Correlation between magnetic resonance diffusion-weighted imaging ADC value of endometrial stromal sarcoma and the malignant biological features

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Abstract

Objective: To study the correlation between magnetic resonance diffusion-weighted imaging ADC value of endometrial stromal sarcoma and the malignant biological features. Methods: A total of 34 patients with endometrial stromal sarcoma who received surgical resection in Hubei Provincial Hospital of Integrated Chinese & Western Medicine between May 2014 and August 2016 were selected as the malignant group of the research, and 58 patients with uterine fibroids who received surgical resection between August 2015 and October 2016 were selected as the control group of the research. Magnetic resonance diffusion-weighted imaging was done before operation to measure apparent diffusion coefficient (ADC value). The lesions were collected after operation to determine the expression of proliferation genes as well as estrogen and progestogen receptors. Results: Endometrial stromal sarcoma ADC value of malignant group was significantly lower than uterine fibroid ADC value of control group; CyclinD1, Rb, Sp1, Survivin, ERα, ERβ, PRA and PRB protein expression in endometrial stromal sarcoma lesions of malignant group were significantly higher than those of control group while SULT1E1 protein expression was significantly lower than that of control group; CyclinD1, Rb, Sp1, Survivin, ERα, ERβ, PRA and PRB protein expression in endometrial stromal sarcoma lesions of subgroup with low ADC value were significantly higher than those of subgroup with high ADC value while SULT1E1 protein expression was significantly lower than that of subgroup with high ADC value. Conclusion: Magnetic resonance diffusion weighted imaging ADC values can be used to evaluate the malignant biological behavior of endometrial stromal sarcoma.

1. Introduction

Endometrial stromal sarcoma is the malignant tumor derived from the uterine mesenchymal tissue, it is clinically rare, and evaluation of its malignant degree is short of effective means[1,2]. Surgical resection is the main way for the clinical treatment of endometrial stromal sarcoma, but the occurrence risk of pelvic recurrence and distant metastasis is high, and to accurately assess the malignant biological characteristics of endometrial stromal sarcoma can provide reference and basis for the judgment of the prognosis. Magnetic resonance diffusion-weighted imaging (DWI) can assess water diffusion ability, and the quantitative index is the apparent diffusion coefficient (ADC)[3]. ADC values is affected by the tissue morphology and cell arrangement, research has shown that ADC value of uterine sarcoma tissue significantly decreases[4], but there is no report on the changes of endometrial stromal sarcoma ADC values, and it is also not clear whether it is able to assess tumor malignancy. In the following study, in order to define the evaluation value of magnetic resonance diffusion-weighted imaging ADC values for endometrial stromal sarcoma malignancy, the correlation between ADC value of endometrial stromal sarcoma and the malignant biological features was analyzed.
2. Research subjects and methods

A total of 34 patients with endometrial stromal sarcoma who received surgical resection in Hubei Provincial Hospital of Integrated Chinese & Western Medicine between May 2014 and August 2016 were selected as the malignant group of the research, and 58 patients with uterine fibroids who received surgical resection in Hubei Provincial Hospital of Integrated Chinese & Western Medicine between August 2015 and October 2016 were selected as the control group of the research. Two groups of patients were with complete clinical data and accepted preoperative magnetic resonance diffusion-weighted imaging, the tumor specimens were kept after operation and the nature of the tumor was confirmed by pathology. Malignant group were 35-59 years old, 11 cases were menopausal and 23 cases were non-menopausal; control group were 41-62 years old, 21 cases were menopausal and 37 cases were non-menopausal. The two groups of patients were not significantly different in general data ($P > 0.05$).

2.1 Magnetic resonance diffusion–weighted imaging methods

Intera model 1.5 T MR Scanner from Philips company was used for inspection, patients received intramuscular injection of 10 mg anisodamine, diffusion-weighted imaging was by EPI sequence, and the parameters were as follows: layer thickness 5 mm, interlayer spacing 1 mm, b value 1 000 s/mm$^2$, TR 3 200 ms, TE 70 ms, matrix $160 \times 160$, FOV $240 \ mm \times 240 \ mm$, and flip Angle $90^\circ$. After the image was obtained, the lesion scope was confirmed, three layers were selected to measure ADC values, and the unit was mm$^2$/s.

2.2 Evaluation methods of the malignant biological features of tumor

About 80-80 mg of endometrial stromal sarcoma tissue and uterine fibroids tissue from surgical resection were taken, added in 300 μL PBS buffer and fully homogenized, the liquid after homogenate was centrifuged at 4 ℃ and 12 000 r/min for 20 min to separate the supernatant, and enzyme-linked immunosorbent assay kits were used to determine CyclinD1, Rb, Sp1, Survivin, ERα, ERβ, PRA, PRB and SULT1E1 contents.

2.3 Statistical processing methods

SPSS 16.0 software was used to input ADC values and gene expression, the median of endometrial stromal sarcoma ADC values was calculated, the endometrial stromal sarcoma with ADC value > median was included in subgroup with high ADC value, the endometrial stromal sarcoma with ADC value ≤ median was included in subgroup with low ADC value, the measurement data analysis between two groups was by t test, and $P < 0.05$ was the standard of statistical significance in differences.

