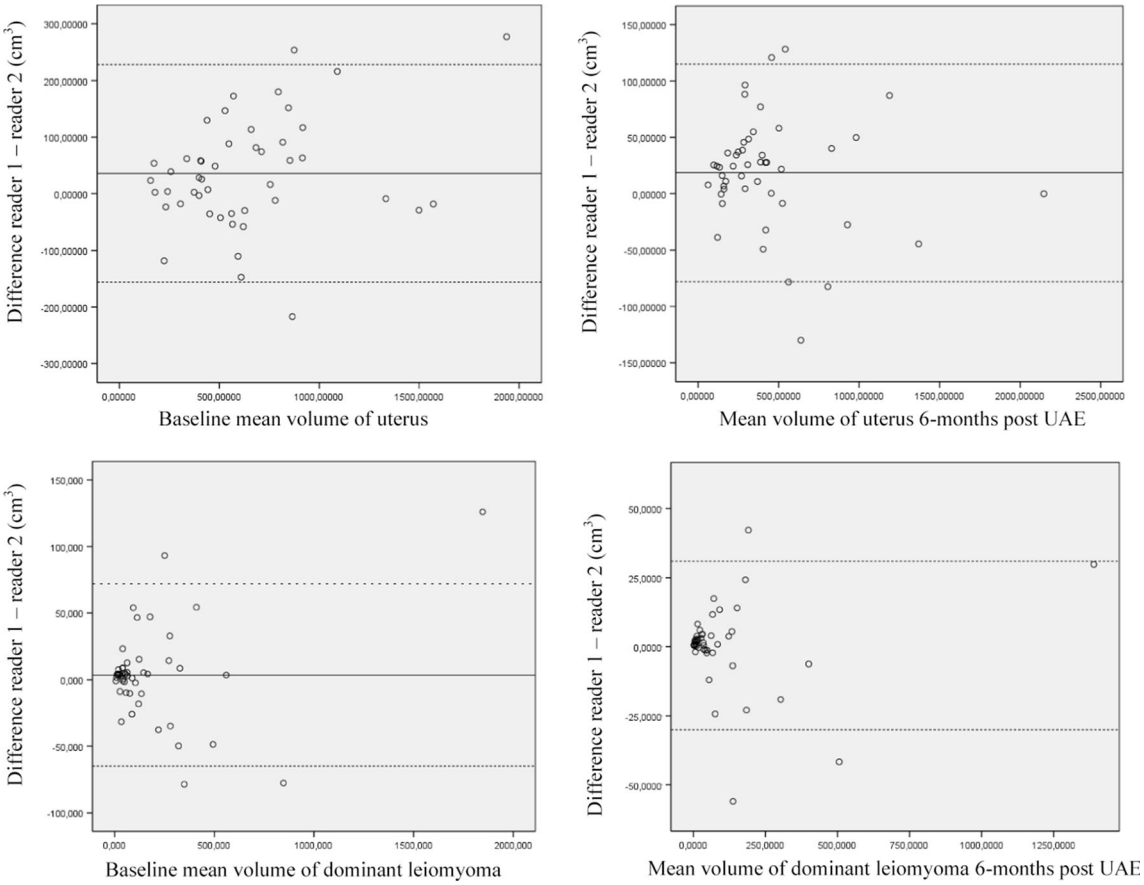

Fig. 5 Bland–Altman plots show interobserver agreement for uterine and dominant leiomyoma volumes using manual (reader 1) and semi-automated segmentation method (reader 2). UAE indicates uterine artery embolization

associated with complete post-UAE devascularization, assuming that such drop in ADC value may be used as a predictor of favourable outcome.

