

〈Regular Article〉

## Dynamic contrast-enhanced MRI for the prediction of volumetric response of uterine leiomyomas following uterine artery embolization

Yuko FUKUHARA<sup>1)</sup>, Takayoshi SHINYA<sup>2)</sup>, Shinsuke KOMAKI<sup>3)</sup>  
Shuichi DENDO<sup>4)</sup>, Susumu KANAZAWA<sup>1)</sup>, Katsuya KATO<sup>1)</sup>

1) Department of Diagnostic and Therapeutic Radiology, Kawasaki Medical School

2) Division of Radiology, Department of Community Medicine and Medical Science Tokushima University Graduate School of Biomedical Sciences, Tokushima University Hospital.

3) Department of Central Radiation Center, Kawasaki Medical School General Medical Center

4) Hori Gynecology Clinic, Uterine Fibroid Okayama UAE Center

**ABSTRACT** This study aimed to evaluate the utility of using contrast enhancement (CE) effects of uterine leiomyoma in dynamic contrast-enhanced (DCE) magnetic resonance imaging (MRI) as a predictor of uterine leiomyoma volume reduction (VR) following uterine artery embolization (UAE). We retrospectively studied 22 women who underwent pre-UAE pelvic MRI with DCE-MRI and post-UAE pelvic MRI without DCE-MRI. The MRI sequences included conventional and fat-suppressed DCE-MRI. Percent volume response was determined using axial and sagittal T2-weighted imaging. The ratio between the signal intensity (SI) of the leiomyoma and that of the psoas major or iliopsoas muscle (SI ratio) was used to measure CE. In addition, the ratio of change in CE ratio during DCE-MRI was used to assess the CE pattern. We divided the target leiomyomas into two groups according to the volume reduction (VR) rate. Next, we examined whether there was a significant correlation between VR rate and SI ratio in each phase on DCE-MRI, we also assessed the ratio of change in CE ratio during DCE-MRI, age, and pre-UAE leiomyoma volume using the Mann-Whitney U test. We grouped leiomyomas in 10% increments from 50% to 90%, VR rates and decided to perform a total of five statistical tests. A total of 57 leiomyomas with preprocedural volumes ranging from 6.27 to 949.15 cm<sup>3</sup> (135.20 ± 197.33 cm<sup>3</sup>) were included. The time between UAE and follow-up MRI was 3 - 14 months (mean, 9.09 months). The leiomyoma VR rate following UAE ranged from -85.51% to 99.94% (55.3 ± 33.85%). We found that between leiomyomas with VR rate of ≥ 90% and those with VR rate of < 90%, there was a significant difference in SI ratio at 35 sec after contrast material injection (CMI) (p = 0.0499), the ratio of change in CE ratio from 35 to 60 sec after CMI (p = 0.0153), and the ratio of change in CE ratio from 35 to 80 sec after CMI (p = 0.0185). Thus, DCE-MRI can be considered an effective and predictive tool for the therapeutic effect of UAE.

doi:10.11482/KMJ-E202147113 (Accepted on June 22, 2021)

Key words : Magnetic resonance imaging, Dynamic contrast enhancement effects,  
Uterine artery embolization, Volume reduction

Corresponding author

Yuko Fukuhara

Department of Diagnostic and Therapeutic Radiology,  
Kawasaki Medical School, Kawasaki Medical School  
General Medical Center, 2-6-1 Nakasange, Kita-ku,  
Okayama, 700-8505, Japan

Phone : 81 86 252 2211

Fax : 81 86 232 8343

E-mail: yutti.s@sky.megaegg.ne.jp

## INTRODUCTION

Uterine artery embolization (UAE) is a safe and effective procedure for treating symptomatic uterine leiomyomas<sup>1)</sup>. However, predicting the volumetric response of leiomyomas following UAE remains a significant challenge despite extensive clinical application. Several factors, including location<sup>2)</sup>, fibroid size<sup>3)</sup>, and patient age<sup>4)</sup>, have been found to be associated with volume reduction (VR) rate.

Only a few studies have so far evaluated the predictive value of magnetic resonance imaging (MRI) [using factors such as signal intensity (SI) on T2-weighted imaging and apparent diffusion coefficient (ADC) value] before UAE. Furthermore, these studies had relatively small sample sizes<sup>5, 6)</sup>. Dynamic contrast-enhanced MRI (DCE-MRI) can help predict the effects of high-intensity focused ultrasound ablation of leiomyomas<sup>7, 8)</sup>. To the best of our knowledge, no study has assessed the quantitative predictive value of DCE-MRI for UAE.

