The Usefulness of MRI and PET Imaging for the Detection of Parametrial Involvement and Lymph Node Metastasis in Patients with Cervical Cancer

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Objective: The purpose of this study is to elucidate the usefulness of magnetic resonance imaging (MRI) and positron emission tomography (PET) for the detection of parametrial involvement and lymph node metastasis in patients with cervical cancer.

Methods: Thirty-six patients with cervical cancer were retrospectively enrolled. MRI and PET scans were performed for all patients within a week before radical surgery. The criterion for malignancy on MRI was >1 cm short axis diameter of the suspected lymph node. On PET, only fluorodeoxyglucose (FDG) uptake was significantly higher than the background and, if this FDG uptake showed on at least two consecutive axial slices, then the lesion was considered as a malignancy. We compared the extent of tumor on the surgical findings with the FIGO staging, MRI and PET scans.

Results: The accuracy of FIGO and MRI staging was 67 and 84.4%, respectively. The accuracy for detecting pelvic lymph node metastasis was better for PET than for MRI (78 versus 67%, respectively). All FDG uptake lymph nodes were confirmed as metastatic lymph nodes by pathological evaluation; this included five lymph nodes <1 cm in diameter.

Conclusion: MRI provides an improved evaluation of local tumor extension, but PET is more useful for the evaluation of pelvic lymph nodes than MRI; however, PET still misses microscopic disease. Further studies are necessary to evaluate the usefulness of PET/computed tomography (CT) for the accuracy of the disease extension and the cost-effectiveness of MRI, PET or PET/CT in patients with cervical cancer.

Key words: cervical cancer – lymph node – MRI – PET

INTRODUCTION

Cervical cancer has been decreasing in incidence for several years, but is still the fifth most frequently diagnosed cancer for women in Korea (1). Although treatment advances have improved the cure rate, a large percentage of women with advanced stage disease will still die of the cancer. Most oncology centers use the International Federation of Gynecology and Obstetrics (FIGO) clinical staging system for classifying the stage of cervical carcinoma (2). A number of non-invasive modalities have been used to evaluate the status of the disease. These recommendations include a clinical examination under anesthesia, chest X-ray, intravenous urography, barium enema, cystoscopy and sigmoidoscopy. Other diagnostic modalities such as computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET) using 2-¹⁸F]fluoro-2-deoxy-D-glucose (FDG) and ultrasonography are used to evaluate the extent of tumor, but the results do not change the clinical staging.

Generally, the treatment plan for cervical cancer is determined by the FIGO stage (3–5). Patients with stage IB and IIA cervical carcinoma can be treated equally with external irradiation and brachytherapy, or by radical hysterectomy. For locally advanced cervical cancer (FIGO stage IIB–IVA), radical hysterectomy is not a therapeutic option. Recommended treatment for these patients has been radiotherapy combined with cisplatin-based chemotherapy (6–8). After radical hysterectomy for early cervical cancer, adjuvant radiotherapy alone or combined with chemotherapy may be required to reduce the local recurrence and to improve the survival of those patients having high risk factors for failure (9–15).
In the FIGO staging system, there are significant inaccuracies of the staging, and cancers are not assessed for lymph node metastasis, which is one of the most important prognostic factors (16–19). Lymphangiogram, CT, MRI or PET scanning have been used for evaluation of tumor extent and the nodal metastasis for cervical cancer. Until now, PET has been known as a reliable alternative to conventional imaging for the detection of lymph node metastasis in patients with cervical cancer (20–22).

In this study, we retrospectively evaluated the diagnostic accuracies of MRI and PET for the detection of parametrial involvement and lymph node metastasis by comparing their results with surgical specimens in patients with early cervical cancer.

PATIENTS AND METHODS

From 1997 to 2003, 36 patients with cervical cancer were retrospectively enrolled in our study. All the patients were evaluated with a clinical examination that included palpation, inspection, colposcopy, endocervical curettage, cystoscopy, proctoscopy, intravenous urography and chest radiography.