Liapi et al., in a study involving 11 women with a total of 32 leiomyomas, found a significant drop in post-UAE ADC values, with a correlation between post-UAE ADC values and the degree of enhancement of each leiomyomas, but no correlations with volume changes [22]. Faye et al. also found in 17 patients with a total of 27 leiomyomas a significant drop in ADC values at 6 months post-UAE, but no correlations with the degree of devascularization or volume reduction of leiomyomas [23]. Ananthakrishnan et al. have studied 15 women with uterine leiomyomas treated with UAE and found a significant drop in ADC values on follow-up MR imaging examinations, with no correlations with volume reduction at 6 months post-UAE or contrast enhancement patterns [24]. However, Ananthakrishnan et al. found a correlation between pre-UAE ADC values and dominant leiomyoma volume reduction at 6 months post-UAE. Their results are consistent with those of other three studies [37–39]. It can be thus hypothesized that pre-UAE leiomyoma ADC values may help predict volume reduction after UAE.

In our study, we did not find any correlation between pre-UAE ADC values of dominant leiomyomas and their volume reduction. It may be assumed that this was because we excluded all cystic or necrotic parts of leiomyomas, both of which have high ADC values due to a liquid content, from ROIs for ADC measurement. In this regard we calculated the ADC values of viable and vascularized portions of dominant leiomyomas that were targeted by UAE.

We found a significant decrease in ADC value of the myometrium at both 48 h and 6 months post-UAE, which is a finding that has not been reported yet. One previous study found a slight drop in myometrium ADC values that did not reach significance [24]. In addition, we observed that myometrium ADC values at 48 h post-UAE were lower in the subset of women with myometrium ischemia, which is a finding that has not been reported yet. It may be reasonably assumed that myometrium ischemia may result from UAE [31]. This result suggests that superselective UAE even with an optimal selection of embolic agents may result in unwanted untargeted embolization of adjacent myometrium [40–42].

In our study, myometrium ischemia was observed in a substantial subset of women (28.5 %). It may be hypothesized that myometrium ischemia resulted from over embolization

