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Original Article

Efficacy of PET/CT to exclude leiomyoma in patients with lesions suspicious for uterine sarcoma on MRI

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ABSTRACT

Objective: To analyze the efficacy of positron emission tomography/computed tomography (PET/CT) for the diagnosis of uterine sarcoma.

Materials and methods: Thirty-four patients evaluated between January 2010 and March 2015 were retrospectively enrolled. All patients in whom uterine sarcoma was suspected based on contrast-enhanced magnetic resonance imaging (MRI) findings (heterogeneous, high signal intensity on T2-weighted images and/or high intensity on T1-weighted images) underwent PET/CT for further assessment. Patients were divided into 2 groups based on postoperative pathological findings: uterine sarcoma (n = 15) and leiomyoma (n = 19). The maximum standardized uptake value (SUVmax) of all lesions was measured using PET/CT; we calculated the optimal cutoff value for diagnosing sarcoma.

Results: The median SUVmax for uterine sarcoma and leiomyoma was 12 and 4.1, respectively; these values were significantly different. An SUVmax of greater than 7.5 was able to exclude leiomyoma with 80.8% sensitivity and 100% specificity (area under the curve, 95.3%). A cutoff SUVmax of 7.5 yields 100% specificity, and a cutoff SUVmax of 4.4 yields a 100% negative predictive value (NPV). The combination of PET/CT and lactate dehydrogenase (LDH) levels had a sensitivity of 86.6%, specificity of 100%, positive predictive value of 100%, and an NPV of 90.4%. No relation between histopathology or International Federation of Gynecology and Obstetrics (FIGO) stage and 18-fluoro-2-deoxy-D-glucose uptake value on PET/CT was seen. The surgical outcome trended toward a correlation with the SUVmax, although this was not statistically significant.

Conclusions: In patients with MRI findings consistent with either uterine sarcoma or leiomyoma, PET/CT can decrease the false-positive rate by setting an optimal cutoff SUVmax of 7.5. Using this cutoff can avoid unnecessary surgery.

Introduction

Uterine sarcomas are rare, accounting for 3–7% of uterine cancers [1]. They are classified as either leiomyosarcoma (LMS), endometrial stromal sarcoma (ESS), undifferentiated endometrial stromal sarcoma (UES), or adenosarcoma (AS). Uterine sarcomas have a poor prognosis, significantly worse than that of endometrial cancer [1], although ESS and AS have more favorable outcomes than the other subtypes, with a low incidence of recurrence. Some subtypes exhibit abnormal bleeding in the early phase and can be diagnosed using endometrial curettage. However, LMS and UES have similar symptoms to leiomyoma, and these subtypes are not amenable to diagnosis by endometrial sampling [2]. To differentiate lesions with a high risk for uterine sarcoma, primary screening is conducted using symptoms, physical examination findings, tumor size, serum lactate dehydrogenase (LDH) levels, and ultrasound; secondary screening uses magnetic resonance imaging (MRI). It is important to distinguish uterine sarcoma from leiomyoma because of the difference in treatment: leiomyomata have the option for conservative management while sarcomas require surgical treatment. An accurate diagnosis can help patients avoid unnecessary surgery. However, once a uterine tumor is suspected of malignancy,

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surgical intervention with histopathological examination is necessary.

MRI is a well-known diagnostic tool for uterine sarcoma. Sarcomas have a heterogeneous appearance of high signal intensity on T2-weighted images (T2-WI) and/or high signal intensity on T1-weighted images (T1-WI). These findings imply necrosis or hemorrhage of muscle or mesenchymal tissue, but they are not specific to sarcomatous lesions.

Positron emission tomography (PET) is a metabolic imaging modality that uses positron tracers such as 18-fluoro-2-deoxy-D-glucose (^{18}F-FDG). Using FDG PET alone or PET combined with computed tomography (PET/CT) has been increasingly employed for the detection of uterine tumors. Although some authors report the efficacy of PET to detect tumor recurrence in patients with uterine sarcoma, the rarity of the tumors means that little is known about the role of PET in the primary assessment of uterine sarcomas [3,4].

In our institution, patients with lesions suspicious for uterine sarcoma on MRI are sent for confirmation with PET/CT. We retrospectively reviewed the surveillance of uterine tumors using PET/CT and determined the optimal cutoff for the maximum standardized uptake value (SUVmax) to differentiate uterine sarcoma from leiomyoma.

Materials and methods

Patients

Thirty-four patients who were evaluated at Juntendo University Hospital between January 2010 and March 2015 were retrospectively enrolled. Informed consent was obtained from all patients. All patients with lesions suspicious for uterine sarcoma on contrast-enhanced MRI (heterogeneous, high signal intensity on T2-WI and/or high intensity on T1-WI) underwent PET/CT for further assessment. All enrolled patients underwent surgery, and the pathological findings were used to divide them into 2 groups: those with uterine sarcoma and those with leiomyoma. We analyzed the clinical symptoms and signs such as uterine enlargement, abnormal bleeding, tumor size, and serum LDH and cancer antigen (CA) 125 levels in both groups.

