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A Network Meta-Analysis on the Diagnostic Value of Different Imaging Methods for Lymph Node Metastases in Patients With Cervical Cancer

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Abstract

Purpose: We performed this network meta-analysis to compare the diagnostic value of 4 imaging methods (magnetic resonance imaging, positron emission tomography, computed tomography, and diffusion-weighted imaging) for diagnosing lymph node metastases in cervical cancer. **Method:** Diagnostic tests regarding different imaging methods to diagnose lymph node metastases in cervical cancer were retrieved from the Cochrane Library, PubMed, and Embase electronic databases from inception to December 2016. Direct and indirect evidence was performed to calculate the odds ratio and to draw the surface under the cumulative ranking curves of the 4 imaging methods for diagnosing lymph node metastases in cervical cancer. **Results:** Sixteen eligible diagnostic tests were included in this network meta-analysis. The results of network meta-analysis demonstrate that in comparison with the diffusion-weighted imaging, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio of positron emission tomography were relatively higher. Additionally, the results further indicate that compared with other diagnosis method, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio of positron emission tomography had a higher trend. The surface under the cumulative ranking curve results indicated that in terms of positive likelihood ratio and diagnostic odds ratio, positron emission tomography had a relatively higher diagnostic value for lymph node metastases in patients with cervical cancer. **Conclusion:** Our findings indicate that positron emission tomography might have a relatively higher diagnostic value for lymph node metastases in patients with cervical cancer.

Keywords

cervical cancer, lymph node metastases, magnetic resonance imaging, computed tomography, diagnostic tests

Abbreviations

AUC, area under the curve; CC, cervical cancer; CT, computed tomography; DWI, diffusion-weighted imaging; HPV, human papillomavirus; LN, lymph node; MRI, magnetic resonance imaging; NMA, network meta-analysis; OR, odds ratio; PET, positron emission tomography; PPV, positive predictive value; QUADAS, Quality Assessment of Diagnostic Accuracy Studies; SROC, summary receiver operating characteristic; SUCRA, surface under the cumulative ranking curve.

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Introduction

Cervical cancer (CC) is a common gynecologic malignancy in women.[1] In 2012, the world cancer statistics showed that CC was the fourth most common cancer globally (528 000 new cases each year) and is also the fourth highest leading cause of death in women worldwide (266 000 deaths).[2] A previous study demonstrated that the etiology of CC is very complex and involved external, genetic, and cellular risk factors.[3] The main

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cause of CC is human papillomavirus (HPV) infection in the whole cervix. Next, the virus substantially metastasizes to the bladder, rectum, and other organs and may result in death.[4] The large growth in HPV and smoking have also been indicated to be vital causes of CC.[5] Cervical cancer is also known as a preventable cancer.[6] Furthermore, a previous study indicated that CC is associated with geographic location and that the incidence of CC has changed over time.[7] Lymph node (LN) metastasis in CC occurs when tumor cells acquire an immune escape mechanism to avoid the host immune system.[8] The presence of LN metastases in patients is common. A study by Sakuragi *et al* showed that out of 208 patients with stages IB, IIA, and IIB CC who had undergone radical hysterectomy and pelvic lymphadenectomy, 11.5% had stage IB lymphatic metastasis of CC, 26.7% had stage IIA metastasis, and 39.2% were in stage IIB.[9] Imaging is frequently used to determine tumor size, parametrial involvement, LN metastasis, and distant metastasis. Most patients with locally advanced CC are treated with definitive chemoradiotherapy in order to identify the disease extent (especially LN involvement).[10]