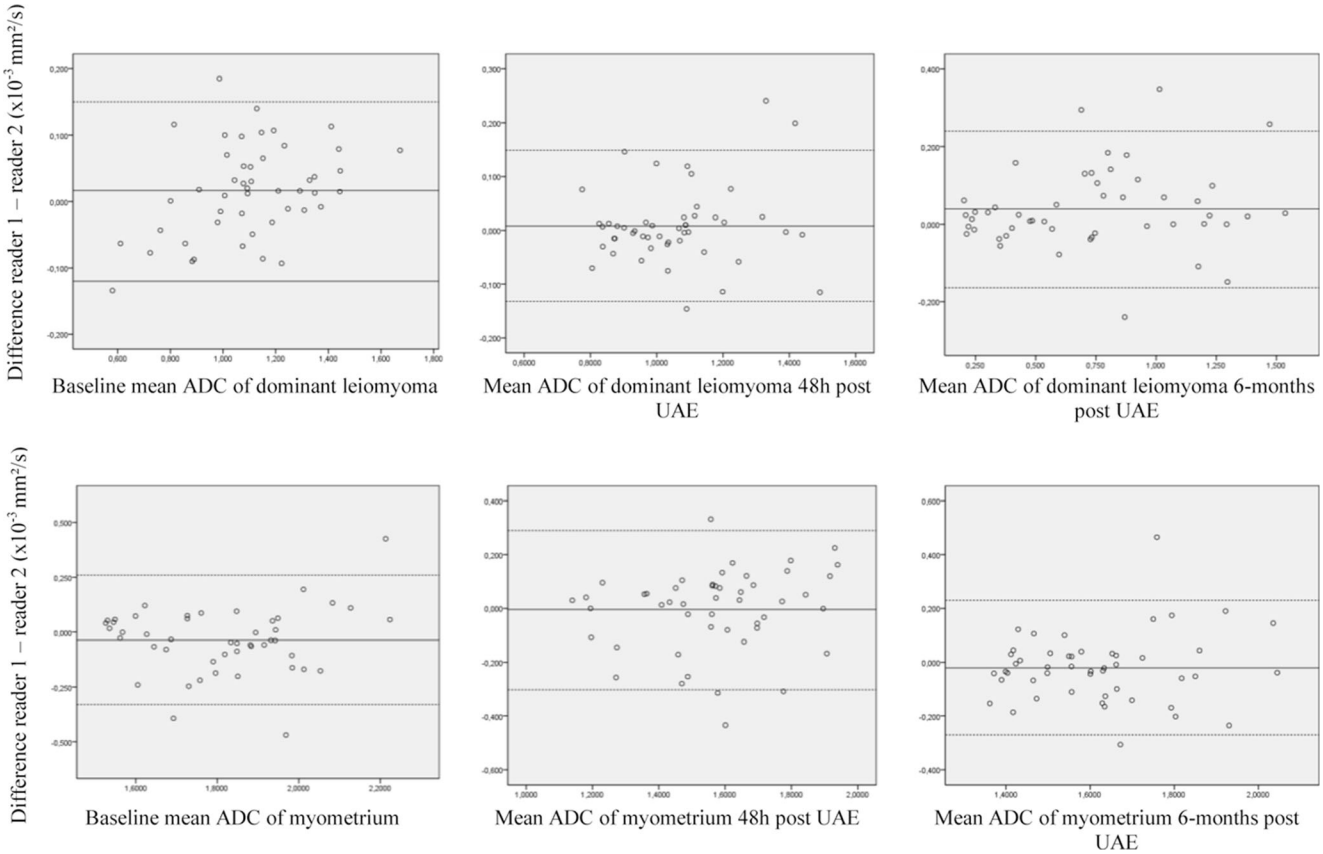

Fig. 6 Bland–Altman plots show interobserver agreement for measurement of ADC values of dominant leiomyoma, and myometrium at baseline, 48-h post-uterine artery embolization (UAE) and 6 months post-UAE

Table 4 ADC values and uterine volume at baseline, 48 h, and 6 months post-UAE according to devascularization at 48 h post-UAE of dominant leiomyoma

	Dominant leiomyoma devascularization at 48 h post-UAE			*p* value*
	Complete (100 %) n =40	Almost complete (90-99 %) n = 2	Incomplete (0-89 %) n = 7	
Dominant leiomyoma ADC				
Baseline	1.08 ± 0.2	0.871 ± 0.32	1.252 ± 0.19	0.08
48 h	1.045 ± 0.16	0.951 ± 0.18	1.115 ± 0.24	0.6
6 months	0.623 ± 0.34	0.986 ± 0.35	1.147 ± 0.25	**0.003**
Dominant leiomyoma ADC_N				
Baseline	2.047 ± 1.48	1.347 ± 0.27	1.624 ± 0.42	0.49
48 h	1.738 ± 0.84	1.782 ± 1.03	1.825 ± 0.47	0.56
6 months	0.987 ± 0.57	1.537 ± 0.48	1.627 ± 0.54	**0.01**
Dominant leiomyoma volume				
Baseline	130 ± 140	457 ± 606	364 ± 638	0.71
6 months	70 ± 85	272 ± 360	289 ± 497	0.4
Variation	-43.2 %	-39.4 %	-29.7 %	0.39
Uterine volume				
Baseline	637 ± 349	3948 ± 5149	905 ± 1037	0.82
6 months	395 ± 266	3365 ± 4448	705 ± 766	0.69
Variation	-39.1 %	-21.2 %	-21.8 %	**0.008**

Note. *ADC* indicates apparent diffusion coefficient. ADC values are expressed $x10^{-3}$ mm^2 /s.

Volumes are expressed in cm^3 ; n = number of patients.