In our practice, we routinely perform pelvic DCE-MRI before UAE to evaluate the vascularity of leiomyomas<sup>9)</sup> and the anatomy of the uterine artery<sup>10)</sup>. During these evaluations, we experienced a more substantial enhancing effect on DCE-MRI in groups wherein the treatment of uterine leiomyoma effectively caused regression or resolution. Considering these factors, we evaluated the relationship between the contrast enhancement (CE) effect of a leiomyoma on DCE-MRI and the effectiveness of UAE. This study aimed to retrospectively examine whether DCE-MRI could be an effective predictor of UAE by examining the relationship between the VR rate and each parameter of DCE-MRI.

## SUBJECTS AND METHODS

This study was approved by the ethics committee of our institution. (5210-00)

### Patients

This retrospective study included 22 women

who underwent pre- and post-UAE pelvic DCE-MRI between January 2017 and March 2021. Patients were aged 35 - 49 years ( $43.95 \pm 4.22$ ). Eighteen women were premenopausal, and four had missing information on the presence or absence of menstruation.

### UAE Technique

All UAE procedures were performed by an experienced interventional radiologist (S.D.) with 27 years of experience in interventional radiological treatment. The embolic agent used was a gelatin sponge fragment 0.5 - 1 mm in size (Spongel; LTL, Tokyo, Japan). The endpoint was defined as sluggish blood flow in the ascending segment of the uterine artery.

### MRI Protocol

MRI was performed with a 1.5T scanner (Achieva, Philips Medical Systems, Best, Netherlands) or a 3T clinical scanner (Ingenia 3T CX, Philips Medical Systems, Best, the Netherlands) using a cardiac coil and a dS anteroposterior coil, respectively.

MRI protocols consisted of axial and sagittal T2-weighted imaging (T2WI), axial T1-weighted imaging (T1WI), axial fat-suppressed T1WI, diffusion-weighted imaging, and DCE-MRI. The MRI parameters for examination at each MRI scanner are shown in Table 1. Multiphase DCE-

Table 1. MRI parameters

|                        | PHILIPS 1.5 T<br>Achieva | PHILIPS Ingenia<br>3 T CX |
|------------------------|--------------------------|---------------------------|
| FOV                    | 280 mm                   | 300 mm                    |
| Matrix size            | 256 * 512 (r)            | 256 * 512 (r)             |
| SENSE reduction factor | 2.0                      | 2.0                       |
| Slices                 | 64                       | 64                        |
| Slice thickness        | 3.0 mm                   | 3.0 mm                    |
| Slice gap              | 0 mm                     | 0 mm                      |
| TR                     | Shortest                 | Shortest                  |
| TE                     | Shortest                 | Shortest                  |
| Flip angle             | 11 deg                   | 13 deg                    |
| NEX                    | 1                        | 1                         |

FOV: Field of view, TR: Repetition time, TE: Echo time, NEX: Number of excitations

MRI images were obtained at pre-contrast as well as 35, 60, and 80 sec after contrast material injection (CMI). Gadolinium-based contrast media (Gadobutrol [Gadovist] Bayer Schering Pharma, Osaka, Japan, and Gadoteridol [ProHance] Eisai, Tokyo, Japan) were intravenously administered at a dose of 0.1 mmol/kg at a rate of 1 ml/sec with 20 ml of saline.

### Image Analysis

Pre-UAE and post-UAE MRI scans were independently reviewed by two radiologists with 14 (Y. F.) and 30 (K. K.) years of clinical experience in pelvic MRI interpretation. The radiologists were blinded to the clinical information after UAE. If they disagreed on the radiological finding, a final decision was reached by consensus.

We evaluated leiomyomas that had a largest diameter of  $\geq 3$  cm among the three measured diameters.

A total of 58 leiomyomas were included in this study. The 58 leiomyomas were in 22 patients and comprised one lesion in eight patients, two lesions in five patients, three lesions in five patients, five lesions in two patients, six lesions in one patient, and nine lesions in one patient.

### Volume Measurements

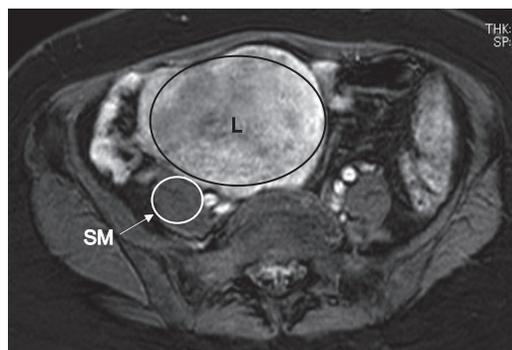
The anteroposterior (AP), craniocaudal (CC), and transverse long axis (TR) dimensions of each lesion were measured using axial and sagittal T2WI. The radiologists individually measured the leiomyoma diameter on the PACS system (SYNAPSE, FUJIFILM, Tokyo, Japan). In cases of discrepancy, the radiologists discussed the findings to resolve the conflict. The leiomyoma volume was calculated using a standard prolate ellipse formula ( $AP \times CC \times TR \times 0.5233$ )<sup>11)</sup>. The VR rate was calculated based on the volume of individual leiomyoma pre- ( $Vol^{pre}$ ) and post- ( $Vol^{post}$ ) UAE, with  $VR = \{(Vol^{pre} - Vol^{post})/Vol^{pre}\} \times 100$ .

