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# Diagnostic performance of computer tomography, magnetic resonance imaging, and positron emission tomography or positron emission tomography/computer tomography for detection of metastatic lymph nodes in patients with cervical cancer: Meta-analysis

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**We performed a meta-analysis to compare diagnostic performances of computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET or PET/CT), for detection of metastatic lymph nodes in patients with cervical cancer. We searched MEDLINE (PubMed), EMBASE and the Cochrane Review database in December 2007. All articles were independently reviewed and selected by three evaluators. We estimated a summary receiver operating characteristic (sROC) curve. The area under the curve (AUC), *Q**, and pooled weighted estimates of sensitivity and specificity for each modality by patient-based and region- or node-based data analyses and conducted pair-wise comparisons between modalities using the two-sample *Z*-test. Forty-one of 768 initially identified studies were included in the meta-analysis. In a patient-based data analysis, PET or PET/CT showed the highest pooled sensitivity (82%) and specificity (95%), while CT showed 50% and 92%; and MRI, 56% and 91%, respectively. The AUC (0.9641) and *Q** (0.9106) of PET or PET/CT were significantly higher than those of MRI (AUC = 0.8270; *Q** = 0.7599), both $P < 0.001$. In region- or node-based data analysis, sensitivities of CT (52%) and PET or PET/CT (54%) were higher than that of MRI (38%), $P < 0.02$ and $P < 0.001$, respectively, while specificities of MRI (97%) and PET or PET/CT (97%) were higher than that of CT (92%), both $P < 0.001$. The AUC and *Q** showed no significant difference among CT, MRI, and PET or PET/CT. PET or PET/CT had an overall higher diagnostic performance than did CT or MRI in detecting metastatic lymph nodes in patients with cervical cancer. (*Cancer Sci* 2010; 101: 1471–1479)**

Uterine cervical carcinoma is the second most common malignancy in women worldwide, and is the only major gynecologic malignancy that is staged clinically according to International Federation of Obstetrics and Gynecology (FIGO) recommendations.[1] However, clinical staging of cervical cancer is accurate in only 29% of patients. Undiagnosed lymph node metastases are a major problem[2–5] because lymph node status is an independent prognostic factor for survival of patients with primary cervical cancer.[6–9] Although lymph node dissection before radiotherapy results in improved survival of patients with macroscopically enlarged pelvic and para-aortic lymph nodes, the routine pretreatment surgical staging is not recommended. Thus, an inaccurate evaluation of lymph node metastasis associated with uterine cervical carcinoma often leads to unsatisfactory treatment.[10–14]

Computed tomography (CT) and magnetic resonance imaging (MRI) have been used to assess the metastatic lymph nodes of cervical cancer patients. A meta-analysis of studies evaluating these diagnostic methods concluded that these methods have only moderate sensitivity and specificity for detection of metastatic lymph nodes.[15] On the contrary, the recent studies have reported that positron emission tomography (PET or PET/CT), employing [$^{18}$F]-fluoro-2-deoxy-D-glucose (FDG), is more sensitive than CT or MRI for detection of metastatic lymph nodes in patients with cervical cancer.[16–33]

Numerous studies have described the use of CT, MRI, and PET or PET/CT for detection of metastatic lymph nodes in patients with cervical cancer, but no studies have compared these three imaging modalities for those patients. Some previous studies have compared PET and MRI and suggested that PET is more accurate than MRI, but the statistical power of the comparisons was too low to assess the significance of this difference.[20,21,25–27,30,34] Scheidler *et al.*[15] performed a meta-analysis of studies performed between 1971 and 1997 that compared the accuracy of CT and MRI for detection of metastatic lymph nodes. However, patient heterogeneity, differences in imaging techniques, and differences in diagnostic criteria for metastatic lymph nodes made it difficult to compare these two imaging modalities directly.

Since Scheidler *et al.*'s meta-analysis, there have been many technical improvements in CT and MRI, and PET has recently become widely available. The aim of our study was to compare diagnostic performances of CT, MRI, and PET or PET/CT for detection of metastatic lymph nodes in patients with cervical cancer, using a meta-analysis.

## Materials and Methods

**Data sources and keywords.** We searched MEDLINE (PubMed), EMBASE, and the Cochrane Library in December 2007, using common keywords relevant to cervical cancer, lymph node, and imaging. The keywords for the literature search were

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''cervical cancer'' and ''lymph node'' for disease factors, and ''computed tomography'' or ''magnetic resonance imaging'' or ''positron emission tomography'' for imaging factors. We scanned bibliographies of relevant articles to identify additional studies. The search period was January 1981 to December 2007 for CT, January 1988 to December 2007 for MRI, and January 2001 to December 2007 for PET or PET/CT, after consideration of the time of introduction of each modality in the clinical setting.

**Selection criteria.** The selection criteria for the relevant studies were: (i) a minimal sample size of 20 patients; (ii) histological examination of lymph nodes by surgery or biopsy; (iii) use of clear diagnostic criteria; (iv) adequate presentation of data (true-positive [TP], false-positive [FP], true-negative [TN], false-negative [FN]); and (v) use of the English language.

**Selection of relevant studies.** All studies retrieved from databases were independently evaluated by the three co-authors of this study. When there was a disagreement concerning inclusion of a study, it was resolved by discussion. When there were insufficient or missing data in a study, we contacted the authors to request the relevant information. We included only one article, when there were two or more articles with the same data.