* Kruskal-Wallis test; Bold indicates significant difference

Table 5 ADC values of dominant leiomyoma and uterine volume on MR examination according to the degree of devascularization at 6 months post-UAE

	Dominant leiomyoma devascularization at 6 months post-UAE			*p* value*
	Complete (100 %) n =37	Almost complete (90-90 %) n = 3	Incomplete (0-89 %) n = 9	
Dominant leiomyoma ADC				
Baseline	1.092 ± 0.2	0.992 ± 0.2	1.149 ± 0.26	0.46
6 months	0.626 ± 0.34	0.704 ± 0.57	1.069 ± 0.25	**0.008**
Dominant leiomyoma ADC_N				
Baseline	2.086 ± 1.53	1.498 ± 0.35	1.585 ± 0.40	0.43
6 months	0.985 ± 0.57	1.204 ± 0.99	1.544 ± 0.43	**0.017**
Dominant leiomyoma volume				
Baseline	132 ± 143	696 ± 942	187 ± 287	0.24
6 months	72 ± 87	509 ± 749	133 ± 193	0.31
Variation	-42.6 %	-41.2 %	-34.9 %	0.79
Uterine volume				
Baseline	621 ± 296	1803 ± 1225	1261 ± 2408	0.08
6 months	383 ± 242	1229 ± 878	1069 ± 2078	0.13
Variation	-39.6 %	-32.3 %	-21.6 %	**0.0056**

Note. *ADC* indicates apparent diffusion coefficient. ADC values are expressed $x10^{-3}$ mm^2 /s.

Volumes are expressed in cm^3 ; n = number of patients.

* Kruskal-Wallis test; Bold indicates significant difference

during UAE. Of interest, women with myometrium ischemia had a smaller pre-UAE uterine volume. Assuming that uterine volume is proportional to the number and size of leiomyomas, the angiographic end-point was reached more quickly during UAE in women with a small uterus, thus exposing them to over-embolization. In our study, myometrium ischemia was not associated with a more marked drop in uterine volume, but was significantly associated with persistent leiomyoma devascularization at 6 months post-UAE. More research is needed to investigate the actual benefit and potential risks of initial myometrium ischemia after UAE.

In our study, we found significant differences in leiomyoma volume reduction between leiomyomas with an initially "typical" appearance and those with an initially "high cellularity" appearance, although we agree that the limited number of "highly cellular" leiomyomas (only four women in our study) does not allow drawing definite conclusions. However, data from the literature indicate that leiomyomas

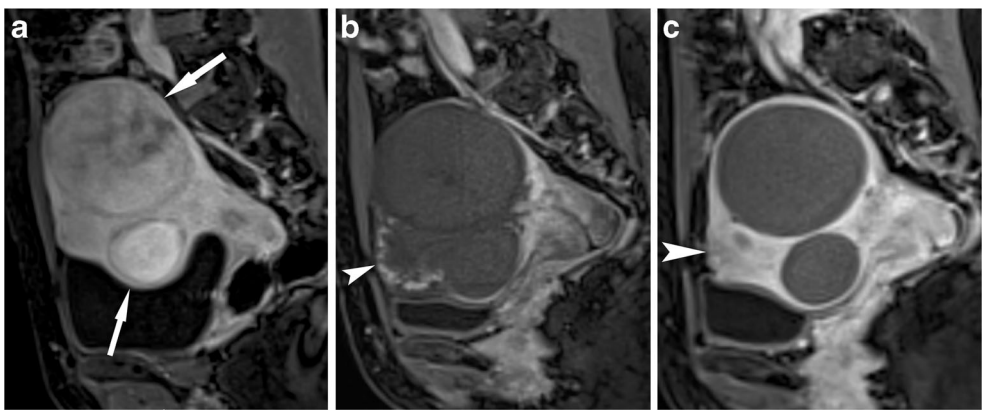

Fig. 7 Imaging features of a 43-year-old woman who had uterine artery embolization (UAE). Gadolinium chelate-enhanced 3D-VIBE® sequences in the sagittal plane were obtained before UAE (**a**), at 48 h (**b**), and 6 months (**c**) after UAE. Two leiomyomas show marked enhancement before UAE (*arrows*) (**a**). There is an initial myometrial enhancement defect (*arrowhead*) on the 48-h examination (**b**) along with complete (100 %) leiomyoma devascularization. This myometrial ischemia was reversible on the 6-month MR images (*arrowhead*) (**c**), and leiomyoma devascularization stays complete (100 %)

