Introduction

Uterine sarcomas are rare tumors with poor prognosis, and the most common subtypes are leiomyosarcoma (LMS), endometrial stromal sarcoma (ESS), and carcinosarcoma (CS). Different subtypes of uterine sarcomas have different operative approaches.[1-6] Such as the standard surgical excision of uterine sarcomas consists of hysterectomy and bilateral salpingo-oophorectomy,[4] but oophorectomy of LMS was not found to have an independent impact on survival by Kapp.[5] Surgical methods consisting of hysterectomy with bilateral salpingo-oophorectomy, lymphadenectomy, and cytoreduction are the initial recommended treatment for CS.[6] With the development of precision medicine, individual treatment is necessary for patients with different subtypes of uterine sarcomas, especially for young women. Accordingly, it is very important to preoperatively distinguish these three uterine sarcomas to guide in the surgical approach to avoid surgical resection of large areas.

Previous studies have reported that 92% of patients with CS presented with abnormal uterine bleeding, and 86.7% of patients with LMS presented with pelvic or abdominal masses.[7] Clinical indexes such as age, menopausal status, and blood type were
proven to be correlated with survival.[8] These clinical characteristics of the patients with different subtypes of uterine sarcomas may be different. Therefore, it is necessary to compare the clinical characteristics of the patients with different subtypes of uterine sarcomas.

Compared with ultrasonography and computed tomography (CT), magnetic resonance imaging (MRI) is the best imaging modality for assessing uterine lesions.[9,10] Some researches have suggested that MRI can help differentiate uterine sarcomas from other tumors.[9–13] Diffusion-weighted imaging (DWI) is a recent technique to reflect the diffusivity of water molecules in tumors. It has been used to differentiate uterine sarcomas from leiomyoma or endometrial carcinoma by measuring mean or minimum apparent diffusion coefficient (ADC) values.[14–17] However, literature is lacking on use of the lesion-muscle ADC ratio (rADC) values on MRI for uterine sarcomas. There was no article about this study was to explore the value of clinical parameters combined with MRI features to differentiate the subtypes of uterine sarcomas. The purpose of

2. Methods

2.1. Study subjects

From January 2011 to December 2018, a total of 80 patients with uterine sarcomas, who underwent preoperative MRI with DWI and had histological results at our institutions, were retrospectively reviewed. Four patients confirmed by pathologic biopsies and 3 patients confirmed by fractional curettage were excluded. Two patients having a history of chemotherapy and/or radiation therapy before surgery were excluded. The remaining 71 patients (15 patients with LMS, 29 patients with ESS, and 27 patients with CS) who were diagnosed by surgery and had complete clinical data and MR images were included. The institutional review board of our hospital approved this retrospective study and waived the requirement for written informed consent of patients.

2.2. Clinical parameters

The following clinical characteristics were collected: age, menopause status, blood type, body mass index (BMI), fertility status, presenting symptoms, and laboratory parameters including CA125, lactic dehydrogenase (LDH). Normal range for LDH was 109 to 245 U/L, and for CA125, the normal value was less than 35 U/ml.

2.3. MRI protocols

MR images were acquired using a 3.0T system (Signa HD Excite, GE healthcare, Milwaukee, USA) through an 8-channel phased array coil. The acquisition protocol is summarized in Table 1. In brief, axial T1-weighted spin-echo images and axial and sagittal T2-weighted fast spin-echo images with fat suppression were obtained. Dynamic contrast-enhanced liver acceleration volume injection was obtained with a gadopentetate dimeglumine injection at a dose of 0.2 ml/kg of body weight at a rate of 2 ml/s. The axial dynamic images were obtained before injection, and at 30 (arterial phase), 47 (venous phase), and 64 (delayed phase) seconds into examination after injection. The sagittal contrast images were obtained at 90 seconds into examination after injection. DWI was performed for the axial plane by using spin-echo type and single-shot echo planar imaging with parallel imaging techniques by setting b value = 0 and 800 s/mm².