**Data extraction.** From the studies finally selected, we extracted the study name (first author, year of publication), journal name, and comparison methods (patient-by-patient, region-by-region and node-by-node comparison). TP, FP, TN, and FN results were recorded. Because different comparison methods led to different results, even within the same study, results were recorded twice for seven MRI studies[19,27,30,35–38] and six PET or PET/CT studies.[19,20,27,28,30,33] In five studies,[20,28,33,36,39] pelvic and para-aortic lymph node metastases were subdivided and results were recorded for each area.

**Statistical analyses.** We conducted all analyses based on two types of comparison method; one is a patient-based data analysis, and the other is a region- or node-based data analysis. A patient-based data analysis uses the pathologically proven positive node in the same patient who had been identified to have metastatic lymph nodes by preoperative imaging, while region- or node- based analyses use the pathologically proven positive node in the corresponding region or node which had been described as containing positive node by preoperative imaging.

Summary receiver operating characteristic (sROC) curve and the area under the curve (AUC) were calculated. The sROC curve was constructed by using an estimated false positive rate (FPR) and true positive rate (TPR) of each study based on a regression model.[40–42] We also calculated another global measure of test efficacy, $Q^*$; the intersection of the estimated sROC curve with the line where sensitivity equals specificity; values of $Q^*$ near 1.0 indicate that sROC curves are snugged up near the desirable north-west corner where sensitivity and specificity are both 1.0.[42]

We obtained summary sensitivity and specificity data with 95% confidence intervals using bivariate analysis for diagnostic meta-analysis.[43] In order to examine heterogeneity in sensitivity and specificity across studies, Higgins *I*-square ($I^2$) was calculated. An $I^2$ value greater than 50% was considered to indicate substantial heterogeneity.

We conducted a two-sample *Z*-test in order to evaluate a significant difference in sensitivity, specificity, AUC, and $Q^*$ values between any two diagnostic modalities. A *P*-value less than 0.05 was considered statistically significant. All of the statistical analyses were conducted using Meta-DiSc version 1.4.[44]

## Results

We initially identified 768 studies from the initial search using the keywords. After exclusion of duplicates ($n = 97$), we reviewed all remaining article titles and abstracts, and 597 additional studies were excluded. We reviewed the remaining 74 articles, and finally included 41 studies in our meta-analysis (Fig. 1). The main reasons for exclusion of studies were as follows: use of a non-English language[45–63] ($n = 19$); insufficient number of patients[17,18,65,69–72] ($n = 7$); insufficient data[64–68] ($n = 5$); use of identical populations[73] ($n = 1$); and non-use of a histopathological gold standard for lymph node evaluation[74] ($n = 1$).

We finally included data from 20 studies for the analysis of CT performance, 31 studies for the analysis of MRI performance, and 20 studies for analysis of PET or PET/CT performance, respectively (Tables 1–3).

**Patient-based data analysis.** Figure 2 shows the sROC curves of the performance of CT, MRI, and PET or PET/CT for detection of metastatic lymph nodes in cervical cancer patients, based on a patient-based data analysis. AUCs (SE) of each modality were 0.8998 (0.042), 0.8270 (0.045), and 0.9641 (0.021) for CT, MRI, and PET or PET/CT, respectively; $Q^*$ values were 0.8310 (0.0456), 0.7599 (0.0409), and 0.9106 (0.0322), respectively. Table 4 shows summary sensitivity and specificity of three modalities by patient-based data. A significant heterogeneity was found in most analyses except for the meta-analysis of CT studies for specificity ($I^2 = 31.6$). Summary sensitivity and specificity of CT were 50% (95% confidence interval [CI]: 43%, 57%) and 92.0% (95% CI: 90%, 94%). For MRI, summary sensitivity and specificity were 56% (95% CI: 51%, 62%) and 91% (95% CI: 90%, 93%). For PET or PET/CT, summary sensitivity and specificity were 82% (95% CI: 75%, 87%) and 95% (95% CI: 93%, 97%).

Table 5 shows pair-wise comparisons between modalities for sensitivity, specificity, AUC, and $Q^*$ values by patient-based data. Statistically significant differences were observed in the following comparisons: CT *versus* PET or PET/CT (50% *vs* 82%, $P < 0.001$) and MRI *versus* PET or PET/CT (56% *vs* 82%, $P < 0.001$) for sensitivity; CT *versus* PET or PET/CT (92% *vs* 95%, $P = 0.04$) and MRI *versus* PET or PET/CT (91% *vs* 95%, $P < 0.001$) for specificity; MRI *versus* PET or PET/CT (0.8270 *vs* 0.9641, <0.001) for AUC; and MRI *versus* PET or PET/CT (0.7599 *vs* 0.9106, $P < 0.001$) for $Q^*$ values.

**Region- or node-based data analysis.** Figure 3 shows the sROC curves of the performance of CT, MRI, and PET or PET/CT for detection of metastatic lymph nodes in cervical cancer patients, based on region- or node-based data analysis. AUCs (SE) of each modality were 0.8085 (0.2273), 0.7450 (0.0877), and 0.8181 (0.1815) for CT, MRI, and PET or PET/CT, respectively; $Q^*$ values were 0.7433 (0.2008), 0.6893 (0.0722), and 0.7519 (0.1626), respectively. Table 4 shows summary sensitivity and specificity of three modalities by region- or node-based data. Summary sensitivity and specificity of CT were 52% (95% CI: 42%, 62%) and 92% (95% CI: 90%, 94%). For MRI, summary sensitivity and specificity were 38% (95% CI: 32%, 43%) and 97% (95% CI: 97%, 98%). For PET or PET/CT, summary sensitivity and specificity were 54% (95% CI: 46%, 61%) and 97% (95% CI: 96%, 98%).