### Analysis of Dynamic CE Effects

We used the leiomyoma-to-skeletal muscle (LSM) signal intensity (SI) ratio to measure CE. The psoas major muscle or iliopsoas muscle in the same slice as the leiomyoma was used for evaluation.

The two regions of interest (ROIs), located at the maximum cross-sectional area of the leiomyoma at each phase of DCE-MRI and the skeletal muscle on the 3T-MRI console, were selected based on consensus between the two radiologists. We first set the ROIs on the pre-contrast phase (if the contour of the leiomyoma in the pre-phase was unclear, we used the 35 sec after CMI image), and then we copied the ROIs and pasted them in each phase. We set the same ROIs on the leiomyoma and skeletal muscle on each phase of the DCE-MRI and calculated the LSM-SI ratio of each phase (Fig. 1). The size of the ROI encompassed the entire leiomyoma. The ROI was measured in circles to cover the entire leiomyoma to the maximum extent. The ROI measurement for skeletal muscle was performed in the same protocol. The LSM-SI ratio (SI ratio) was calculated by dividing the SI of the leiomyoma by the SI of the skeletal muscle.

To measure the CE pattern, the ratio of change in CE ratio during DCE-MRI was calculated in each



ROI: regions of interest. L: leiomyoma SM: skeletal muscle

Fig. 1. Dynamic contrast-enhanced fat-suppressed axial T1-weighted imaging of leiomyoma and skeletal muscle with regions of interest (ROI) placement

dynamic phase, i.e., between pre-CE and after 35 sec; pre-CE and after 60 sec; pre-CE and after 80 sec; after 35 sec and after 60 sec; after 35 sec and after 80 sec; and after 60 sec and after 80 sec. It was measured using the formula:

$$\frac{\text{The ratio of change in CE ratio between phase a and phase b} = (\text{SI ratio of phase b} - \text{SI ratio of phase a})}{\text{SI ratio of phase a}} \times 100.$$

### Statistical Analysis

We divided the target leiomyomas into two groups each in the following pattern: VR rate of  $\geq 50\%$  and  $< 50\%$ ,  $\geq 60\%$  and  $< 60\%$ ,  $\geq 70\%$  and  $< 70\%$ ,  $\geq 80\%$  and  $< 80\%$ , and  $\geq 90\%$  and  $< 90\%$ . The Mann-Whitney U test was used to assess the significance of differences between the two groups categorized by VR rate using various parameters from DCE-MRI as well as age and pre-UAE volume. The parameters from DCE-MRI included SI ratio (35 sec), SI ratio (60 sec), SI ratio (80 sec), the ratio of change in CE ratio (pre-35 sec), the ratio of change in CE ratio (pre-60 sec), the ratio of change in CE ratio (pre-80 sec), the ratio of change in CE ratio (35 sec-60 sec), the ratio of change in CE ratio (35 sec-80 sec), and the ratio of change in CE ratio (60 sec-80 sec). Statistical significance was at a  $p < 0.05$ .

Furthermore, if a significant difference was

observed for each parameter between the groups, an additional receiver operating characteristic (ROC) curve was used to evaluate the variables. Discrimination was assessed using the area under the ROC curve (AUC), which was also used to determine the optimal cut-off values that maximized the sensitivity and specificity for each index. Significant differences between AUCs, as determined from the ROC curve, were assessed with Delong's test.

All statistical analyses were performed using the EZR software<sup>12)</sup>, a modified version of R designed to provide a simplified graphical user interface with statistical functions frequently used in biostatistics.

### RESULTS

Initially, 22 patients with 58 leiomyomas were included in the study. The mean follow-up period was 9.09 months (range, 3 - 14 months). During follow-up, one leiomyoma was excluded from the study as it disappeared following fibroid delivery.

Pre- and post-UAE MRI examinations were completed without complications.