2.4. MRI analyses

Two radiologists with 26 and 13 years of experience in gynecologic radiology reviewed the MR images without prior knowledge of the clinical and histological information. The two reviewers looked at all MR images individually and agreement was reached after careful evaluation. The main location, shape, maximum tumor diameters, band sign, cystic change or necrosis, hemorrhage (high signal on T1WI), T1WI and T2WI signals of solid tumor component, enhancement, mean ADC, minimum ADC, and rADC values were noted. Maximum tumor diameters were measured in 3 orthogonal planes: anteroposterior, transverse diameters on axial T2WI, and craniocaudal diameters on sagittal T2WI. The band sign was defined as the bands of low-signal intensity on T2WI within the area of myometrial invasion. On T1WI, hypo-, iso-, and hyperintensity were similar to the intravasical liquid, myometrium, and fat signal; on T2WI, hypo-, iso-, and hyperintensity were similar for the bone, myometrium, and intravasical liquid; on contrast-enhanced MRI (CE-MRI), mild, moderate, and marked enhancement were less than, equal to, and superior to the myometrium. The mean and minimum ADC values within the solid components of the tumors were measured in a circular region of interest (ROI) in the maximum tumor slice from the ADC maps on the ADC software (AW 4.6 workstation, GEMS). Necrotic, cystic, or hemorrhagic areas in the ROI were avoided as much as possible. For the rADC values, internal obturator muscle was used as the reference site, and the same method mentioned above was used to measure the mean ADC values of the muscles. ADC values for each patient were averaged from three repetitions. The readers were blinded to the types of tumors. The mean and

| Parameters | Sag T2WI | Ax T2WI | Ax T1 | Ax DWI | Ax LAVA+c | Sag LAVA+c |
|------------|----------|---------|-------|--------|-----------|------------|
| TR (ms)    | 3040     | 4400    | 175   | 4375   | 4         | 3.9        |
| TE (ms)    | 107.5    | 106.6   | 1.8   | 65.6   | 1.9       | 1.8        |
| Slice thickness (mm) | 6     | 5       | 5     | 5      | 4         | 4          |
| Slice gap (mm) | 1    | 1.5     | 1     | 1.5    | 0         | 0          |
| FOV (cm)   | 28 × 22.4 | 28 × 22.4 | 40 × 28 | 36 × 27 | 40 × 32   | 35 × 28    |
| Matrix     | 288 × 224 | 320 × 224 | 320 × 224 | 128 × 128 | 320 × 224 | 288 × 224 |
| NEX        | 1        | 1       | 1     | 5      | 0.72      | 0.71       |

FOV = field of view, LAVA = liver acceleration volume acquisition, NEX = number of excitation, TE = echo time, TR = repetition time.
Clinical characteristics of 57 uterine sarcomas as regards different types of uterine sarcoma.

|                  | LMS (N = 15) | ESS (N = 29) | CS (N = 27) | P   | P1  | P2  | P3  |
|------------------|--------------|--------------|-------------|-----|-----|-----|-----|
| Average age (years),range | 48±8.33–66   | 43±12.20–71  | 59±9.39–75  | <.001 | .09 | .001 | <.001 |
| Menopausal status  |              |              |             |     |     |     |     |
| Premenopausal     | 12           | 25           | 5           | <.001 | .68 | <.001 | <.001 |
| Postmenopausal    | 3            | 4            | 22          | .94  |     |     |     |
| Blood type        |              |              |             |     |     |     |     |
| A                | 5            | 9            | 10          |      |     |     |     |
| B                | 5            | 7            | 9           |      |     |     |     |
| AB               | 1            | 4            | 3           |      |     |     |     |
| O                | 4            | 9            | 5           |      |     |     |     |
| BMI (kg/m²)       | 23.5±3.9     | 23.3±4.4     | 24.2±3.6    | .53  |     |     |     |
| Childbearing history |            |              |             |     |     |     |     |
| Nulliparity       | 1            | 5            | 1           | .27  |     |     |     |
| Abortion          | 9            | 22           | 22          | .32  |     |     |     |
| Clinical manifestation |          |              |             |     |     |     |     |
| Irregular vaginal bleeding | 4          | 11           | 24          |      |     |     |     |
| Menstrual disorder | 5            | 7            | 1           |      |     |     |     |
| Abdominal pain    | 3            | 6            | 1           |      |     |     |     |
| Pelvic mass       | 3            | 2            | 0           |      |     |     |     |
| Physical examinations |          | 3            | 1           |      |     |     |     |
| Laboratory investigation |     |              |             |     |     |     |     |
| CA125†            | 5            | 6*           | 8†          | 1    |     |     |     |
| LDH†              | 3†           | 3*           | 3†          | .65  |     |     |     |

BMI = body mass index, CS = carcinosarcoma, ESS = endometrial stromal sarcoma, LDH = lactic dehydrogenase, LMS = leiomyosarcoma.