Table 5 shows pair-wise comparisons between modalities for sensitivity, specificity, AUC, and $Q^*$ values by region- or node-based data. Statistically significant differences were observed in the following comparisons: CT *versus* MRI (52% *vs* 38%, $P = 0.02$) and MRI *versus* PET or PET/CT (38% *vs* 54%, $P < 0.001$) for sensitivity; and CT *versus* MRI (92% *vs* 97%, $P < 0.001$) and CT *versus* PET or PET/CT (92% *vs* 97%, $P < 0.001$) for specificity. However, there was no significant difference regarding AUC and $Q^*$ values.

## Discussion

Positron emission tomography using FDG is well known for a technique being used for the assessment of primary tumors and


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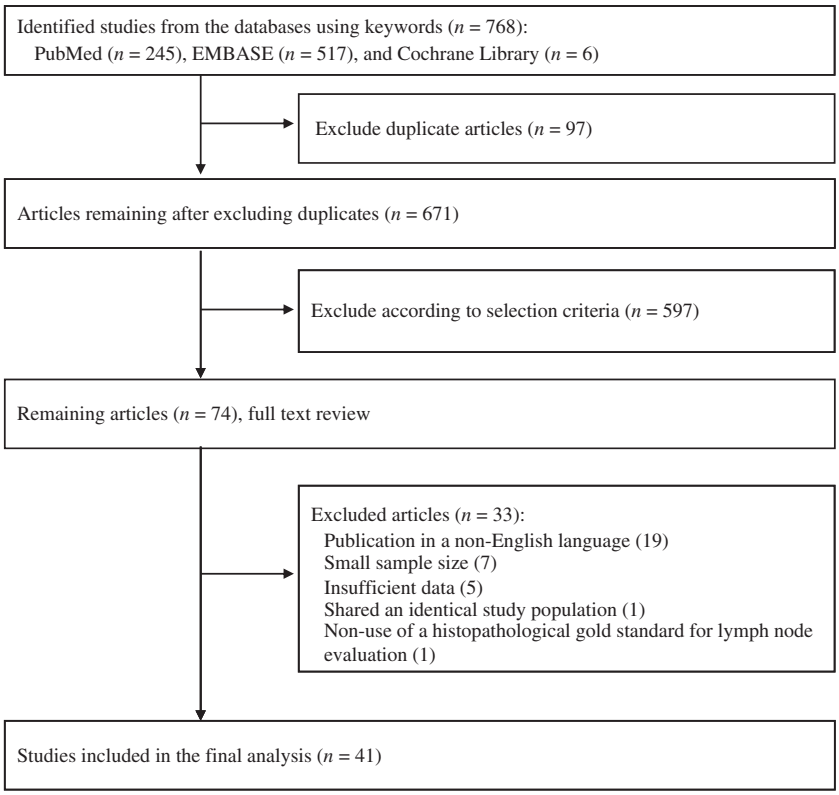


**Fig. 1.** Flow diagram for identification of relevant studies.

**Table 1. Computed tomography studies included in the meta-analysis (*n* = 20)***

| Study, year (reference) | Journal | Type of scanner | Comparison | *N* | Sensitivity, no. (%) | Specificity, no. (%) | Positive likelihood ratio | Negative likelihood ratio |
|---|---|---|---|---|---|---|---|---|
| Grumbine *et al.*, 1981[83] | Gynecol Oncol | Non-helical | p | 24 | 0/6 (0) | 17/18 (94) | 0.90 | 1.01 |
| Walsh *et al.*, 1981[84] | Am J Roentgenol | Non-helical | p | 25 | 12/15 (80) | 7/10 (70) | 2.67 | 0.29 |
| Brenner *et al.*, 1982[85] | Cancer | Non-helical | p | 20 | 4/6 (67) | 13/14 (93) | 9.33 | 0.36 |
| Villasanta *et al.*, 1983[86] | Obstet Gynecol | Non-helical | p | 42 | 10/13 (77) | 25/29 (86) | 5.58 | 0.27 |
| Van engelshoven *et al.*, 1984[87] | Gynecol Obstet Invest | Non-helical | p | 20 | 3/7 (43) | 12/13 (92) | 5.57 | 0.62 |
| Bandy *et al.*, 1985[88] | Obstet Gynecol | Non-helical | p | 44 | 9/12 (75) | 29/32 (91) | 8.00 | 0.28 |
| Vas *et al.*, 1985†[39] | J Comput Tomogr | Non-helical | p | 30 | 10/16 (63) | 11/14 (79) | 2.92 | 0.48 |
| Vas *et al.*, 1985‡[39] | J Comput Tomogr | Non-helical | p | 33 | 10/12 (83) | 20/21 (95) | 17.5 | 0.18 |
| Camilien *et al.*, 1988[89] | Gynecol Oncol | Non-helical | p | 51 | 3/12 (25) | 38/39 (97) | 9.75 | 0.77 |
| Janus *et al.*, 1989[90] | Clin Imaging | Non-helical | p | 22 | 1/3 (33) | 18/19 (95) | 6.33 | 1.85 |
| Matsukuma *et al.*, 1989[91] | Gynecol Oncol | Non-helical | p | 70 | 5/7 (71) | 61/63 (97) | 22.50. | 0.30 |
| Kim *et al.*, 1990[92] | Radiology | Single helical | r | 30 | 6/12 (50) | 36/48 (75) | 2.00 | 0.67 |
| Heller *et al.*, 1990[93] | Gynecol Oncol | Single helical | p | 253 | 31/61 (34) | 184/192 (96) | 22.50 | 0.30 |
| Kim *et al.*, 1993[94] | J Comput Tomogr | Single helical | r | 99 | 7/29 (24) | 158/169 (93) | 3.71 | 0.81 |
| Subak *et al.*, 1995[95] | Obstet Gynecol | Single helical | p | 37 | 3/5 (60) | 29/32 (91) | 6.40 | 0.44 |
| Chu *et al.*, 1997‡[96] | Gynecol Oncol | Single helical | p | 28 | 4/10 (40) | 17/18 (94) | 6.67 | 0.64 |
| Yang *et al.*, 2000[97] | Am J Roentgenol | Single helical | r | 43 | 11/17 (62) | 57/59 (97) | 20.67 | 0.39 |
| Hertel *et al.*, 2002†[36] | Gynecol Oncol | Not presented | p | 75 | 3/20 (15) | 47/55 (85) | 1.00 | 1.00 |
| Hertel *et al.*, 2002‡[36] | Gynecol Oncol | Not presented | p | 91 | 3/16 (19) | 66/75 (88) | 1.58 | 0.92 |
| Bellomi *et al.*, 2005[34] | Eur Radiol | Single helical | r | 62 | 31/48 (65) | 418/448 (93) | 9.29 | 0.38 |