The pre-UAE volume of the leiomyomas ranged from 6.27 to 949.15 cm<sup>3</sup> (135.20  $\pm$  197.33 cm<sup>3</sup>). The leiomyoma VR rate following UAE ranged from -85.51% to 99.94% (55.3  $\pm$  33.85%). All

Table 2. Baseline characteristics and leiomyoma volume reduction

| Characteristics  | Value                               |
|--|-------------------------------------|
| Number of patients                                     | 22                                  |
| Age (years)  | 35 - 49 (43.95 $\pm$ 4.22).         |
| Follow-up period (months)                              | 3 - 14 (mean, 9.09)                 |
| Number of leiomyomas (> 3 cm in diameter)              | 58 (one leiomyoma was excluded)     |
| Tumor volume (cm <sup>3</sup> ) <pre-procedural>       | 6.27 - 949.15 (135.20 $\pm$ 197.33) |
| Tumor volume (cm <sup>3</sup> ) <post-procedural>      | 0.07 - 801.01 (62.23 $\pm$ 127.31)  |
| Volume reduction rate (%)                              | -85.51 - 99.94 (55.3 $\pm$ 33.85)   |
| Number of leiomyomas with reduction rate $\leq 0\%$ .  | 3                                   |
| Number of leiomyomas with reduction rate 0 - 20%.      | 4                                   |
| Number of leiomyomas with reduction rate 20 - 50%.     | 20                                  |
| Number of leiomyomas with reduction rate 50 - 70%.     | 10                                  |
| Number of leiomyomas with reduction rate 70 - 90%.     | 15                                  |
| Number of leiomyomas with reduction rate $\geq 90\%$ . | 5                                   |

Table 3. Results of the parameters of contrast enhancement effects

| Measure (sec)                                 | Group with<br>≥ 50% VR rate | Group with<br>< 50% VR rate | Group with<br>≥ 60% VR rate | Group with<br>< 60% VR rate | Group with<br>≥ 70% VR rate | Group with<br>< 70% VR rate | Group with<br>≥ 80% VR rate | Group with<br>< 80% VR rate | Group with<br>≥ 90% VR rate | Group with<br>< 90% VR rate |
|---|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
|   | median ± SEM<br>n = 30      | median ± SEM<br>n = 27      | median ± SEM<br>n = 24      | median ± SEM<br>n = 33      | median ± SEM<br>n = 20      | median ± SEM<br>n = 37      | median ± SEM<br>n = 13      | median ± SEM<br>n = 44      | median ± SEM<br>n = 5       | median ± SEM<br>n = 52      |
| SI ratio (35)                                 | 2.036 ± 0.104               | 2.225 ± 0.100               | 1.858 ± 0.113               | 2.240 ± 0.093               | 1.761 ± 0.121               | 2.225 ± 0.088               | 2.109 ± 0.153               | 2.082 ± 0.082               | 1.387 ± 0.211               | 2.160 ± 0.073               |
| SI ratio (60)                                 | 2.270 ± 0.099               | 2.203 ± 0.112               | 2.243 ± 0.118               | 2.268 ± 0.095               | 2.243 ± 0.107               | 2.268 ± 0.098               | 2.264 ± 0.101               | 2.244 ± 0.091               | 2.046 ± 0.127               | 2.268 ± 0.079               |
| SI ratio (80)                                 | 2.320 ± 0.091               | 2.267 ± 0.108               | 2.275 ± 0.109               | 2.339 ± 0.091               | 2.225 ± 0.097               | 2.313 ± 0.093               | 2.242 ± 0.088               | 2.311 ± 0.086               | 2.108 ± 0.126               | 2.313 ± 0.074               |
| the ratio of change in<br>CE ratio (pre - 35) | 77.517 ± 8.259              | 77.266 ± 9.916              | 68.891 ± 9.619              | 77.266 ± 8.537              | 69.085 ± 9.504              | 77.266 ± 8.357              | 78.955 ± 9.063              | 76.202 ± 7.830              | 55.485 ± 13.470             | 78.955 ± 6.708              |
| the ratio of change in<br>CE ratio (pre - 60) | 86.810 ± 10.919             | 74.798 ± 15.023             | 86.810 ± 13.129             | 76.000 ± 12.591             | 86.810 ± 12.200             | 76.000 ± 12.434             | 91.025 ± 11.122             | 76.093 ± 11.372             | 91.02 ± 19.41               | 76.186 ± 9.679              |
| the ratio of change in<br>CE ratio (pre - 80) | 95.193 ± 8.861              | 85.387 ± 12.649             | 95.193 ± 10.609             | 91.843 ± 10.595             | 96.421 ± 8.791              | 91.843 ± 10.665             | 97.190 ± 6.158              | 91.034 ± 9.643              | 103.776 ± 6.698             | 92.024 ± 8.144              |
| the ratio of change in<br>CE ratio (35 - 60)  | 8.254 ± 4.133               | 9.908 ± 2.971               | 9.074 ± 4.040               | 5.608 ± 3.409               | 13.004 ± 4.610              | 5.608 ± 3.112               | 10.189 ± 6.220              | 5.777 ± 2.833               | 47.467 ± 10.146             | 5.608 ± 2.455               |
| the ratio of change in<br>CE ratio (35 - 80)  | 12.493 ± 5.184              | 5.608 ± 3.002               | 16.705 ± 4.800              | 9.651 ± 4.037               | 18.050 ± 5.588              | 9.651 ± 3.645               | 13.932 ± 7.327              | 10.178 ± 3.377              | 51.967 ± 11.519             | 10.08 ± 2.945               |
| the ratio of change in<br>CE ratio (60 - 80)  | 2.449 ± 1.036               | 2.535 ± 0.942               | 2.592 ± 1.151               | 2.535 ± 0.892               | 3.224 ± 1.191               | 2.060 ± 0.886               | 2.132 ± 1.181               | 2.650 ± 0.854               | 5.481 ± 0.955               | 2.060 ± 0.756               |