* 8 cases unknown.
† 2 cases unknown.
‡ 2 cases unknown.
§ 6 cases unknown.
¶ 1 case unknown.

P, comparing data among the three groups with a value of P <.05; P1, comparing data between LMS and ESS; P2, comparing data between LMS and CS; P3, comparing data between ESS and CS. *P1-P3, all using an adjusted significant level, α = .017.

Bold fonts, considering statistically significant.

Continuous variables were expressed as arithmetic means and standard deviations.

minimum ADC values with the area of each ROI were recorded. The rADC values for each patient were calculated using the following formula: lesion ADC values/muscular ADC values (rADC = mean ADC values of uterine sarcoma/ADC values of internal obturator muscle).

### 2.5. Statistical analyses

Statistical analyses were performed with SPSS base 20.0 (SPSS, Inc, Chicago, IL) for Windows. Continuous variables were expressed as arithmetic means and standard deviations. Kolmogorov-Smirnov tests were used to test the normality of the data distributions. The data were not normally distributed, so nonparametric tests were performed. The Fisher’s exact test was used to compare the categorical variables among/between the groups with a value of P <.05 or .017. The Kruskal-Wallis H test was used to compare continuous variables among the three groups. A value of P <.05 was considered statistically significant. The Mann-Whitney U tests were used to compare continuous variables between two groups with an adjusted significant level, α’ = .017.

### 3. Results

#### 3.1. Clinical characteristics

The relational data of the patients are listed in Table 2. Patients with CS were significantly older than the patients with LMS and ESS (P =.001 and P <.001, respectively). Most patients with CS (81.5%) were postmenopausal with a mean age of 59 years old. Most patients with ESS (86.2%) were premenopausal with a wide range of 20 to 71 years old. Clinical manifestations of patients with CS were significantly different from the presentations of LMS or ESS (P <.001 and P =.001, respectively). Almost all patients with CS (88.9%) presented with irregular vaginal bleeding. Menstrual disorder was the most common presenting symptoms for patients with LMS (33.3%). There were no significant differences between subtypes of uterine sarcomas regarding blood type, BMI, childbearing history, and laboratory parameters. However, there were some similarities among the three groups. Forty-five patients (63.4%) with uterine sarcomas were type A and B, and 53 patients (74.6%) had a history of abortion.

#### 3.2. MRI characteristics and ADC values

The principal MRI characteristics of each type of sarcoma are shown in Table 3 and Figures 1–3. Twenty-three CS (85.2%) were mainly located in the uterine cavity (Fig. 1), which was obvious significantly different from LMS or ESS (P <.001 and P =.01, respectively). There was a significant difference in the tumor shape between CS and LMS or ESS (P <.001 and P =.002, respectively). All the LMS were lobulated or round (Fig. 2), 14 lesions (51.9%) with CS were endometrioid (Fig. 1). Cystic change or necrosis was found in most uterine sarcomas (84.5%), in which most cystic change or necrosis (80.0%) was patchy.
Continuous variables were expressed as arithmetic means and standard deviations. Bold fonts, considering statistically significant using an adjusted significance level, \( P < .017 \).