*All studies used contrast agents. †Pelvic lymph nodes; ‡para-aortic lymph nodes. *N*, number of patients who fulfilled the inclusion criteria; p, patient-based comparison; r, region-specific comparison.

metastases, and prognostic stratifications and planning and monitoring of tumor therapy, as well as for the early detection of recurrent tumor growth.[75] Also, simultaneous acquisition of co-registered PET and CT images (PET/CT) enables more precise discrimination between physiologic and malignant FDG uptake and more accurate localization of lesions.[76] Our meta-analysis showed that PET or PET/CT had overall higher sensitivity, specificity, AUC, and $Q^*$ than did CT or MRI in a patient-based data analysis; and a higher sensitivity than did MRI and a higher specificity than did CT in region- or node-based data analyses, for detection of metastatic lymph nodes in patients with cervical cancer. Our findings are similar to those of the previous meta-analyses. Regarding the performance of PET or PET/CT, a recent meta-analysis by Gu *et al.*

**Table 2. Magnetic resonance imaging studies included in the meta-analysis (*n* = 31)**

| Study, year (reference) | Journal | Strength of magnetic field | Comparison | *N* | Sensitivity, no. (%) | Specificity, no. (%) | Positive likelihood ratio | Negative likelihood ratio |
|---|---|---|---|---|---|---|---|---|
| Hricak *et al.*, 1988 [98] | Radiology | 1.5 tesla | p | 57 | 9/11 (82) | 44/46 (96) | 18.82 | 0.19 |
| Waggenspack *et al.*, 1988[99] | J Comput Assist Tomogr | 1.5 tesla | p | 20 | 3/3 (100) | 17/17 (100) | NA | 0 |
| Greco *et al.*, 1989[100] | Clinical Radiology | 1.5 tesla | p | 46 | 3/8 (38) | 32/38 (84) | 2.38 | 0.74 |
| Janus *et al.*, 1989[90] | Clin Imaging | 1.5 tesla | p | 22 | 3/4 (75) | 16/18 (89) | 6.75 | 0.74 |
| Kim *et al.*, 1990[92] | Radiology | 2.0 tesla | p | 30 | 3/15 (20) | 44/45 (98) | 4.00 | 0.79 |
| Ho *et al.*, 1992[64] | J Fromos Med Assoc | 1.5 tesla | p | 20 | 0/5 (0) | 15/15 (100) | 2.67 | 0.95 |
| Kim *et al.*, 1993[94] | J Comput Assist Tomogr | 2.0 tesla | p | 99 | 7/29 (24) | 167/169 (99) | 20.40 | 0.77 |
| Hawnaur *et al.*, 1994[101] | Clin Radiol | 1.5 tesla | p | 49 | 12/16 (75) | 29/33 (88) | 6.19 | 0.28 |
| Kim *et al.*, 1994[102] | Radiology | 1.5 tesla | p | 272 | 23/37 (62) | 223/235 (98) | 29.22 | 0.39 |
| Subak *et al.*, 1995[95] | Obstet Gynecol | 1.5 tesla | p | 71 | 8/13 (62) | 53/58 (91) | 7.14 | 0.42 |
| Hawighorst *et al.*, 1998[103] | J Comput Assist Tomogr | 1.5 tesla | p | 33 | 13/19 (68) | 11/14 (78) | 3.09 | 0.41 |
| Yu *et al.*, 1998[104] | Am J Roentgenol | 1.5 tesla | p | 94 | 9/14 (64) | 73/80 (91) | 7.11 | 0.40 |
| Yang *et al.*, 2000[97] | Am J Roentgenol | 1.5 tesla | r | 43 | 12/17 (71) | 53/59 (90) | 7.11 | 0.32 |
| Narayan *et al.*, 2001[20] | Int J Gynecol Cancer | 1.5 tesla | p | 24 | 6/12 (50) | 12/12 (100) | 6.25 | 0.54 |
| Reinhardt *et al.*, 2001[19] | Radiology | 1.5 tesla | p | 35 | 8/11 (73) | 20/24 (83) | 4.29 | 0.33 |
| Reinhardt *et al.*, 2001[19] | Radiology | 1.5 tesla | r | 35 | 14/22 (67) | 263/270 (97) | 22.33 | 0.34 |
| Sheu *et al.*, 2001[105] | Eur Radiol | 1.5 tesla | p | 41 | 9/11 (82) | 26/30 (87) | 6.31 | 0.21 |
| Hertel *et al.*, 2002†[36] | Gynecol Oncol | Not presented | p | 67 | 3/12 (25) | 48/55 (87) | 1.92 | 0.86 |
| Hertel *et al.*, 2002‡[36] | Gynecol Oncol | Not presented | p | 67 | 0/6 (0) | 60/61 (98) | 0.00 | 1.02 |
| Choi *et al.*, 2004[106] | J Comput Assist Tomogr | 1.5 tesla | r | 113 | 8/22 (36) | 198/204 (97) | 12.00 | 0.29 |