PET/CT

All scans were performed using a GE Discovery STE PET/CT (GE Medical Systems, Inc., Milwaukee, WI). Each patient was administered 3.7 MBq/kg ^{18}F-FDG after a 6-h fast and imaged after a 60-min uptake period. Whole-body PET imaging was then performed from the skull base to the upper thighs using 2-dimensional mode, at 3.5 min per each of 6 bed positions, depending on the size of the patient. CT images were acquired over the same range using a pitch of 1.375 mm, 140 kV (peak), 20–300 mA current, and 3.75-mm slices.

MRI

All examinations were performed using a 3 T MRI scanner (MAGNETOM Spectra; Siemens Healthcare GmbH, Erlangen, Germany) equipped with a 16-channel phased array body coil. The pelvic MRI protocol included axial T1-WI sequences (repetition time [TR]/echo time [TE], 550/10 ms; matrix size, 448 × 269; field of view [FOV], 250 mm), T1-WI with fat suppression (TR/TE, 650/13 ms; matrix size, 384 × 230; FOV, 250 mm), diffusion-weighted imaging (DWI) (TR/TE, 6000/77 ms; matrix size, 128 × 80; b values, 0 and 800 s/mm^2; FOV, 400 mm), sagittal T2-WI sequences (TR/TE, 4000/90 ms; matrix size, 448 × 314; FOV, 250 mm), and axial and sagittal contrast-enhanced T1-WI with fat suppression (axial TR/TE, 700/10 ms; matrix size, 384 × 230; FOV, 250 mm; sagittal TR/TE, 680/10 ms; matrix size, 384 × 230; FOV, 250 mm). All images used 5–6 mm section thickness.

SUVmax

The SUVmax of all lesions was measured using PET/CT and compared between groups. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cutoff value for differentiating uterine sarcoma from leiomyoma. Overall survival was analyzed by distribution into low and high SUVmax values, divided by the optimal cutoff value.

Statistical analysis

All statistical analyses were performed using XL STAT software (Addinsoft, Paris, France). Student's t-test was used to compare differences between groups. ROC curve analysis was performed to determine the optimal SUVmax cutoff points for differentiation between uterine sarcoma and leiomyoma. A P value of <0.05 was defined as significant.

Results

Patient characteristics are listed in Tables 1–3. Of the 34 patients with MRI findings suspicious for uterine sarcoma, 15 were diagnosed with sarcoma and 19 were diagnosed with leiomyoma. Of the 15 patients in the sarcoma group, 6 had LMS, 4 had UES, 4 had ESS, and 1 had AS (Figs. 1 and 2); of the 19 patients in the leiomyoma group, 10 had ordinary leiomyomata, 6 had degenerated leiomyomata, and 3 had cellular leiomyomata. The patients in the sarcoma group were significantly older ($P = 0.001$) and had higher LDH levels ($P = 0.001$) and higher FDG uptake values on PET/CT ($P = 0.001$) than those in the leiomyoma group.

Using the ROC curve, a SUVmax greater than 7.5 was able to exclude leiomyoma with 73.3% sensitivity, 100% specificity, 100% positive predictive value (PPV), and 82.6% negative predictive value (NPV) (area under the curve, 93.3%) (Fig. 3).

The sensitivity, specificity, PPV, and NPV of the LDH level were 53.3%, 86.3%, 72.7%, and 73%, respectively; the respective values for CA125 levels were 64.2%, 70.5%, 64.2%, and 70.5%. The combination of PET/CT and LDH had a sensitivity of 86.6%, specificity of 100%, PPV of 100%, and NPV of 90.4%. The histopathology and

Table 1
Characteristics of patients.

	Uterine sarcoma (n = 15)	Leimyoma (n = 19)	*P*-value
Age, mean ± SD, years	55.8 ± 11.4	45 ± 7.0	$P = 0.001$
Tumor size, mean ± SD, cm	12.0 ± 6.5	13.8 ± 4.9	N.S
Metrorrhagia	12	3	N.S
Level of LDH (mean ± SD)	343 ± 188	183.1 ± 44	$P = 0.001$
Lavel of CA125 median (range)	44 (7–206)	26 (7–108)	N.S
SUVmax of PET/CT	15.1 ± 12.6	4.0 ± 2.4	$P = 0.001$
Histopathological			
LMS	6		
ESS	4		
UES	4		
Adenosarcoma	1		
Originary leiomyoma		10	
Degenerated leiomyoma		6	
Cellular leiomyoma		3	

LMS: Leiomyosarcoma, ESS: Endometrial stromal sarcoma, UES: Undifferentiated endometrial sarcoma.