There are multiple imaging methods that are widely used to diagnose LN metastasis in CC. These include magnetic resonance imaging (MRI), positron emission tomography (PET), computed tomography (CT), and diffusion-weighted imaging (DWI). Diffusion-weighted imaging is a noninvasive imaging method which aims to observe the molecular mobility of biological tissues (especially the water molecule).[11] It is characterized by diffusion gradients, homogeneous or converse imaging, high amplitude, and a short acquisition time. Diffusion-weighted imaging is generally accepted worldwide to be the standardized imaging technique.[12] This study evaluated the usefulness of tumor volume measurement with PET in patients with advanced CC treated by radiation therapy.[13] In terms of treatment planning in radiotherapy, PET has the advantage of tumor delineation and incorporation of biological process descriptions.[14] Hancke *et al* proposed that a clinical examination is more effective than an MRI or CT in the pretreatment assessment of early invasive CC.[15] The positive predictive value (PPV) of PET in the pelvis and para-aortic region appears sufficient to obviate lymph nodal sampling, but sampling is still required to exclude small-volume disease cranial to sites of abnormality on PET, while MRI has insufficient accuracy for nodal staging to impact management.[16] Furthermore, Exner *et al* demonstrated that DWI is more useful than a conventional MRI.[17] A larger prospective trial will determine whether this modality should be used routinely in conjunction with, or in lieu of, other imaging studies to detect recurrent disease in a broader population of patients with CC.[18] Despite the abundant literature submitted, there was no comprehensive literature regarding the optimal imaging method to diagnose LN metastasis in CC. The aim of our study is to conduct a systematic review (including a traditional meta-analysis and network meta-analysis [NMA]) on the diagnostic value of 4 imaging methods of diagnosing LN metastasis in CC. We also expected this study to be helpful to physicians in the diagnosis of LN metastasis in CC.

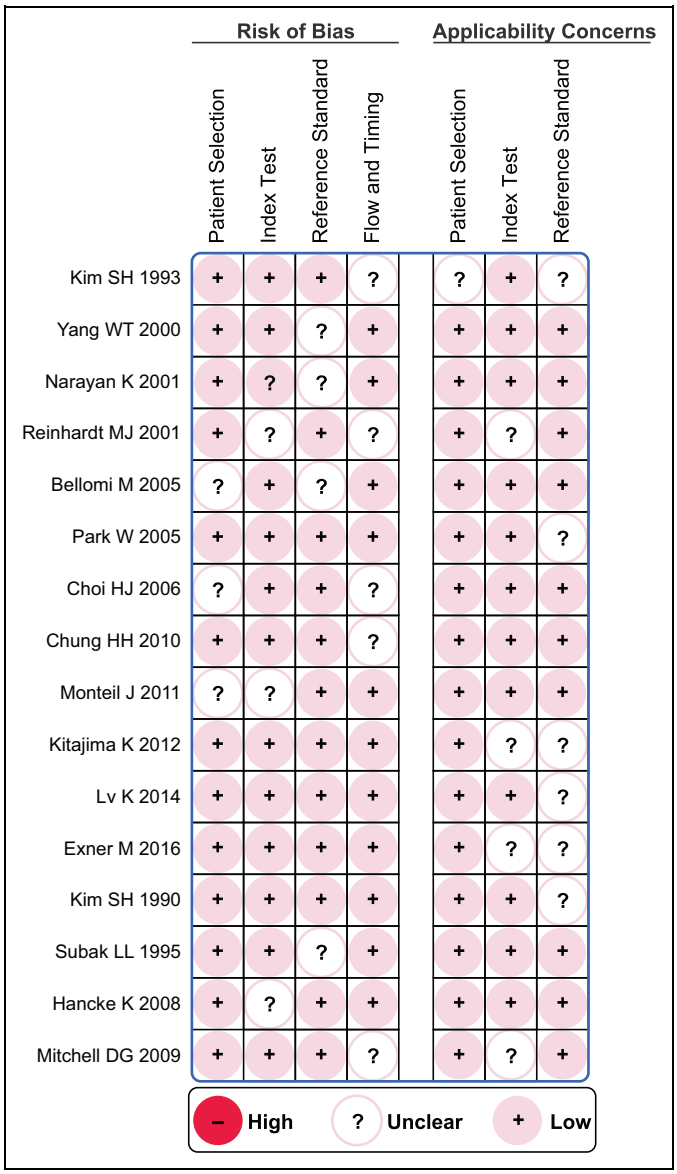

Figure 1. Quality Assessment of Diagnostic Accuracy Studies (QUADAS) included in the network meta-analysis checklist.