Table 6 Characteristics of women with or without myometrium ischemia on MR examination 48 h post-UAE

	Myometrium ischemia n = 14	No myometrium ischemia n = 35	*p* value*
Uterine volume			
Baseline	481.2 ± 175	942.7 ± 1285	**0.04**
6 months	286 ± 140	671 ± 1102	0.05
Variation	-42.6 %	-33.2 %	0.07
Dominant leiomyoma volume			
Baseline	91.7 ± 106	210.5 ± 333	0.07
6 months	51 ± 51	133 ± 250	0.07
Variation	-41 %	-41.2 %	0.98
Dominant leiomyoma ADC			
Baseline	1.072 ± 0.19	1.106 ± 0.22	0.55
6 months	0.56 ± 0.37	0.773 ± 0.36	0.08
Dominant leiomyoma ADC_N			
Baseline	2.544 ± 2.24	1.724 ± 0.67	0.12
6 months	0.933 ± 0.64	1.168 ± 0.58	0.24
Myometrium ADC			
Baseline	1.756 ± 0.19	1.874 ± 0.19	0.07
48 h	1.38 ± 0.18	1.646 ± 0.17	**0.0001**
6 months	1.598 ± 0.16	1.637 ± 0.18	0.59
Dominant leiomyoma devascularization at 6 months	100 %: n = 14 (100 %) 90 - 99 %: n = 0 0 - 89 % : n = 0	100 %: n = 23 (66 %) 90 - 99 %: n = 3 (8 %) 0 - 89 %: n = 9 (26 %)	**0.01**§

Note. *ADC* indicates apparent diffusion coefficient. ADC values are expressed $\times 10^{-3}$ mm^2/s.

Volumes are expressed in cm^3 ; n = number of patients.

* Student's t-test; § Kruskal-Wallis test; *Bold* indicates significant difference

with high signal intensity on T2-weighted MR images are more prone to more marked volume reduction after UAE [36, 38, 43]. One explanation may be that high cellularity is associated with high degrees of vascularization and may thus increase susceptibility to embolization.

The long-term drop in ADC values of leiomyomas following UAE likely depends on several phenomena and largely on microscopic changes like cellular dehydration, hyaline degeneration, and fibrosis [44].

Our results confirm using a larger scale study population those of previous studies with regard to the decrease in ADC value of leiomyomas after embolization [23]. Moreover, we highlighted a correlation between the decrease in ADC value of dominant leiomyoma with post-UAE long-term devascularization. Our study is the first to evidence a decrease in myometrium ADC at 48 h and 6 months post-UAE associated with an ischemia of myometrium, which is relatively frequent after UAE especially in women with small uterus.

Our study has several limitations. First, we used a visual, semi-quantitative evaluation of dominant leiomyoma devascularization. We agree that this method does not provide a precise quantification of leiomyoma devascularization, but it is commonly used in clinical practice [28–30]. Second, we used a monoexponential algorithm for ADC calculation with three diffusion factors ($b = 0$, 500, 1000 s/mm^2). We agree that further studies should be performed using intra-voxel incoherent motion [45, 46]. Finally, due to the retrospective design of the study with lack of long term clinical data, we were not able to determine the proportion of women who were pushed into menopause after UAE. It could be hypothesized that the long-term changes in myometrium ADC that we highlighted may be partially influenced by menopause or age-related uterine changes.