All MRI and PET scannings were performed within a week before surgery. MRI scanning was performed using a 1.5 T system (GE Medical System, USA). All patients were scanned in the supine position from the pelvis to the abdomen using a 5 mm section thickness and 2 mm intervals for the transverse plane, and using a 4 mm section thickness and 1 mm intervals for the sagittal and coronal planes. The MRI scans were read by an experienced radiologist who did not know the results of the clinical examination and PET scanning. The criterion for malignancy on MRI was finding a >1 cm short axis diameter of a lymph node. PET scanning was performed with a whole-body PET system (Advance, GE Medical System, USA). After the patients underwent an 8 h fast, 5 MBq of FDG/kg of body weight (322–47 MBq) was administered intravenously. After a 45 min delay, scanning of the entire body, including the abdomen and pelvis, was performed. To avoid artifacts due to urinary tract activity, a Foley catheter was placed in the bladder and bladder irrigation was done with normal saline prior to administration of FDG to allow drainage of high-activity urine prior to scanning. Attenuation correction was done by transmission scan using a $^{68}$Ge rod source. Tomographic images were reconstructed by filtered back-projection or by an ordered subset expectation maximization algorithm. The PET scans were read by a nuclear medicine physician who did not know the results of the clinical examination and PET scanning. The criterion for malignancy on MRI was finding a >1 cm short axis diameter of a lymph node. PET scanning was performed with a whole-body PET system (Advance, GE Medical System, USA). After the patients underwent an 8 h fast, 5 MBq of FDG/kg of body weight (322 ± 47 MBq) was administered intravenously. After a 45 min delay, scanning of the entire body, including the abdomen and pelvis, was performed. To avoid artifacts due to urinary tract activity, a Foley catheter was placed in the bladder and bladder irrigation was done with normal saline prior to administration of FDG to allow drainage of high-activity urine prior to scanning. Attenuation correction was done by transmission scan using a $^{68}$Ge rod source. Tomographic images were reconstructed by filtered back-projection or by an ordered subset expectation maximization algorithm. The PET scans were read by a nuclear medicine physician who was experienced with PET scans but was blinded to the clinical and MRI findings. Only if the FDG uptake was significantly higher than the background and if this was shown in at least two consecutive axial slices was a lesion considered as malignant. Unclear and equivocal uptakes were interpreted as negative findings.

Radical surgery was performed in all patients. This included class III hysterectomy and the removal of all lymph nodes from the common, external and internal iliac vessels and the obturator fossa nodes. The number of pelvic lymph nodes dissected was from nine to 55 (mean 24 ± 11). The para-aortic lymph node dissection was performed in two patients when the para-aortic lymph nodes were suspicious for malignancy during the operation. Adjuvant radiotherapy were performed for 28 patients who had more than one risk factor such as lymph node metastasis, deep stromal invasion, lymphovascular tumor emboli, parametrial involvement, tumor diameter >4 cm or positive resection margins.

We compared the extent of tumor in the surgical findings with the FIGO and MRI staging. We used Fisher’s exact test to analyze the association between discrete variables. A $P$-value of <0.05 was considered significant. MRI and PET findings on lymph node metastasis were analyzed on the basis of the pathological findings as true-positive, true-negative, false-positive or false-negative, and the findings were judged for sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy.