| Bellomi *et al.*, 2005[34] | Eur Radiol | 1.0 tesla | r | 62 | 35/48 (73) | 417/448 (93) | 10.43 | 0.29 |
| Park *et al.*, 2005[27] | Jpn J Clin Oncol | 1.5 tesla | p | 36 | 8/14 (57) | 16/22 (73) | 2.11 | 0.59 |
| Park *et al.*, 2005[27] | Jpn J Clin Oncol | 1.5 tesla | r | 36 | 12/22 (55) | 40/50 (80) | 2.75 | 0.56 |
| Choi *et al.*, 2006[37] | Am J Roentgenol | 1.5 tesla | r | 55 | 12/36 (33) | 346/349 (97) | 11.00 | 0.69 |
| Choi *et al.*, 2006[37] | Am J Roentgenol | 1.5 tesla | n | 55 | 15/62 (24) | 1830/1847 (99) | 24.00 | 0.77 |
| Choi *et al.*, 2006[30] | Cancer | 1.5 tesla | p | 22 | 4/13 (39) | 4/9 (44) | 0.70 | 1.39 |
| Choi *et al.*, 2006[30] | Cancer | 1.5 tesla | r | 22 | 10/33 (30) | 112/121 (93) | 4.29 | 0.75 |
| Chung *et al.*, 2007[35] | Jpn J Clin Oncol | 1.5 tesla | p | 119 | 24/34 (71) | 59/85 (69) | 2.29 | 0.42 |
| Chung *et al.*, 2007[35] | Jpn J Clin Oncol | 1.5 tesla | r | 119 | 30/74 (41) | 693/759 (91) | 4.56 | 0.65 |
| Sahdev *et al.*, 2007[38] | Int J Gynecol Cancer | 1.5 tesla | p | 150 | 7/19 (37) | 120/131 (92) | 4.63 | 0.68 |
| Sahdev *et al.*, 2007[38] | Int J Gynecol Cancer | 1.5 tesla | n | 150 | 12/44 (27) | 1427/1442 (99) | 27.00 | 0.74 |

†Pelvic lymph nodes; ‡para-aortic lymph nodes. *N*, number of patients who fulfilled the inclusion criteria; NA, not available: Positive likelihood could not be calculated because specificity was 1.0; p, patient-based comparison; r, region-specific comparison; n, node-based comparison.

**Table 3. PET or PET/CT studies included in the meta-analysis (*n* = 20)**

| Study, year (reference) | Journal | Comparison | *N* | Sensitivity, no. (%) | Specificity, no. (%) | Positive likelihood ratio | Negative likelihood ratio |
|---|---|---|---|---|---|---|---|
| Narayan *et al.*, 2001†[20] | Int J Gynecol Cancer | p | 24 | 10/12 (83) | 11/12 (92) | 10.38 | 0.18 |
| Narayan *et al.*, 2001‡[20] | Int J Gynecol Cancer | r | 24 | 4/7 (57) | 16/17 (94) | 9.5 | 0.46 |
| Reinhardt *et al.*, 2001[19] | Radiology | p | 35 | 10/11 (91) | 24/24 (100) | NA | 0.09 |
| Reinhardt *et al.*, 2001[19] | Radiology | r | 35 | 17/21 (81) | 269/271 (99) | 81 | 0.19 |
| Belhocine *et al.*, 2002[22] | Gynecol Oncol | n | 22 | 19/27 (70) | 184/190 (97) | 23.33 | 0.31 |
| Yeh *et al.*, 2002‡[21] | Oncol Rep | p | 42 | 10/12 (83) | 29/30 (97) | 27.67 | 0.18 |
| Lin *et al.*, 2003‡[107] | Gynecol Oncol | p | 50 | 12/14 (86) | 34/36 (94) | 14.33 | 0.15 |
| Ma *et al.*, 2003[24] | J Nucl Med | p | 104 | 38/38 (100) | 66/66 (100) | NA | 0 |
| Park *et al.*, 2005[27] | Jpn J Clin Oncol | p | 36 | 6/14 (43) | 22/22 (100) | NA | 0.57 |
| Park *et al.*, 2005[27] | Jpn J Clin Oncol | r | 36 | 9/22 (41) | 50/50 (100) | NA | 0.59 |
| Roh *et al.*, 2005[26] | Eur J Cancer | r | 54 | 14/37 (38) | 383/395 (97) | 12.67 | 0.64 |
| Wright *et al.*, 2005†[28] | Cancer | p | 59 | 10/19 (53) | 36/40 (90) | 5.30 | 0.52 |
| Wright *et al.*, 2005‡[28] | Cancer | p | 45 | 1/4 (25) | 40/41 (98) | 12.50 | 0.77 |
| Wright *et al.*, 2005†[28] | Cancer | r | 59 | 12/26 (46) | 84/92 (91) | 5.11 | 5.9 |
| Wright *et al.*, 2005‡[28] | Cancer | r | 45 | 2/5 (40) | 84/85 (99) | 40 | 0.61 |
| Choi *et al.*, 2006[30] | Cancer | p | 22 | 10/13 (77) | 5/9 (56) | 1.75 | 0.41 |
| Choi *et al.*, 2006[30] | Cancer | r | 22 | 19/33 (58) | 112/121 (93) | 8.29 | 0.45 |
| Sironi *et al.*, 2006[31] | Radiology | p | 47 | 13/18 (72) | 18/19 (95) | 14.40 | 0.29 |
| Loft *et al.*, 2007†[33] | Gynecol Oncol | p | 78 | 21/21 (100) | 50/57 (87) | 7.69 | 0 |
| Loft *et al.*, 2007‡[33] | Gynecol Oncol | p | 119 | 15/15 (100) | 103/104 (99) | 100 | 0 |