Magnetic resonance imaging characteristics of 57 uterine sarcomas as regards different types of uterine sarcoma.

| Location          | LMS (N = 15) | ESS (N = 29) | CS (N = 27) | \( P \) | \( P_1 \) | \( P_2 \) | \( P_3 \) |
|-------------------|--------------|--------------|-------------|--------|--------|--------|--------|
| Subserosa         | 0            | 2            | 0           | .001   | .46    | < .001 | .01    |
| Myometrium        | 5            | 7            | 0           |        |        |        |        |
| Uterine cavity    | 5            | 15           | 23          |        |        |        |        |
| Cervical canal    | 1            | 2            | 3           |        |        |        |        |
| Extraterine       | 4            | 3            | 1           |        |        |        |        |
| Shape             |              |              |             |        | < .001 | .16    | < .001 | .002   |
| Lobulated         | 13           | 16           | 12          |        |        |        |        |
| Round             | 2            | 5            | 0           |        |        |        |        |
| Endometrioid      | 0            | 4            | 14          |        |        |        |        |
| Other shape       | 0            | 4            | 1           |        |        |        |        |

| Maximum tumor diameters (mm) | Transverse | Anteroposterior | Cranio-caudal | \( P \) | \( P_1 \) | \( P_2 \) | \( P_3 \) |
|------------------------------|------------|-----------------|---------------|--------|--------|--------|--------|
| LMS                          | 63.3 ± 27.5| 56.7 ± 20.5     | 54.1 ± 28.9   | .52    |        |        |        |
| ESS                          | 64.0 ± 27.3| 51.0 ± 25.6     | 47.0 ± 22.0   | .16    |        |        |        |
| CS                           | 69.6 ± 28.3| 61.3 ± 20.6     | 63.0 ± 35.9   | .67    |        |        |        |

| Band sign                  | 0 | 18 | 1 | < .001 | < .001 | 1 | < .001 |
| Solid component on T1WI    |   |    |   |        | < .001 | .29 | < .001 |
| Slight hyperintensity      | 2 | 9  | 0 |        |        |    |        |
| Isointensity               | 13| 18 | 13|        |        |    |        |
| Slight hypointensity       | 0 | 2  | 14|        |        |    |        |
| Solid component on T2WI    |   |    |   |        | < .001 | .07 | < .001 |
| Slight hyperintensity      | 4 | 17 | 23|        |        |    |        |
| Isointensity               | 0 | 0  | 0 |        |        |    |        |
| Slight hypointensity       | 0 | 1  | 0 |        |        |    |        |
| Mixed signal               | 11| 11 | 4 |        |        |    |        |
| Enhancement                |   |    |   |        | < .001 | < .001 | < .001 | .04    |
| Marked enhancement in arterial phase | 12 | 4 | 0 |        |        |    |        |
| Marked enhancement in venous phase | 0 | 2 | 0 |        |        |    |        |
| Mild and delayed enhancement | 3  | 23 | 27|        |        |    |        |

| Mean ADC (\(10^{-3}\text{mm}^2/\text{s}\)) | 0.99 ± 0.21 | 1.03 ± 0.20 | 0.93 ± 0.21 | .20    |
| Minimum ADC (\(10^{-3}\text{mm}^2/\text{s}\)) | 0.82 ± 0.21 | 0.83 ± 0.15 | 0.72 ± 0.20 | .06    |
| rADC                         | 0.70 ± 0.15 | 0.74 ± 0.15 | 0.64 ± 0.14 | .02    |

ADC = apparent diffusion coefficient, CS = carcinosarcoma, ESS = endometrial stromal sarcoma, LMS = leiomyosarcoma, rADC = mean ADC values of uterine sarcoma/ADC values of internal obturator muscle.

\( P \), comparing data among the three groups with a value of \( P < .05 \); \( P_1 \), comparing data between LMS and ESS; \( P_2 \), comparing data between LMS and CS; \( P_3 \), comparing data between ESS and CS. \( P_1 \)–\( P_3 \), all using an adjusted significant level, \( \alpha = .017 \).

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(Fig. 3). Six lesions (40.0%) with LMS had slit-like cystic change or necrosis (Fig. 2). A statistically significant difference in the shape of cystic change or necrosis was found between LMS and ESS or CS (\( P < .003 \) and \( P < .001 \), respectively). Eighteen patients (62.1%) with ESS displayed the band sign on T2WI (Fig. 3). The presence of band sign was significantly higher in ESS than in LMS or CS (both \( P < .001 \)). Maximum tumor diameters in the 3 orthogonal planes in the MR images of patients with LMS were the largest. Forty-five patients (45.1%) with uterine sarcomas exist hemorrhage (Fig. 2). However, there was no obvious significant difference in the maximum tumor diameters or hemorrhage between subtypes of uterine sarcomas.