In conclusion, a drop in leiomyoma ADC values on 6 months post-UAE DW-MR imaging is significantly associated with leiomyoma devascularization, which is an indicator of favourable outcome. In this regard, DW-MR imaging should be routinely used before and after UAE. We assume that a drop in ADC values of all leiomyomas associated with a significant volume reduction on follow-up MR examination is probably sufficient to assess efficacy and may avoid intravenous administration of contrast material when devascularization was evidenced on the early post-UAE MR examination. On the other hand, the absence of long-term drop in leiomyoma ADC values may often indicate treatment failure or recurrence that should be confirmed by contrast-enhanced MRI. Thus, an early post-UAE MRI examination performed at 48-72 h may be useful to have an assessment of leiomyoma devascularization, but DW-MR imaging at this

step does not help predict outcome. Moreover, there is an effect of the UAE on the normal myometrium that is indirectly evidenced by a drop in ADC values and transient perfusion defect on gadolinium chelate-enhanced dynamic T1-weighted MR images. More studies are needed, however, to investigate fully to what extent these findings may be used as predictors of long-term outcome.

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References

1. Pelage JP, Le Dref O, Soyer P, Kardache M, Dahan H, Abitbol M et al (2000) Fibroid-related menorrhagia: treatment with superselective embolization of the uterine arteries and midterm follow-up. Radiology 215:428–431
2. Walker WJ, Pelage JP (2002) Uterine artery embolisation for symptomatic fibroids: clinical results in 400 women with imaging follow up. BJOG Int J Obstet Gynaecol 109:1262–1272
3. Hirst A, Dutton S, Wu O, Briggs A, Edwards C (2008) A multicentre retrospective cohort study comparing the efficacy, safety and cost-effectiveness of hysterectomy and uterine artery embolisation for the treatment of symptomatic uterine fibroids. The HOPEFUL study. Health Technol Assess 12:248
4. Malartic C, Morel O, Fargeaudou Y, Le Dref O, Fazel A, Barranger E et al (2012) Conservative two-step procedure including uterine artery embolization with embosphere and surgical myomectomy for the treatment of multiple fibroids: preliminary experience. Eur J Radiol 81:1–5
5. Edwards RD, Moss JG, Lumsden MA, Wu O, Murray LS, Twaddle S et al (2007) Uterine artery embolization versus surgery for symptomatic uterine fibroids. N Engl J Med 356:360–370
6. Ananthakrishnan G, Murray L, Ritchie M, Murray G, Bryden F, Lassman S et al (2013) Randomized comparison of uterine artery embolization (UAE) with surgical treatment in patients with symptomatic uterine fibroids (REST trial): subanalysis of 5-year MRI findings. Cardiovasc Intervent Radiol 36:676–681
7. Malartic C, Morel O, Rivain A-L, Placé V, Le Dref O, Dohan A et al (2013) Evaluation of symptomatic uterine fibroids in candidates for uterine artery embolization: comparison between ultrasonographic and MR imaging findings in 68 consecutive patients. Clin Imaging 37:83–90
8. Siddiqui N, Nikolaidis P, Hammond N, Miller FH (2013) Uterine artery embolization: pre- and post-procedural evaluation using magnetic resonance imaging. Abdom Imaging 38:1161–1177
9. Deshmukh SP, Gonsalves CF, Guglielmo FF, Mitchell DG (2012) Role of MR imaging of uterine leiomyomas before and after embolization. Radiographics 32:E251–E281
10. Thomassin-Naggara I, Siles P, Balvay D, Cuenod CA, Carette MF, Bazot M (2013) MR perfusion for pelvic female imaging. Diagn Interv Imaging 94:1291–1298
11. Bihan DL (2007) The "wet mind": water and functional neuroimaging. Phys Med Biol 52:R57–R90