Materials and Method

Literature Search

The Cochrane Library, PubMed, and Embase databases were searched via computer-based and manual retrieval for related references of CC with LN metastasis from inception to December 2016. The combination of keywords and individual words including cervical carcinoma, magnetic resonance imaging, LN metastases, computed tomography, positron emission tomography, anddiffusion-weighted imaging were used as the search terms.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) study design was via diagnostic tests; (2) imaging methods included MRI, PET, CT,

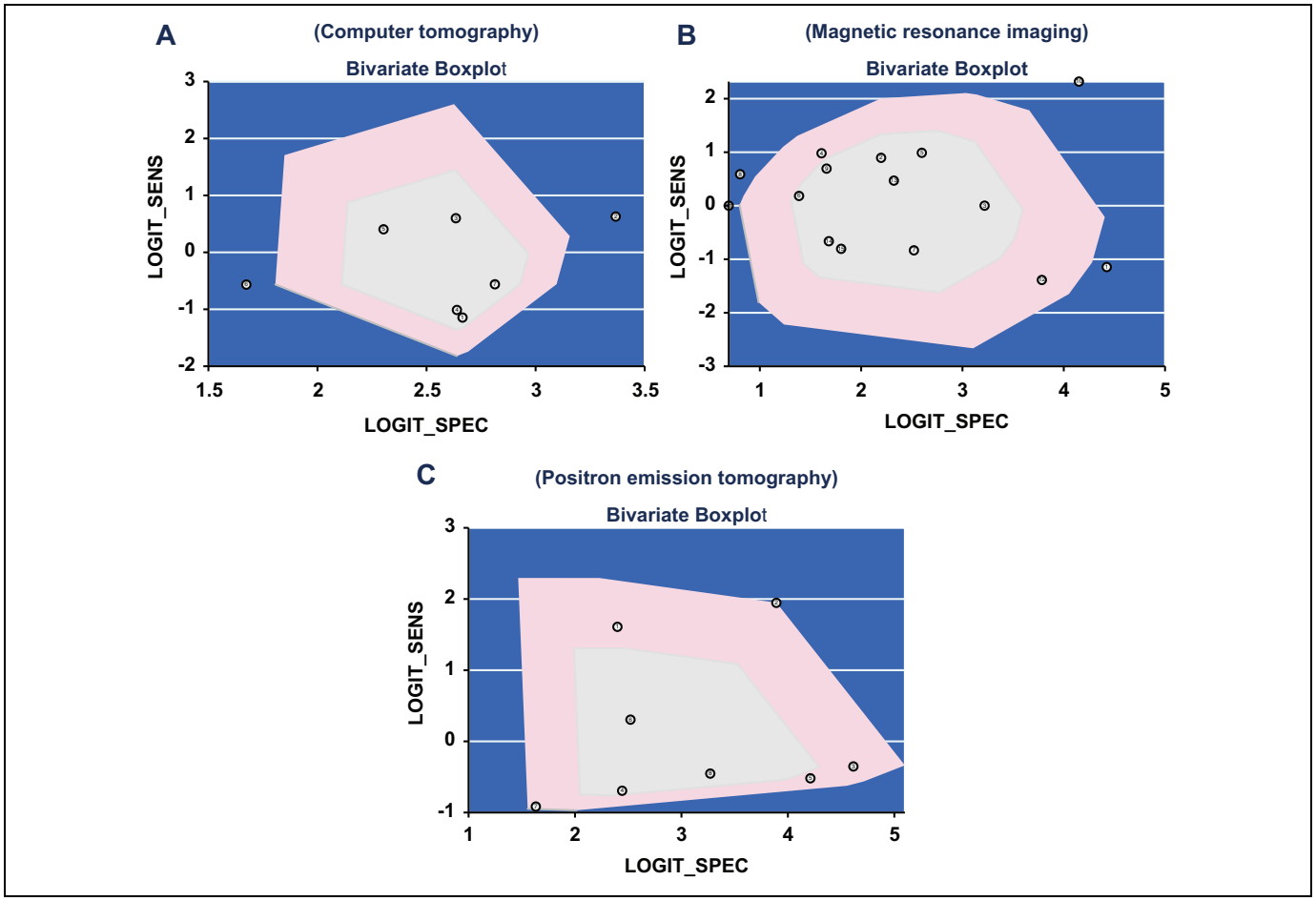

Figure 2. Bivariate box plot diagnostic value for 4 imaging methods in the diagnosis of lymph node metastasis in patients with CC. CC indicates cervical cancer.

and DWI; (3) the age of patients with CC ranged from 21 to 82 years; (4) outcomes included positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio (OR). The exclusion criteria were (1) studies lacking data integrity or are not related to CC and (2) duplicate studies, conference reports, systematic reviews, summary articles, case–control studies, non-English studies, or nonhuman studies.

Data Extraction and Quality Assessment

Data from included studies were extracted by 2 researchers independently using the standard data collection forms. The main data included the first author, publication time, country, race, age, the gold standard, and so on. Any disagreements were resolved through discussion. Risk of bias of included cohort studies was assessed by 2 or more researchers according to the Quality Assessment of Diagnostic Accuracy Studies (QUADAS).[19] The QUADAS tool includes 4 key domains: discuss patient selection, reference standard, index test, and flow and timing (flow of patients through the study, time of the index tests, and reference standard). The Review Manager 5 software (RevMan 5.2.3; Cochrane Collaboration, Oxford, United Kingdom) was applied to evaluate quality and investigate publication bias.

Statistical Analysis

Firstly, we performed a traditional pairwise meta-analysis of studies that directly compared different diagnostic modalities. Statistics were combined by meta-analysis, and threshold effect should be considered at first, which was tested by calculating logarithm of sensitivity and logarithm of 1 − specificity. A $P > .05$ indicated nonthreshold effect, while $P < .05$ showed threshold effect. Sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio could be combined directly if there was no threshold effect. Merge statistics were analyzed via meta-analysis, and if there was heterogeneity caused by threshold effects, data merging was conducted by summary receiver operating characteristic (SROC) curve and then the SROC value was calculated. Area under the curve (AUC) was close to 1, indicating that the clinical value is greater. Area under the curve was between 0.5 and −0.7, indicating that the clinical value was lower. An AUC > 0.7 indicates that the clinical value is good. The straight line of the Deek funnel plot was used as the regression line, and if the