RESULTS

CLINICOPATHOLOGICAL CHARACTERISTICS

The median age of the women was 50 years, and their ages ranged from 22 to 74 years. Table 1 shows the clinicopathological characteristics of the 36 enrolled patients. Among the 36 patients, 27 tumors (75.0%) were squamous cell carcinoma and six tumors (16.7%) were adenocarcinoma. Clinical FIGO stage was as follows: Ib1 in 12 (33.3%), Ib2 in nine (25.0%)...
and IIa in 15 (41.7%). Among the 36 MRI scans, 14 patients (38.9%) and 22 pelvic sides (30.6%) were considered to have pelvic lymph node metastasis. On PET scanning, six patients (16.7%) and nine pelvic sides (12.5%) were suspected to have pelvic lymph node metastasis. On MRI and PET scanning, there were no patients suspected of para-aortic lymph node metastasis. Among the 32 MRI scans, 28 tumors (77.8%) were confined to the cervix, six tumors (16.7%) had invaded into the parametrium, and two patients (5.6%) had tumor infiltration into the parametrium. The mean size of the cervical tumor on the pathological specimen was 4.2 ± 1.6 cm (1.5–8.0 cm). On MRI and PET scanning, 32 primary tumors were measured except four tumors where the patients had the cervix removed by conization before the imaging studies. Among the 32 MRIs, 23 tumors (71.9%) were confined to the cervix, six tumors (18.8%) had invaded into the upper vagina and two tumors (6.3%) had infiltrated into the parametrium, but one superficial infiltrative tumor was not visible on MRI. The mean size of the cervical tumors on MRI was 3.6 ± 1.5 cm, with the maximum tumor size being 6.5 cm. On PET scanning, the primary cervical tumors were not detected in three cases (9.4%), and these three cases were all superficial infiltrative tumors, and two of the tumors were adenocarcinoma. The mean size of the cervical tumors on PET was 3.5 ± 1.9 cm with a maximum tumor size of 9.0 cm.

### Staging Accuracy

Comparison of the pathological findings with FIGO staging and MRI staging is shown in Table 2. In the FIGO staging, there were significant inaccuracies, with a 33.3% error rate. Nine patients (25.0%) were up-staged, but three patients (9.4%) including one patient with no visible tumor on MRI were down-staged on MRI scans. Two patients (6.3%) showed a cervical carcinoma with disruption of the stromal ring and an extension into the parametrium on the axial T2-weighted images. In these tumors, one patient was surgically confirmed to have parametrial infiltration.

### Detection of Pelvic Lymph Node Metastasis

Para-aortic lymph node metastasis was not present in all but two patients on the surgical specimen. Pelvic lymph node metastases were present in 14 patients (38.9%) and in 22 pelvic sides (30.6%) on surgical specimens. Ten patients (71.4%) and 15 pelvic lymph nodes (68.2%) had a metastatic lymph node with a diameter <1 cm. On a patient basis, the sensitivity, specificity, PPV and NPV for detecting lymph node metastasis on MRI were 57, 73, 57 and 73, respectively. For PET scanning, the respective values were 43, 100, 100 and 73%. PET had a greater accuracy than MRI for metastatic lymph node detection (78 versus 67%). The lymph nodes suspected as metastasis on MRI had reactive hyperplasia or inflammation in the surgical specimens (Fig. 1). False-negative nodes were interpreted as non-metastatic lymph nodes because they were smaller than 1 cm in diameter on MRI. For the PET scanning, all lymph nodes taking up FDG were confirmed as metastatic by pathological evaluation including five lymph nodes <1 cm in diameter (Fig. 2).

### Discussion

For pre-treatment evaluation of cervical cancer, the accurate staging and the detection of prognostic factors are highly important to predict the patient’s prognosis and to determine the optimal treatment modality. The FIGO staging system is often inaccurate, with an ~25% error rate for stage I and II disease and with an increasing error rate for more advanced diseases (23,24). In our study, ~33% patients showed a discrepancy between FIGO staging and pathological findings. Therefore, CT and MRI are widely accepted as the optimal staging modality.

<table>
<thead>
<tr>
<th>Pathological stage*</th>
<th>MRI stage*</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Ib</td>
<td>Ib</td>
<td>19</td>
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<tr>
<td>IIa</td>
<td>IIa</td>
<td>9</td>
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</tbody>
</table>

nP.0001

*According to FIGO staging.