†Pelvic lymph nodes; ‡para-aortic lymph nodes. *N*, number of patients who fulfilled the inclusion criteria; NA, not available: Positive likelihood could not be calculated because specificity was 1.0; p, patient-based comparison; r, region-specific comparison; n, node-based comparison; CT, computed tomography; PET, positron emission tomography.


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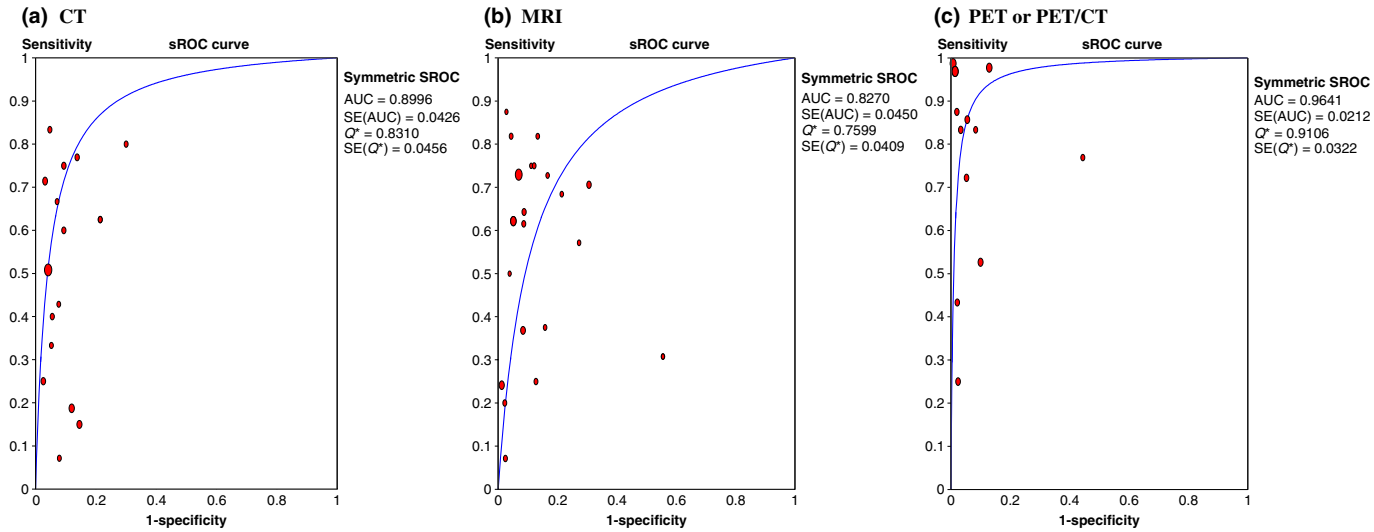


**Fig. 2.** Summary receiver operating characteristic (sROC) curve of the performance of (a) computed tomography (CT), (b) magnetic resonance imaging (MRI), and (c) positron emission tomography (PET or PET/CT) for detection of metastatic lymph nodes in patients with cervical cancer based on a patient-based data analysis. AUC, area under the curve; *Q**, *Q** value.