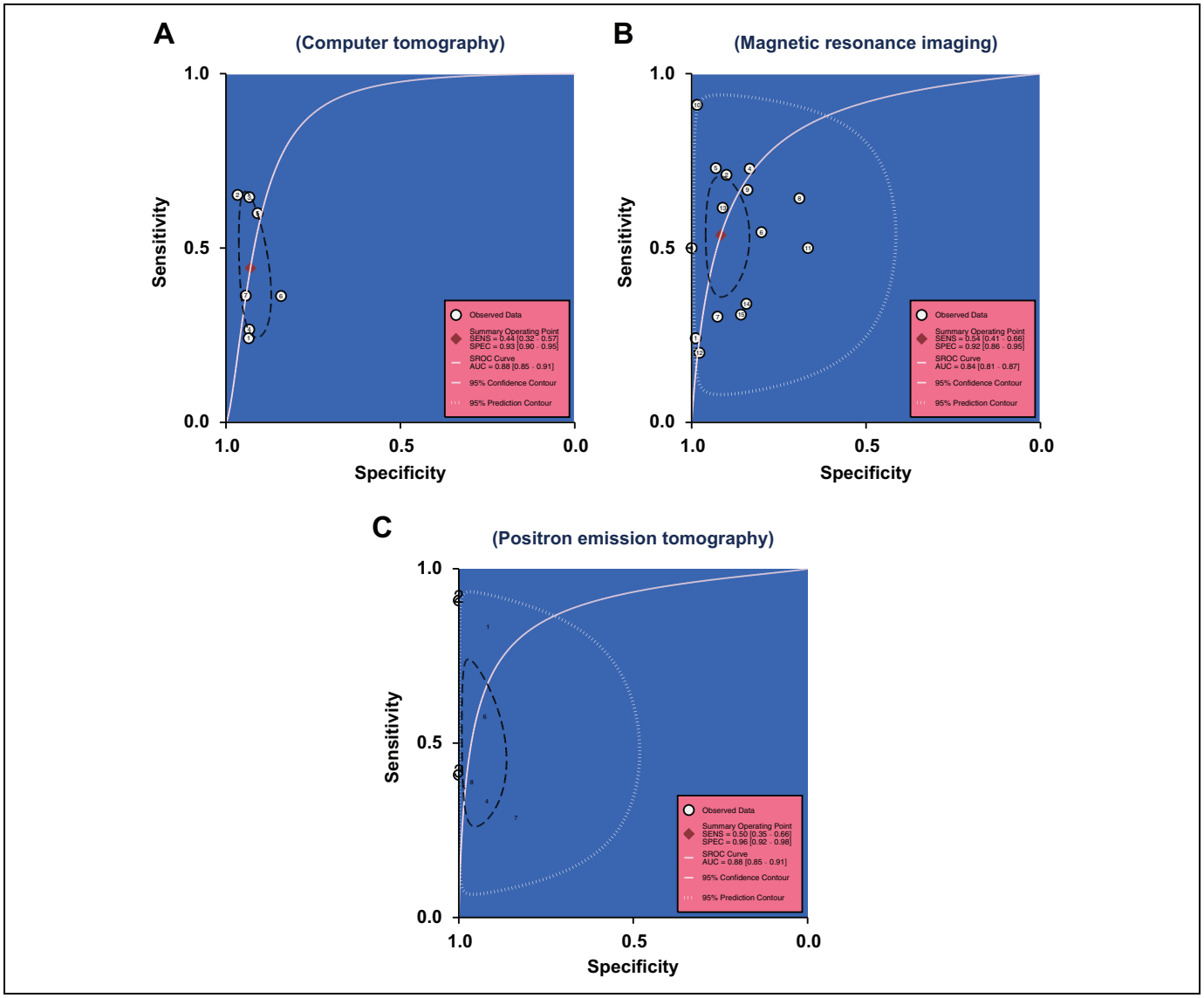

Figure 3. Summary receiver operating characteristic diagram of diagnostic value for 4 imaging methods in the diagnosis of lymph node metastasis in patients with CC. CC indicates cervical cancer.

included angle of the diagnostic odds ratio (DOR) axis was close to 90°, it indicates that the possibility of publication bias is smaller.[20] The OR and 95% credible interval estimates of CC are also shown. The χ^2 and I^2 tests were used to test heterogeneity of the studies.[21] Secondly, R 3.2.1 software was used to draw a network evidence diagram, whereby each node represented a different intervention, node size reflected sample size, and the thickness of the line between nodes represented the number of included studies. Thirdly, a Bayesian NMA was conducted by comparing different diagnostic modalities. Each analysis was based on noninformative priors for effect sizes and precision. We checked and confirmed convergence and lack of autocorrelation after 4 chains and a 20 000-simulation burn-in phase. Eventually, direct probability statements were derived from an additional 50 000-simulation phase.[22] The node splitting method was adopted to evaluate the consistency between direct and indirect evidence, and the decision to use either the consistency or inconsistency model was based on the results.[23] To assist in the interpretation of OR, we calculated the probability of each diagnostic modality. The most effective method was found to be based on a Bayesian approach adopting probability values summarized as surface under the cumulative ranking curve (SUCRA). The larger the SUCRA value, the better the rank of the intervention.[24,25] The cluster analysis method was adopted to evaluate the value of 5 imaging methods in the diagnosis of LN metastasis in CC. This involved clustering different interventions according to the similarity of 2 variables and then determining the advantages and disadvantages of different imaging methods.[24] All computations were conducted using the R (V.3.2.1), package gemtc (V.0.6), and Markov Chain Monte Carlo engine Open BUGS (V.3.4.0) software.