**Table 2.** Comparison of pathological staging with FIGO staging and MRI staging

**Table 3.** Comparison of MRI and PET results with pathological finding on pelvic lymph node metastasis

<table>
<thead>
<tr>
<th></th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
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<tbody>
<tr>
<td>Patient basis (n = 36)</td>
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<tr>
<td>MRI</td>
<td>8</td>
<td>16</td>
<td>6</td>
<td>6</td>
<td>57%</td>
<td>73%</td>
<td>57%</td>
<td>73%</td>
<td>67%</td>
</tr>
<tr>
<td>PET</td>
<td>6</td>
<td>22</td>
<td>0</td>
<td>8</td>
<td>43%</td>
<td>100%</td>
<td>100%</td>
<td>73%</td>
<td>78%</td>
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<tr>
<td>Pelvic side basis (n = 72)</td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td>MRI</td>
<td>12</td>
<td>40</td>
<td>10</td>
<td>10</td>
<td>55%</td>
<td>80%</td>
<td>55%</td>
<td>80%</td>
<td>72%</td>
</tr>
<tr>
<td>PET</td>
<td>9</td>
<td>50</td>
<td>13</td>
<td>4</td>
<td>41%</td>
<td>100%</td>
<td>100%</td>
<td>79%</td>
<td>82%</td>
</tr>
</tbody>
</table>

TP = true-positive, TN = true-negative, FP = false-positive, FN = false-negative, PPV = positive predictive value, NPV = negative predictive value.
modality to evaluate the status of tumor extensions. The accuracy of CT and MRI for the staging of cervical cancer has been reported as being from 63 to 69% for CT and from 77 to 90% for MRI (16,17,25,26). The accuracy obtained with MRI has advantages over that of FIGO staging and CT, especially in the evaluation of parametrial status. The overall accuracy of MRI in our study was comparable with previous reports, but the accuracy for parametrial evaluation was 50% (one in two patients with surgically determined parametrial involvement). However, CT and MRI were comparable for lymph node evaluation, with an accuracy of 70–88%, because this should be based on the size of the lymph nodes. In our study, the accuracy of lymph node evaluation by MRI was ~67%, which was slightly less optimal than in previous reports.

Current data show that metabolic imaging with PET is a reliable alternative to conventional imaging for lymph node evaluation in patients with cervical cancer. Rose et al. (20) have reported that for the para-aortic nodes, PET had a sensitivity of 75% and a specificity of 92%. Lin et al. (27) have also reported 86% sensitivity, 94% specificity and 92% accuracy for PET in detecting para-aortic lymph node metastasis. Reinhardt et al. (22) have compared the diagnostic accuracy of MRI with that of PET for detecting metastatic lymph nodes in patients with cervical cancer; the sensitivity was 91% with PET and 73% with MRI, and the specificity was 100% with PET and 83% with MRI. The PPV of PET was superior to that of MRI (100 versus 67%) and the accuracy of PET was 97% and that of MRI was 80%. In our study, the specificity, PPV and accuracy of PET for detecting lymph node metastasis were superior to MRI, and all of the abnormal lymph nodes detected with PET were confirmed as lymph node metastases in the surgical specimens. PET may be superior to MRI in detecting lymph node metastasis because it evaluates tissue metabolism rather than using only size criteria to diagnose lymph node metastasis. However, in this study, the sensitivity for metastatic lymph nodes with PET was much lower than in the reports previously discussed. We think this may be due to the poor spatial resolution in PET scanning. Since the
sensitivity of PET fails rather remarkably for infracentimetric nodal metastasis, which is much more the case for microscopic disease, the large percentage of small size lymph nodes of <1 cm (~70%) could lower the sensitivity (28).

In conclusion, to evaluate the disease extension at the time of diagnosis is highly important for predicting the prognosis and determining the therapeutic strategy and for patients with cervical cancer. MRI provides an improved evaluation of local tumor extension, but has a lower accuracy in detecting lymph node metastasis than does PET. PET is a non-invasive and more useful method for the evaluation of pelvic lymph nodes or extra-pelvic metastases than MRI, but it still has high a probability of missing microscopic disease, as shown in this study. Recent technological improvements in imaging have led to the development of PET/CT combining the advantages of PET in reflecting metabolism and of CT in anatomical precision. Further studies are necessary not only to evaluate the usefulness of PET/CT for the accuracy in determining the tumor extension or detecting the lymph node metastasis, but also for the cost-effectiveness of MRI, PET or PET/CT in patients with cervical cancer.

References