SI: signal intensity, CE: contrast enhancement, VR: volume reduction, SEM: standard error of the mean

Table 4. The statistical results in each group

| Measure (sec)                                 | Between group<br>with ≥ 50% VR<br>rate and group<br>with < 50% VR<br>rate. | Between group<br>with ≥ 60% VR<br>rate and group<br>with < 60% VR<br>rate. | Between group<br>with ≥ 70% VR<br>rate and group<br>with < 70% VR<br>rate. | Between group<br>with ≥ 80% VR<br>rate and group<br>with < 80% VR<br>rate. | Between group with ≥ 90% VR rate and group with < 90% VR rate. |       |             |             |               |
|---|--|--|--|--|--|-------|-------------|-------------|---------------|
|   | p-value  | p-value  | p-value  | p-value  | p-value  | AUC   | sensitivity | specificity | cut-off value |
| SI ratio (35)                                 | 0.507  | 0.196  | 0.112  | 0.351  | 0.0499   | 0.778 | 0.6         | 0.885       | 1.388         |
| SI ratio (60)                                 | 0.743  | 0.349  | 0.332  | 0.53   | 0.359  | -     | -           | -           | -             |
| SI ratio (80)                                 | 0.955  | 0.383  | 0.308  | 0.506  | 0.421  | -     | -           | -           | -             |
| the ratio of change in<br>CE ratio (pre - 35) | 0.792  | 0.572  | 0.539  | 0.718  | 0.29   | -     | -           | -           | -             |
| the ratio of change in<br>CE ratio (pre - 60) | 0.603  | 0.759  | 0.854  | 0.648  | 0.563  | -     | -           | -           | -             |
| the ratio of change in<br>CE ratio (pre - 80) | 0.517  | 0.834  | 0.616  | 0.648  | 0.163  | -     | -           | -           | -             |
| the ratio of change in<br>CE ratio (35 - 60)  | 0.581  | 0.438  | 0.285  | 0.775  | 0.0153   | 0.797 | 1           | 0.577       | 7.959         |
| the ratio of change in<br>CE ratio (35 - 80)  | 0.538  | 0.332  | 0.263  | 0.849  | 0.0185   | 0.794 | 0.6         | 0.962       | 51.969        |
| the ratio of change in<br>CE ratio (60 - 80)  | 0.326  | 0.301  | 0.263  | 0.985  | 0.0933   | -     | -           | -           | -             |
| Age   | 0.716  | 0.523  | 0.242  | 0.454  | 0.217  | -     | -           | -           | -             |
| pre-UAE volume                                | 0.379  | 0.265  | 0.108  | 1  | 0.592  | -     | -           | -           | -             |

SI: signal intensity, CE: contrast enhancement, UAE: uterine artery embolization, VR: volume reduction, AUC: area under the curve

results are shown in Table 2.

Table 3 shows the results of detailed measurement of the parameters of CE effects divided into groups according to the VR rate.

Detailed results of the Man-Whitney U test are shown in Table 4.

No significant difference was found between the groups in terms of age and pre-UAE volume.

Regarding comparisons of the CE effects, we found that between leiomyomas with VR rate of ≥ 90% and those with VR rate of < 90%, there was a

significant difference in SI ratio at 35 sec after CMI ( $p = 0.0499$ ), ratio of change in CE ratio from 35 to 60 sec after CMI ( $p = 0.0153$ ), and ratio of change in CE ratio from 35 to 80 sec after CMI ( $p = 0.0185$ ).