On T1WI, most solid LMS (86.7%) and ESS (62.1%) showed isointensity (Figs. 2–3) and 14 CS (51.9%) showed slight hypointensity (Fig. 1). The difference in T1WI of CS compared to LMS or ESS is statistically significant (both \( P < .001 \)). On T2WI, the solid LMS (73.3%) usually appeared mixed signals (Fig. 2), which was significantly different from the solid CS (85.2%) that mainly showed slight hyperintensity (\( P < .001 \)) (Fig. 1). On CE-MRI, most LMS (80.0%) showed marked enhancement in the arterial phase (Fig. 2). All CS appeared mild and delayed enhancement (Fig. 1). There was a statistically significant difference in the enhancement between LMS and ESS or CS on CE-MRI (both \( P < .001 \)). A statistically significant difference in the rADC values was observed between ESS and CS (\( P = .004 \)). There were no significant differences among the groups in mean ADC and minimum ADC values. But the mean ADC, minimum ADC, and rADC values of ESS were higher than other groups.

4. Discussion

This research demonstrated that clinical parameters (age and clinical manifestation) and MRI characteristics (tumor location, shape, band sign, cystic change or necrosis, rADC values, and so on) of different types of uterine sarcoma are different.
T1WI and T2WI signals of the solid components were helpful to distinguish different subtypes of uterine sarcomas. The most common subtype of uterine sarcomas in previous studies is LMS. There were only 15 patients with LMS in our study. One possible reason for this discrepancy is that some patients with LMS were only tested by ultrasound examination rather than MRI before surgeries.

CS is a very aggressive tumor that was composed of both epithelial and mesenchymal elements. According to the revised FIGO 2009, CS is regarded as a subset of endometrial carcinoma, since CS has the same precursor cell origin as endometrial carcinoma. But because it has a higher incidence of distant metastasis, lymphatic spread, and a poorer prognosis than endometrial carcinoma, it is still considered as one of the common subtypes of uterine sarcomas. CS often occurs in the postmenopausal woman and generally presented as irregular vaginal bleeding just like endometrial carcinoma. LMS and ESS are often seen in perimenopausal patients, both younger than CS. ESS also occurs more commonly in premenopausal women with a wide age range. These results are consistent with this study.

MRI is an option for qualitatively and quantitatively assessing the lesion, detecting malignancy, and characterizing features of tumors. The location of the uterine sarcomas correlates with distant metastasis, lymphatic spread, and a poorer prognosis than endometrial carcinoma, it is still considered as one of the common subtypes of uterine sarcomas. CS often occurs in the postmenopausal woman and generally presented as irregular vaginal bleeding just like endometrial carcinoma. LMS and ESS are often seen in perimenopausal patients, both younger than CS. ESS also occurs more commonly in premenopausal women with a wide age range. These results are consistent with this study.

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the origin of tumor cells or tissue.\textsuperscript{19,25,26} CS and ESS are stemmed from endometrium epithelial cells and/or endometrial stromal cells,\textsuperscript{19,26} so they are mainly located in the uterine cavity. The shape of most cases with CS was endometrioid in our investigation. This is also related to the endometrial origin of tumor cells because endometrium-derived tumors are often characterized by irregular thickening of the endometrium, which leads to the formation of endometrioid masses.\textsuperscript{19} While a lot of LMS and ESS were lobulated or round, the revised FIGO 2009 classified CS along with endometrial carcinoma to distinguish from other USs.\textsuperscript{20} Lesions with ESS displayed the band sign, which was first noted by Koyama.\textsuperscript{27} The band sign shows that bands of low signal intensity within areas of myometrial involvement on T2WI are equivalent to the relict bundles of bands of low signal intensity within areas of myometrial hypointensity on T1-weighted image.\textsuperscript{27} Axial diffusion-weighted imaging showed hyperintensity in the solid component of tumor.\textsuperscript{27} Axial ADC map revealed the solid component of ESS showed restricted diffusion, and the mean ADC, minimum ADC, and rADC values were $1.12 \times 10^{-3} \text{mm}^2/\text{s}$, $0.80 \times 10^{-3} \text{mm}^2/\text{s}$, 0.74 respectively.\textsuperscript{27} Axial T1-weighted image revealed the solid component of ESS showed slight hyperintensity.\textsuperscript{27} Axial contrast-enhanced magnetic resonance imaging including arterial phase, venous phase, and delayed phase, and ESS displayed mild and delayed enhancement. ESS=endometrial stromal sarcoma, ADC=apparent diffusion coefficient, rADC=lesion-muscle ADC ratio.