3. Results

3.1 ADC value of malignant group and control group

Endometrial stromal sarcoma ADC value of malignant group was $(0.84\pm0.11) \times 10^{-2} \ mm^2/s$ and endometrial stromal sarcoma ADC value of control group was $(1.47\pm0.23) \times 10^{-2} \ mm^2/s$. t test showed that endometrial stromal sarcoma ADC value of malignant group was significantly lower than uterine fibroid ADC value of control group, and differences in ADC value were statistically significant between two groups ($P < 0.05$).

3.2 Proliferation gene expression in lesions of malignant group and control group and the correlation with ADC value

Analysis of proliferation genes CyclinD1, Rb, Sp1 and Survivin expression in lesions between malignant group and control group was as follows: CyclinD1, Rb, Sp1 and Survivin protein expression in endometrial stromal sarcoma lesions of malignant group were significantly higher than those of control group, and differences in CyclinD1, Rb, Sp1 and Survivin protein expression in lesions were statistically significant between malignant group and control group ($P < 0.05$), shown in Table 1.

Analysis of CyclinD1, Rb, Sp1 and Survivin expression in endometrial stromal sarcoma lesions between subgroups with different ADC values was as follows: CyclinD1, Rb, Sp1 and Survivin protein expression in endometrial stromal sarcoma lesions of subgroup with low ADC value were significantly higher than those of subgroup with high ADC value, and differences in CyclinD1, Rb, Sp1 and Survivin expression in endometrial stromal sarcoma lesions were statistically significant between subgroups with different ADC values ($P < 0.05$), shown in Table 2.

Table 1. Comparison of proliferation gene expression in lesions between malignant group and control group (ng/mL).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>CyclinD1</th>
<th>Rb</th>
<th>Sp1</th>
<th>Survivin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant group</td>
<td>34</td>
<td>7.94±1.03</td>
<td>4.51±0.62</td>
<td>2.18±0.32</td>
<td>3.53±0.51</td>
</tr>
<tr>
<td>Control group</td>
<td>58</td>
<td>3.25±0.52</td>
<td>2.03±0.34</td>
<td>0.94±0.12</td>
<td>1.57±0.33</td>
</tr>
<tr>
<td>$P$</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 2. Comparison of proliferation gene expression in endometrial stromal sarcoma lesions between subgroups with different ADC values (ng/mL).

<table>
<thead>
<tr>
<th>Subgroups with different ADC values</th>
<th>n</th>
<th>CyclinD1</th>
<th>Rb</th>
<th>Sp1</th>
<th>Survivin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgroup with low ADC value</td>
<td>17</td>
<td>9.51±1.24</td>
<td>5.77±0.93</td>
<td>2.94±0.39</td>
<td>4.31±0.62</td>
</tr>
<tr>
<td>Subgroup with high ADC value</td>
<td>17</td>
<td>6.02±0.87</td>
<td>3.14±0.45</td>
<td>1.37±0.23</td>
<td>2.65±0.35</td>
</tr>
<tr>
<td>$T$</td>
<td></td>
<td>7.482</td>
<td>8.175</td>
<td>13.271</td>
<td>8.495</td>
</tr>
<tr>
<td>$P$</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
3.3 Estrogen and progestogen receptor expression in lesions of malignant group and control group and the correlation with ADC value

Analysis of estrogen and progestogen receptors ERα, ERβ, PRA, PRB and SULT1E1 expression in lesions between malignant group and control group was as follows: ERα, ERβ, PRA and PRB protein expression in endometrial stromal sarcoma lesions of malignant group were significantly higher than those of control group while SULT1E1 protein expression was significantly lower than that of control group, and differences in ERα, ERβ, PRA, PRB and SULT1E1 protein expression in lesions were statistically significant between malignant group and control group (P<0.05), shown in Table 3.

Analysis of ERα, ERβ, PRA, PRB and SULT1E1 expression in endometrial stromal sarcoma lesions between subgroups with different ADC values was as follows: ERα, ERβ, PRA and PRB protein expression in endometrial stromal sarcoma lesions of subgroup with low ADC value were significantly higher than those of subgroup with high ADC value while SULT1E1 protein expression was significantly lower than that of subgroup with high ADC value, and differences in ERα, ERβ, PRA, PRB and SULT1E1 expression in endometrial stromal sarcoma lesions were statistically significant between subgroups with different ADC values (P<0.05), shown in Table 4.