**Table 4. Summary sensitivity and specificity of CT, MRI, and PET or PET/CT**

| Category | No. of studies | Summary sensitivity, % (95% CI) | $I^2$* (%) | Summary specificity, % (95% CI) | $I^2$* (%) |
|---|---|---|---|---|---|
| Patient-based comparison | | | | | |
| CT | 16 | 50 (43–57) | 71.1 | 92 (90–94) | 31.6 |
| MRI | 21 | 56 (51–62) | 70.7 | 91 (90–93) | 80.1 |
| PET or PET/CT | 12 | 82 (75–87) | 80.7 | 95 (93–97) | 69.7 |
| Region/node-based comparison | | | | | |
| CT | 4 | 52 (42–62) | 78.0 | 92 (90–94) | 81.5 |
| MRI | 9 | 38 (32–43) | 67.7 | 97 (97–98) | 95.0 |
| PET or PET/CT | 8 | 54 (46–61) | 57.3 | 97 (96–98) | 70.9 |

*Test for heterogeneity: An $I^2$ value greater than 50% was considered to indicate substantial heterogeneity across the studies included in the analysis. CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

**Table 5. Pair-wise comparisons between modalities for sensitivity, specificity, AUC, and *Q**

| Category | Sensitivity | Specificity | AUC | *Q** |
|---|---|---|---|---|
| Patient-based comparison | | | | |
| CT *vs* MRI | 50% *vs* 56% (0.19) | 92% *vs* 91% (0.43) | 0.8998 *vs* 0.8270 (0.28) | 0.8310 *vs* 0.7599 (0.25) |
| CT *vs* PET or PET/CT | 50% *vs* 82% (<0.001†) | 92% *vs* 95% (0.04†) | 0.8998 *vs* 0.9641 (0.18) | 0.8310 *vs* 0.9160 (0.15) |
| MRI *vs* PET or PET/CT | 56% *vs* 82% (<0.001†) | 91% *vs* 95% (<0.001†) | 0.8270 *vs* 0.9641 (<0.001†) | 0.7599 *vs* 0.9160 (<0.001†) |
| Region/node-based comparison | | | | |
| CT *vs* MRI | 52% *vs* 38% (0.02†) | 92% *vs* 97% (<0.001†) | 0.8085 *vs* 0.7450 (0.79) | 0.7433 *vs* 0.6893 (0.80) |
| CT *vs* PET or PET/CT | 52% *vs* 54% (0.75) | 92% *vs* 97% (<0.001†) | 0.8085 *vs* 0.8181 (0.97) | 0.7433 *vs* 0.7519 (0.97) |
| MRI *vs* PET or PET/CT | 38% *vs* 54% (<0.001†) | 97% *vs* 97% (1.00) | 0.7450 *vs* 0.8181 (0.72) | 0.6893 *vs* 0.7519 (0.72) |

*By two-sample *Z*-test, values of parenthesis indicate *P*-value; †significant, $P < 0.05$. *Q** corresponds to the point on the sROC curve where sensitivity and specificity are equal. AUC, area under the curve; CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography; sROC, summary receiver operating characteristic curve.

reported that AUC of PET, whether interpreted with or without the use of CT, was higher than that of CT or MR ($P < 0.05$) in diagnosing recurrent ovarian carcinoma.[77] Also, Zhang *et al.*'s meta-analysis reported that PET had a quite high sensitivity (0.91) and specificity (0.83) for detecting distant metastasis in recurrent colorectal carcinoma.[78]

Clinically, the presence of metastatic lymph nodes significantly influences the prognosis of cervical cancer patients.[12–14,79–81] In patients with surgically staged and locally advanced cervical carcinoma, 5-year survival rates of patients without a metastatic lymph node, with a pelvic metastatic lymph node, or with a para-aortic metastatic lymph node, were reported to be 57%, 34%, and 12%, respectively.[82] Nevertheless, lymph node metastasis is not used in the FIGO staging of cervical cancer.[1]

Before the use of PET, three diagnostic modalities such as lymphangiography (LAG), CT, and MRI had been used to assess the metastatic lymph nodes of cervical cancer patients. Scheidler *et al.* compared the utility of LAG, CT, and MRI for the diagnosis of metastatic lymph nodes in patients with cervical cancer via a meta-analysis in 1997.[15] They reported a trend toward

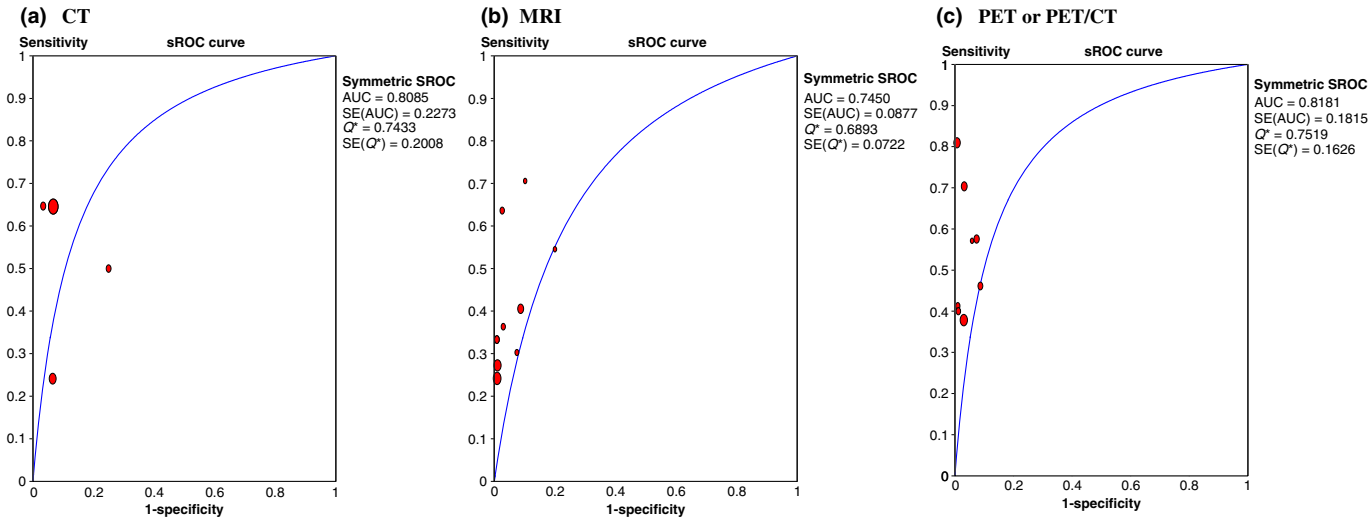


**Fig. 3.** Summary receiver operating characteristic curve of the performance of (a) computed tomography (CT), (b) magnetic resonance imaging (MRI), and (c) positron emission tomography (PET or PET/CT) for detection of metastatic lymph nodes in patients with cervical cancer based on a region- or node-based analysis. AUC, area under the curve; $Q^*$, $Q^*$ value.