Each ROC curve is shown in Figs. 2, 3, and 4. The SI ratio after 35 sec had an AUC of 0.778, a sensitivity of 0.6, and a specificity of 0.885. The ratio of change in CE ratio from 35 to 60 sec showed an AUC of 0.797, a sensitivity of 1, and a specificity of 0.577. The ratio of change in CE ratio from 35 to 80 sec had an AUC of 0.794, a sensitivity

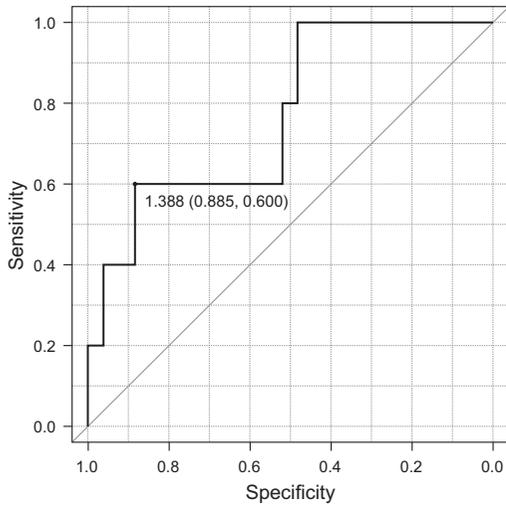


Fig. 2. The receiver operating characteristics (ROC) curve for the leiomyoma-to-skeletal muscle (LSM) signal intensity (SI) ratio (35 sec) shows that the area under the ROC curve (AUC) was 0.778 (95% confidence interval (CI), 0.5405-0.998), with a sensitivity of 0.6, a specificity of 0.885, and a cut-off value of 1.388.

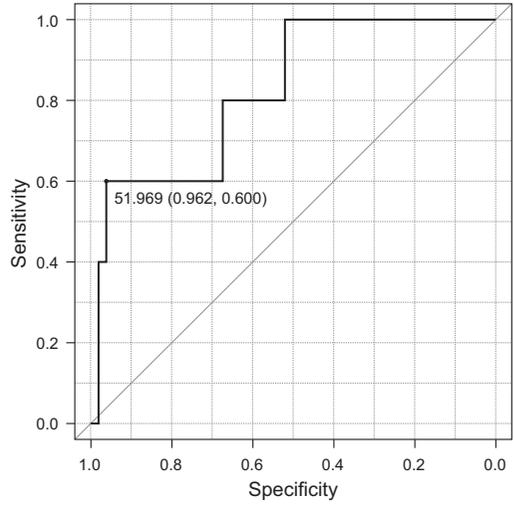


Fig. 4. The receiver operating characteristics (ROC) curve for the ratio of change in contrast enhancement effects (CE) ratio during dynamic contrast enhanced (DCE)-MRI (from 35 to 80 sec) shows that the area under the ROC curve (AUC) was 0.794 (95% confidence interval CI, 0.626-1), with a sensitivity of 0.6, a specificity of 0.962, and a cut-off value of 51.969.

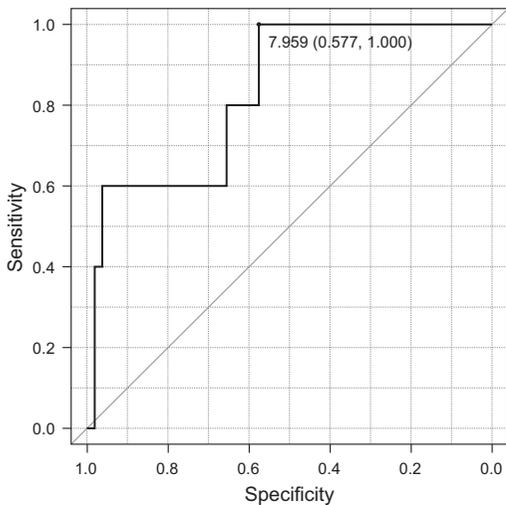


Fig. 3. The receiver operating characteristics (ROC) curve for the ratio of change in contrast enhancement effects (CE) ratio during dynamic contrast enhanced (DCE) -MRI (from 35 to 60 sec) shows that the area under the ROC curve (AUC) was 0.797 (95% confidence interval CI, 0.646-1), with a sensitivity of 1, a specificity of 0.577, and a cut-off value of 7.959.

of 0.6, and a specificity of 0.962. Delong's test did not reveal any significant differences between AUCs for all parameters (Table 5).