Uterine sarcoma generally appears with heterogeneous intensity on MRI due to the existence of abundant cystic, hemorrhagic, and necrotic areas.\textsuperscript{35} Accordingly, we only observed the solid component of lesions on T1WI or T2WI in this study. Most patients with uterine sarcomas show isointensity on T1WI.\textsuperscript{24} As a subtype of endometrial carcinoma, CS usually presents hyperintensity on T1WI, it may be related to the abundance of glands in the endometrium.\textsuperscript{20,29} This study found forty-five patients (45.1%) with uterine sarcomas exist hemorrhage. It was hard to avoid containing microscopic hemorrhage in the solid component of tumors, so we could observe slight hyperintensity with some solid tumors on T1WI. On T2WI, the solid component of most LMS (73.3%) usually appeared with mixed signals. It may be that LMS has complicated compositions, including uterine smooth muscle and mesenchymal tissue.\textsuperscript{10} We found that most LMS showed marked and rapid enhancement, similar to previous studies.\textsuperscript{24} The marked and rapid enhancement is related to the higher microvessel density in LMS.\textsuperscript{131} ESS and CS originated from endometrial stromal tissues, which are usually hypovascular,\textsuperscript{132} and all CS and 79.3% ESS appeared mild with delayed enhancement in our study. There was a statistically significant difference in enhancement between LMS and ESS or CS. Consequently, CE-MRI could also be used as a parameter to distinguish the different subtypes of uterine sarcomas.\textsuperscript{133} DWI is able to determine malignant lesions as a hyperintense area with excellent tissue contrast. Additionally, the quantitative measurement of ADC values could also be provided to assist in more accurate diagnosis of uterine sarcomas.\textsuperscript{133} Uterine sarcoma has high cellularity and high nuclear-to-cytoplasm ratio of tumor cells, which limit the diffusivity of water molecules, leading to high signals on DWI and low ADC values.\textsuperscript{114,17,24,33} However, the minimum ADC values only represent the water molecular diffusive rate of a small part of the total tumor, and the mean ADC value may be influenced by the ROI positioning and size.\textsuperscript{114} Factors such as scanning time, environmental temperature, and individual differences of patients may also react on ADC values. Therefore, the concept of rADC values using internal obturator muscle as the reference site was introduced in this study. Karakas et al\textsuperscript{133} discovered that there was a significant difference in tumor-myometrium ADC ratios between endometrial carcinoma and other benign lesions. Menstrual cycle and hormonal variation may affect myometrial ADC values,\textsuperscript{136} and completely normal myometrium is rare due to strong tumor infiltration. Internal obturator muscle is unlikely to be infiltrated by the lesions or affected by hormones. Accordingly, using internal obturator muscle as the reference site is more stable than using myometrium. And our results proved that there was a significant difference between ESS and CS in the rADC values. One reason is that CS is a highly malignant tumor.\textsuperscript{139} On the other hand, ESS is more likely to appear cystic change and necrosis,\textsuperscript{19} microscopic necrotic areas or cystic components may increase the ADC values of the solid tumor component.\textsuperscript{114} A few limitations should be considered when interpreting the results of this study. First, the numbers of patients with uterine...
sarcoma with preoperative MR images were limited, although the number of uterine sarcoma with MRI data reported from a single center was relatively large. Future studies should be performed with a greater number of patients. Second, our team has done some research on using clinical parameters with MRI to differentiate uterine sarcomas from leiomyoma, which included lots of available contents. So, we only incorporated 3 histopathological subtypes of uterine sarcoma and did not compare with leiomyoma in this study.

In conclusion, clinical characteristics combined with MRI features could help narrowing preoperative diagnostic possibilities. These multiple parameters preliminary proved to be beneficial in the preoperative identification of different subtypes of uterine sarcoma. Large samples or prospective studies will be needed to verify our conclusions in the future.

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