4. Discussion

Endometrial stromal sarcoma is a rare malignant gynecology tumor[5], and accurate assessment of lesion malignancy helps to judge the prognosis of disease. Magnetic resonance diffusion-weighted imaging is the imageological examination means to assess the water diffusion ability within tissue, and ADC value is the quantitative parameter of the examination means. The cell volume, number and arrangement as well as extracellular matrix and capillary number within tissue will influence the water diffusion[6,7]. In the occurrence and development of malignant tumor, abnormal cell proliferation can increase the number and change the arrangement, abnormal invasion can cause extracellular matrix degradation and micro-angiogenesis increase, and above changes will reduce the water diffusion space and decrease the ADC value[8,9]. Studies have shown that the ADC values of magnetic resonance diffusion-weighted imaging can be used to evaluate the malignant degree of uterine sarcoma[4], but the ADC value change of endometrial stromal sarcoma tissue is not yet clear. In the study, ADC values of endometrial stromal sarcoma and uterine fibroids lesions were compared, and the results showed that endometrial stromal sarcoma ADC value of malignant group was significantly lower than uterine fibroid ADC value of control group. It illustrates that the ADC values of endometrial stromal sarcoma decrease significantly, this is associated with the strong heterogeneity as well as dense and irregular arrangement of cells within the sarcoma lesion, and it will lead to the weakened water diffusion ability and decreased ADC values.

Malignant proliferation is the most basic biological feature of endometrial stromal sarcoma, and the continuously proliferated sarcoma cells are not only the pathological basis for lesion growth, recurrence and metastasis, but may also affect the cell number and arrangement within the lesions, and cause changes in ADC values. Endometrial stromal sarcoma cell proliferation is regulated by multiple genes, CyclinD1 can participate in regulation of cell cycle, and it forms complexes with CDK4 and CDK6 to activate downstream Rb protein, accelerate cell cycle progression and promote cell proliferation[10,11]. Sp1 is the transcription factor involved in regulation of cellular biological behaviors, and it can regulate the expression of a variety of downstream genes to promote cell growth[12,13]; the product encoded by Survivin gene is a class of powerful anti-apoptotic protein in cells, and it can restrain the caspase cascade activation and the apoptosis mediated by it[13,14]. In the study, the analysis of above proliferation gene expression in endometrial stromal sarcoma tissues showed that CyclinD1, Rb, Sp1 and Survivin protein expression in endometrial stromal sarcoma lesions of malignant group were significantly higher than those of control group. Further analysis of the correlation between ADC value and proliferation gene expression showed that CyclinD1, Rb, Sp1 and Survivin protein expression in endometrial stromal sarcoma lesions of subgroup with low ADC value were significantly

Table 3.
Comparison of estrogen and progestogen receptor expression in lesions between malignant group and control group (ng/mL).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>ER</th>
<th>ERβ</th>
<th>PRA</th>
<th>PRB</th>
<th>SULT1E1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant group</td>
<td>34</td>
<td>1.85±0.22</td>
<td>1.26±0.18</td>
<td>2.31±0.35</td>
<td>1.56±0.20</td>
<td>0.42±0.08</td>
</tr>
<tr>
<td>Control group</td>
<td>58</td>
<td>0.74±0.09</td>
<td>0.54±0.07</td>
<td>1.02±0.15</td>
<td>0.64±0.09</td>
<td>1.24±0.19</td>
</tr>
<tr>
<td>T</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 4.
Comparison of estrogen and progestogen receptor expression in endometrial stromal sarcoma lesions between subgroups with different ADC values (ng/mL).

<table>
<thead>
<tr>
<th>Subgroups</th>
<th>n</th>
<th>ER</th>
<th>ERβ</th>
<th>PRA</th>
<th>PRB</th>
<th>SULT1E1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgroup with low ADC value</td>
<td>17</td>
<td>2.33±0.31</td>
<td>1.65±0.22</td>
<td>2.89±0.39</td>
<td>1.94±0.26</td>
<td>0.28±0.05</td>
</tr>
<tr>
<td>Subgroup with high ADC value</td>
<td>17</td>
<td>1.29±0.17</td>
<td>0.81±0.12</td>
<td>1.78±0.22</td>
<td>1.01±0.14</td>
<td>0.61±0.11</td>
</tr>
<tr>
<td>T</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
higher than those of subgroup with high ADC value. It means that the high expression of proliferation genes in endometrial stromal sarcoma lesions is associated with the reduction of ADC values, and the changes of proliferation gene expression can promote cell proliferation so as to change the water diffusion capacity and reduce the ADC values.

Endometrium is the target organ of estrogen and progesterone, and the occurrence of endometrial cancer, endometrial stromal sarcoma and various other malignant tumors is related to the excessive exposure of estrogen and progesterone. The physiological role of estrogen and progesterone in local tissue depends on estrogen receptors ER and ERβ as well as progesterone receptors PRA and PRB, the high expression of estrogen receptors and progesterone receptors can enhance the effect of sex hormones in local lesions and promote cells to obtain malignant biological characteristics, proliferate and invade to the distance. SULT1E1 is a new regulatory enzyme of estrogen and progesterone discovered in recent years, and it can catalyze the of estrogen and progesterone sulfation, the value of DWI and dynamic enhanced MRI for differential diagnosis of uterine sarcoma and the degenerated uterine fibroids. Chin J Med Imaging Technol 2016; 32(2): 274-278.

References