Table 5. Results of Delong's test

|   | p-value |
|---|---------|
| AUC of SI ratio (35 sec) and AUC of the ratio of change in CE ratio (from 35 to 60 sec)                                   | 0.235   |
| AUC of SI ratio (35 sec) and AUC of the ratio of change in CE ratio (from 35 to 80 sec)                                   | 0.297   |
| AUC of the ratio of change in CE ratio (from 35 to 60 sec) and AUC of the ratio of change in CE ratio (from 35 to 80 sec) | 0.667   |

SI: signal intensity. CE: contrast enhancement. AUC: area under the curve

## DISCUSSION

In this study, we evaluated the predictive value of DCE-MRI for VR of leiomyomas in post-UAE. A high VR rate of  $\geq 90\%$  was observed in leiomyomas with a weak CE effect at 35 sec after CMI and a faster increase in the ratio of change in CE ratio from 35 to 60 sec after CMI and 35 to 80 sec after CMI.

Predicting clinical outcomes after UAE allows better patient selection and counseling. The clinical improvement related to greater VR remains

contentious with no immediate association with symptom improvement<sup>13)</sup>. However, leiomyoma VR after UAE is considered an important outcome for patient satisfaction.

Harman *et al.*<sup>14)</sup> stated that the CE effect of lesions before UAE aids in patient selection and prognosis determination; this was supported by Jha *et al.*<sup>4)</sup>, who identified hypervascularity of leiomyoma as a strong predictor of high VR rate. In contrast, several studies found no significant correlation between the CE effect of leiomyoma and VR<sup>5, 6, 15)</sup>. Hecht *et al.*<sup>6)</sup> suspected that a single time point measurement of the CE effect might be insufficient to predict the VR of leiomyoma. Additionally, MR perfusion has been found to have no significant effect on the mean VR<sup>13)</sup>.

Our study demonstrated that leiomyomas with weak CE effects at 35 sec after CMI and a subsequent high rate of increase in the ratio of change in CE ratio might have a high VR rate of  $\geq 90\%$ . These results suggest that the weak CE effects at 35 sec after CMI could be a good predictors of a high VR rate of uterine leiomyoma regardless of the contrast effect at 60 and 80 sec after CMI, in addition to the high ratio of change in CE ratio during the dynamic MRI scans.

A previous study reported that increased CE is associated with several factors, such as higher cellularity, higher vessel density, and lower degeneration (measured as hyalinization in leiomyomas)<sup>16)</sup>. Shimada *et al.*<sup>17)</sup> found that the leiomyoma vascularity on DCE-MRI were closely related to the number of vessels and the degree of hyalinization in uterine leiomyoma. Furthermore, they found that contrast effects after 60 and 180 sec correlated with intra-tumoral vessel density.

Taking our results into consideration, leiomyomas with slowly increasing CE patterns, weak CE effects in the early phase reflecting the arterial blood flow, and strong CE effects in the late phase reflecting the intra-tumoral vessel density, may have a high VR

rate.

We suspected that leiomyomas with gradual enhancement from 35 to 60 or 80 sec could have a high VR rate because embolic agents enter the leiomyoma slowly and are less likely to be washed out due to the development of the intra-tumoral vascular network compared with leiomyomas with strong enhancement at 35 sec. However, this was only a speculation as there has been no pathological verification.

From our observations, it can be deduced that DCE-MRI, which can evaluate multiple phases, may be useful in predicting VR rate of UAE.

Our study had several limitations. First, this study utilized a retrospective design with a relatively small sample and a small number of leiomyomas. In particular, only a small number of patients demonstrating a VR rate of  $\geq 90\%$  were found. Next, it was not possible to unify the observations of all target leiomyomas into the same MRI device, the same timing of MRI after UAE, and the same imaging protocol, due to the study's retrospective nature. Further prospective studies with larger populations are necessary to validate the results of this study. Third, the ROI used to evaluate the CE effect is set based on the consensus between two radiologists; therefore, reproducibility might be low. Finally, since the ROI is set to surround the entire leiomyoma, it is possible that the CE effects reflected tumor vascularity and degeneration.

In conclusion, DCE-MRI can be a safe tool for predicting the therapeutic effect of UAE, particularly in patients with excellent therapeutic effects with increased contrast effect from 35 to 60 sec and from 35 to 80 sec after CMI.

## REFERENCES

- 1) Keung JJ, Spies JB, Caridi TM: Uterine artery embolization: A review of current concepts. *Best Pract Res Clin Obstet Gynaecol.* 2018; 46: 66-73. doi: 10.1016/j.bpobgyn.2017.09.003.