better performance for MRI than for LAG or CT, even though sROC analyses showed no significant differences in the overall performance of these modalities. However, those findings are less informative for the following reasons: first, LAG is no longer used in clinical settings because of significant improvements in CT and MRI techniques; second, many of the studies included in the cited overview adopted per-patient-based comparisons and this makes it difficult to directly compare the diagnostic performance of CT or MRI in the detection of metastatic lymph nodes when researchers adopt per-region or per-node-based comparisons; third, since 2001, a lot of studies have reported that PET or PET/CT, as a state-of-the art noninvasive diagnostic tool, showed a better diagnostic performance for the detection of metastatic lymph nodes in patients with cervical cancer, compared with CT or MRI.

To the best of our knowledge, the current study is the first meta-analysis of the diagnostic performance of CT, MRI, and PET in the detection of metastatic lymph nodes in cervical cancer patients. In our study, we subdivided the included studies into a per-patient comparison group and per-region or per-node comparison groups. CT and MRI had similar diagnostic performance but both had lower sensitivity and higher specificity than had PET. This may be because the criteria of the lymph node size were used differently in each study, and also CT and MRI cannot readily differentiate metastatic nodes from hyperplastic nodes of the similar size. In some studies, the mean size of a metastatic lymph node was smaller than 1 cm (largest short axis diameter).[37] This may also explain the low performance of CT and MRI when the largest short axis diameter is the diagnostic size criterion. Even though our study showed that the diagnostic performance of PET was significantly better than that of CT and MRI in both a per-patient based data analysis and region- or node-based data analyses, PET has a lower diagnostic performance than surgical staging for the detection of metastatic lymph nodes in cervical cancer patients.

Also, we performed subgroup analyses based on the type of CT scanner (not shown due to space limitation). Sensitivity was 39% (95% CI: 30%, 49%; $n = 5$) for helical CT (per-patient based comparison) and 61% (95% CI: 52%, 71%; $n = 11$) for non-helical CT (per-patient based comparison), while specificity was similar between them: 92% (95% CI: 89%, 95%) and 92% (88%, 95%), respectively. We could guess that a possible reason for the discrepancy between helical and non-helical CT might be associated with publication bias in the early period. That is, studies showing low sensitivity might not be published.

More importantly, especially in regard to the detection of metastatic lymph nodes, we think that diagnostic performance in CT imaging is not that much related with technical development because the important criteria for metastatic lymph nodes is only the size of lymph node; CT imaging in the early period might also be able to detect metastatic lymph nodes more than 1 cm in size as well as those modalities in the recent period. Again, although recent studies involved more advanced imaging with higher image quality than the previous ones, and lymph nodes detected additionally tended to be smaller (<1 cm in a short axis diameter), these additionally detected lymph nodes might not change the diagnostic decision (size criteria for lymph node metastasis is usually more than 1 cm) in imaging analyses (CT or MRI).

Our study had several limitations. First, we did not evaluate a region-based or node-based data analysis separately because only three studies[22,37,38] had reported the findings from a node-based data analysis. This could be evaluated after more individual studies are conducted. Second, we could not present the exact reasons for heterogeneity which was observed in the meta-analysis for most summary sensitivity and specificity of CT, MRI, and PET, except for summary specificity of CT ($I^2 = 31.6$). However, this may be associated with the variation in patient characteristics or quality of studies. Third, we did not evaluate diagnostic performances by type of MRI scanner. It is not likely that subgroup analyses by type of MRI scanner would provide additional useful information because most studies (26 of 32 MRI studies) used 1.5-tesla MR scanners. Last, there could be reporting or publication bias on this topic. Further research is required to determine this.

In conclusion, this meta-analysis is the first study to evaluate the diagnostic performance of CT, MRI, and PET in the detection of metastatic lymph nodes in cervical cancer patients. Our study showed that PET or PET/CT had an overall higher diagnostic performance than those of CT or MRI in detecting metastatic lymph nodes in patients with cervical cancer. These findings have a clinical implication in that they may give useful information to not only radiologists in interpretation of images but also gynecologic oncologists in choosing imaging modality in the management of cervical cancer patients.


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## Contributorship statement and guarantor

S.K. Myung and H.J. Choi were responsible for the initial plan, study design, statistical analysis, and the conduct of the study. H.J. Choi, S.K. Myung, and W. Ju were responsible for data collection, data extraction, data interpretation, and manuscript drafting. H.J. Choi, W. Ju, Y. Kim, and S.K. Myung were responsible for data interpretation and manuscript drafting. S.K. Myung is the guarantor for this paper and has full responsibility for this study.

## Disclosure Statement

The authors have no conflict of interest.

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