12. Le Bihan D, Turner R, Douek P, Patronas N (1992) Diffusion MR imaging: clinical applications. AJR Am J Roentgenol 159:591–599
13. Padhani AR, Liu G, Mu-Koh D, Chenevert TL, Thoeny HC, Takahara T et al (2008) Diffusion-weighted magnetic resonance imaging as a cancer biomarker: consensus and recommendations. Neoplasia 11:102–125
14. Soyer P, Kanematsu M, Taouli B, Koh D-M, Manfredi R, Vilgrain V et al (2013) ADC normalization: a promising research track for diffusion-weighted MR imaging of the abdomen. Diagn Interv Imaging 94:571–573
15. Soyer P, Corno L, Boudiaf M, Aout M, Sirol M, Placé V et al (2011) Differentiation between cavernous hemangiomas and untreated malignant neoplasms of the liver with free-breathing diffusion-weighted MR imaging: comparison with T2-weighted fast spin-echo MR imaging. Eur J Radiol 80:316–324
16. Barral M, Cornud F, Neuzillet Y, Lonchampt E, Lassalle L, Delonchamp NB et al (2015) Characteristics of undetected prostate cancer on diffusion-weighted MR Imaging at 3-Tesla with a b-value of 2000s/mm^2: imaging-pathologic correlation. Diagn Interv Imaging 96:923–929
17. Taouli B (2012) Diffusion-weighted MR, imaging for liver lesion characterization: a critical look. Radiology 262:378–380
18. Dallaudière B, Lecouvet F, Vande Berg B, Omoumi P, Perlepe V, Cerny M et al (2015) Diffusion-weighted MR imaging in musculoskeletal diseases: current concepts. Diagn Interv Imaging 96:327–340
19. Barral M, Sebbag-Sfez D, Hoeffel C, Chaput U, Dohan A, Eveno C et al (2013) Characterization of focal pancreatic lesions using normalized apparent diffusion coefficient at 1.5-Tesla: preliminary experience. Diagn Interv Imaging 94:619–627
20. Barral M, Taouli B, Guiu B, Koh D-M, Luciani A, Manfredi R et al (2015) Diffusion-weighted MR imaging of the pancreas: current status and recommendations. Radiology 274:45–63
21. Thoeny HC, Forstner R, De Keyzer F (2012) Genitourinary applications of diffusion-weighted MR imaging in the pelvis. Radiology 263:326–342
22. Liapi E, Kamel IR, Bluemke DA, Jacobs MA, Kim HS (2005) Assessment of response of uterine fibroids and myometrium to embolization using diffusion-weighted echoplanar MR imaging. J Comput Assist Tomogr 29:83–86
23. Faye N, Pellerin O, Thiam R, Chammings F, Brisa M, Marques E et al (2013) Diffusion-weighted imaging for evaluation of uterine arterial embolization of fibroids: DWI for evaluation of UAE of fibroids. Magn Reson Med 70:1739–1747
24. Ananthakrishnan G, Macnaught G, Hinksman L, Gilmour H, Forbes KP, Moss JG (2012) Diffusion-weighted imaging in uterine artery embolisation: do findings correlate with contrast enhancement and volume reduction? Br J Radiol 85:e1046–e1050
25. Pelage JP, Le Dref O, Soyer P, Jacob D, Kardache M, Dahan H et al (1999) Arterial anatomy of the female genital tract: variations and relevance to transcatheter embolization of the uterus. AJR Am J Roentgenol 172:989–994
26. Pelage JP, Cazejust J, Pluot E, Dref OL, Laurent A, Spies JB et al (2005) Uterine fibroid vascularization and clinical relevance to uterine fibroid embolization. Radiographics 25:S99–S117
27. Joffre F, Tubiana JM, Pelage JP (2004) Groupe FEMIC*. FEMIC (Fibromes Embolisés aux MICrosphères calibrées): uterine fibroid embolization using tris-acryl microspheres. A French multicenter study. Cardiovasc Intervent Radiol 27:600–606
28. Katsumori T, Kasahara T, Kin Y, Nozaki T (2008) Infarction of uterine fibroids after embolization: relationship between postprocedural enhanced MRI findings and long-term clinical outcomes. Cardiovasc Intervent Radiol 31:66–72
29. Kroencke TJ, Scheurig C, Poellinger A, Gronewold M, Hamm B (2010) Uterine artery embolization for leiomyomas: percentage of infarction predicts clinical outcome. Radiology 255:834–841