- 2) Katsumori T, Yoshikawa T, Miura H: Insufficient Leiomyoma Infarction in Uterine Artery Embolization: Relationship with Tumor Location. *J Vasc Interv Radiol.* 2019; 30: 668-675. doi: 10.1016/j.jvir.2018.11.041.
- 3) Gabriel-Cox K, Jacobson GF, Armstrong MA, Hung YY, Learman LA: Predictors of hysterectomy after uterine artery embolization for leiomyoma. *Am J Obstet Gynecol.* 2007; 196: 588. e1-588. e6. doi: 10.1016/j.ajog.2007.03.014.
- 4) Jha RC, Ascher SM, Imaoka I, Spies JB: Symptomatic fibroleiomyomata: MR imaging of the uterus before and after uterine arterial embolization. *Radiology.* 2000; 217: 228-235. doi: 10.1148/radiology.217.1.r00se49228.
- 5) Burn PR, McCall JM, Chinn RJ, Vashisht A, Smith JR, Healy JC: Uterine fibroleiomyoma: MR imaging appearances before and after embolization of uterine arteries. *Radiology.* 2000; 214: 729-734. doi: 10.1148/radiology.214.3.r00fe07729.
- 6) Hecht EM, Do RK, Kang SK, Bennett GL, Babb JS, Clark TW: Diffusion-weighted imaging for prediction of volumetric response of leiomyomas following uterine artery embolization: a preliminary study. *J Magn Reson Imaging.* 2011; 33: 641-646. doi: 10.1002/jmri.22459.
- 7) Kim YS, Lim HK, Kim JH, *et al.*: Dynamic contrast-enhanced magnetic resonance imaging predicts immediate therapeutic response of magnetic resonance-guided high-intensity focused ultrasound ablation of symptomatic uterine fibroids. *Invest Radiol.* 2011; 46: 639-647. doi: 10.1097/RLI.0b013e318220785c.
- 8) Wei C, Fang X, Wang CB, Chen Y, Xu X, Dong JN: The predictive value of quantitative DCE metrics for immediate therapeutic response of high-intensity focused ultrasound ablation (HIFU) of symptomatic uterine fibroids. *Abdom Radiol (NY).* 2018; 43: 2169-2175. doi: 10.1007/s00261-017-1426-7.
- 9) Deshmukh SP, Gonsalves CF, Guglielmo FF, Mitchell DG: Role of MR imaging of uterine leiomyomas before and after embolization. *Radiographics.* 2012; 32: E251-E281. doi: 10.1148/rg.326125517.
- 10) Nikolaidis P, Siddiqi AJ, Carr JC, Vogelzang RL, Miller FH, Chrisman HB, Nemcek AA Jr, Omary RA: Incidence of nonviable leiomyomas on contrast material-enhanced pelvic MR imaging in patients referred for uterine artery embolization. *J Vasc Interv Radiol.* 2005; 16: 1465-1471. doi: 10.1097/01.RVI.0000175333.41751.71.
- 11) Orsini LF, Salardi S, Pilu G, Bovicelli L, Cacciari E: Pelvic organs in premenarcheal girls: real-time ultrasonography. *Radiology.* 1984; 153: 113-116. doi: 10.1148/radiology.153.1.6473771.
- 12) Kanda Y: Investigation of the freely available easy-to-use software 'EZR' for medical statistics. *Bone Marrow Transplant.* 2013; 48: 452-458. doi: 10.1038/bmt.2012.244.
- 13) deSouza NM, Williams AD: Uterine arterial embolization for leiomyomas: perfusion and volume changes at MR imaging and relation to clinical outcome. *Radiology.* 2002; 222: 367-374. doi: 10.1148/radiol.2222010584.
- 14) Harman M, Zeteroğlu S, Arslan H, Sengül M, Etlik O: Predictive value of magnetic resonance imaging signal and contrast-enhancement characteristics on post-embolization volume reduction of uterine fibroids. *Acta Radiol.* 2006; 47: 427-435. doi: 10.1080/02841850600557117.
- 15) Duvnjak S, Ravn P, Green A, Andersen PE: Magnetic Resonance Signal Intensity Ratio Measurement Before Uterine Artery Embolization: Ability to Predict Fibroid Size Reduction. *Cardiovasc Intervent Radiol.* 2017; 40: 1839-1844. doi: 10.1007/s00270-017-1721-2.
- 16) Yamashita Y, Torashima M, Takahashi M, Tanaka N, Katabuchi H, Miyazaki K, Ito M, Okamura H: Hyperintense uterine leiomyoma at T2-weighted MR imaging: differentiation with dynamic enhanced MR imaging and clinical implications. *Radiology.* 1993; 189: 721-725. doi: 10.1148/radiology.189.3.8234695.
- 17) Shimada K, Ohashi I, Kasahara I, Miyasaka N, Shibuya H: Triple-phase dynamic MRI of intratumoral vessel density and hyalinization grade in uterine leiomyomas. *AJR Am J Roentgenol.* 2004; 182: 1043-1050. doi: 10.2214/ajr.182.4.1821043.