30. Scheurig-Muenkler C, Koesters C, Grieser C, Hamm B, Kroencke TJ (2012) Treatment failure after uterine artery embolization: prospective cohort study with multifactorial analysis of possible predictors of long-term outcome. Eur J Radiol 81:e727–e731
31. Scheurig-Muenkler C, Wagner M, Franiel T, Hamm B, Kroencke TJ (2010) Effect of uterine artery embolization on uterine and leiomyoma perfusion: evidence of transient myometrial ischemia on magnetic resonance imaging. J Vasc Interv Radiol 21:1347–1353
32. Ruuskanen A, Sipola P, Hippeläinen M, Wüstefeld M, Manninen H (2009) Pain after uterine fibroid embolisation is associated with the severity of myometrial ischaemia on magnetic resonance imaging. Eur Radiol 19:2977–2985
33. Murase E, Siegelman ES, Outwater EK, Perez-Jaffe LA, Tureck RW (1999) Uterine leiomyomas: histopathologic features, MR imaging findings, differential diagnosis, and treatment. Radiographics 19:1179–1197
34. Bland JM, Altman DG (1986) Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1:307–310
35. Bland JM, Altman DG (2003) Applying the right statistics: analyses of measurement studies. Ultrasound Obstet Gynecol 22:85–93
36. de Souza NM, Williams AD (2002) Uterine arterial embolization for leiomyomas: perfusion and volume changes at MR imaging and relation to clinical outcome. Radiology 222:367–374
37. Hecht EM, Do RKG, Kang SK, Bennett GL, Babb JS, Clark TWI (2011) Diffusion-weighted imaging for prediction of volumetric response of leiomyomas following uterine artery embolization: a preliminary study. J Magn Reson Imaging 33:641–646
38. Cao MQ, Suo ST, Zhang X-B, Zhong YC, Zhuang ZG, Cheng JJ et al (2014) Entropy of T2-weighted imaging combined with apparent diffusion coefficient in prediction of uterine leiomyoma volume response after uterine artery embolization. Acad Radiol 21:437–444
39. Lee MS, Kim MD, Jung DC, Lee M, Won JY, Park SI et al (2013) Apparent diffusion coefficient of uterine leiomyoma as a predictor of the potential response to uterine artery embolization. J Vasc Interv Radiol 24:1361–1365
40. Laurent A, Wassef M, Namur J, Ghegediban H, Pelage JP (2010) Arterial distribution of calibrated tris-acryl gelatin and polyvinyl alcohol embolization microspheres in sheep uterus. Cardiovasc Intervent Radiol 33:995–1000
41. Pelage JP, Laurent A, Wassef M, Bonneau M, Germain D, Rymer R et al (2002) Uterine artery embolization in sheep: comparison of acute effects with polyvinyl alcohol particles and calibrated microspheres. Radiology 224:436–445
42. Kitamura Y, Ascher SM, Cooper C, Allison SJ, Jha RC, Flick PA et al (2005) Imaging manifestations of complications associated with uterine artery embolization. Radiographics 25:S119–S132
43. Burn PR, McCall JM, Chinn RJ, Vashisht A, Smith JR, Healy JC (2000) Uterine fibroleiomyoma: MR imaging appearances before and after embolization of uterine arteries. Radiology 214:729–734
44. Weichert W, Denkert C, Gauruder-Burmester A, Kurzeja R, Hamm B, Dietel M, et al (2005) Uterine arterial embolization with tris-acryl gelatin microspheres: a histopathologic evaluation. Am J Surg Pathol 29
45. Le Bihan D, Breton E, Lallemand D, Aubin ML, Vignaud J, Laval-Jeantet M (1988) Separation of diffusion and perfusion in intravoxel incoherent motion MR imaging. Radiology 168:497–505
46. Le Bihan D (2008) Intravoxel incoherent motion perfusion MR imaging: a wake-up call. Radiology 249:748–752