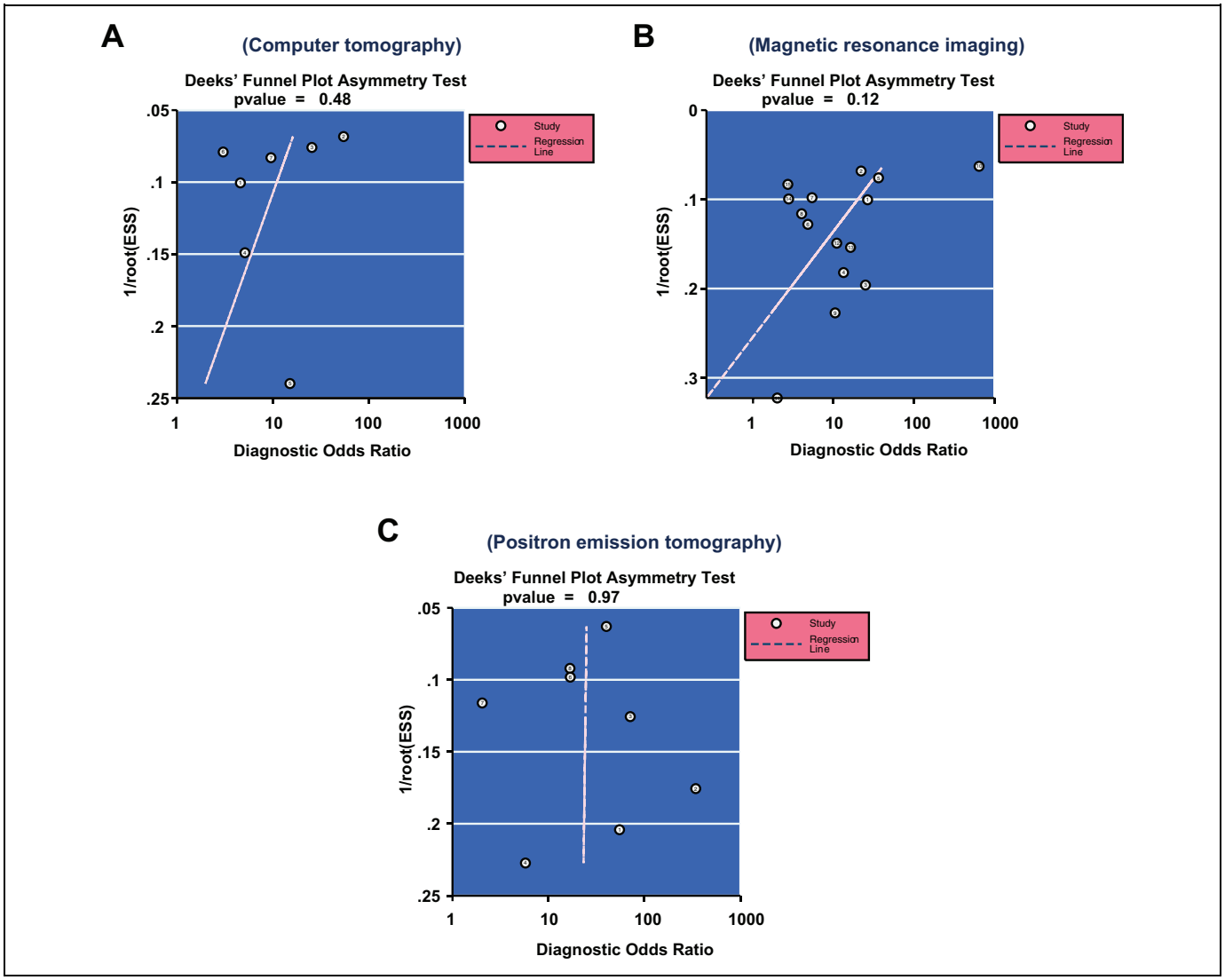

Figure 4. Deek funnel plot of diagnostic value for 4 imaging methods in the diagnosis of lymph node metastasis in patients with CC. CC indicates cervical cancer.

Results

Baseline Characteristics of Included Studies

A total of 5184 relevant studies were initially retrieved from the databases. We excluded 26 duplicate studies, 191 letters and reviews, 22 nonhuman studies, and 604 non-English studies. After a full-text review, we ruled out 156 case–control studies, 1630 cases unrelated to CC, 2538 cases unrelated to imaging methods, and 1 which had low data integrity. Finally, 16 diagnostic tests were eligible and included in this meta-analysis[15-17,26-38] (Supplemental Figure 1). These studies included 1172 patients with CC, most adopted MRI, and were published from 1990 to 2016. There were 8 studies on Caucasians and 8 on Asians. All 16 diagnostic tests were 2-arm trials. The baseline characteristics of included studies are displayed in Supplemental Table 1. The Cochrane risk of bias assessment of included studies is shown in Figure 1.

Pairwise Meta-Analysis of the Diagnostic Value of 4 Imaging Methods in the Diagnosis of LN Metastasis in CC

In CT, Spearman correlation coefficient = −0.179, calculated by logarithm of sensitivity and logarithm of 1 − specificity, P = .702; in MRI, Spearman correlation coefficient = 0.188, calculated by logarithm of sensitivity and logarithm of 1 − specificity, P = .503; in PET, Spearman correlation coefficient = −0.143, calculated by logarithm of sensitivity and logarithm of 1 − specificity, P = .736. Results of threshold testing indicated that there was no threshold effect in each research, so the sensitivity, specificity, PPV, and negative predictive value could be combined. Bivariate box plot showed that there was heterogeneity in each research (Figure 2). The area of the SROC curve showed that diagnostic value of CT, MRI, and PET was good (AUC = 0. 88, AUC = 0. 84, AUC = 0.88; Figure 3). Deek funnel plot

Table 1. Estimated OR and 95% CI of Pairwise Meta-Analysis for 4 Modalities in the Detection of Lymph Node Metastases in Cervical Cancer.[a]

		Heterogeneity Test		Pairwise Meta-Analysis		
Included Studies	Comparisons	I^2	P_h	OR (95% CI)	Z	P
Positive likelihood ratio						
7 Studies	A vs C	99.3%	<.001	1.04 (0.52-2.08)	0.12	.904
7 Studies	B vs A	98.8%	<.001	1.85 (0.78-4.39)	1.39	.165
1 Study	B vs D	**NA**	**NA**	**13.67 (11.75-15.90)**	**33.9**	**<.001**
1 Study	D vs A	NA	NA	0.80 (0.25-2.55)	0.38	.706
Negative likelihood ratio						
7 Studies	C vs A	99.3%	<.001	0.98 (0.74-1.31)	0.12	.903
7 Studies	A vs B	98.8%	<.001	0.79 (0.12-5.08)	0.25	.804
1 Study	D vs B	**NA**	**NA**	**0.28 (0.25-0.31)**	**26.78**	**<.001**
1 Study	A vs D	NA	NA	1.80 (0.58-5.55)	1.02	.307
Diagnostic odds ratio						
7 Studies	A vs C	98.9%	<.001	1.09 (0.50-2.39)	0.21	.832
7 Studies	B vs A	99.2%	<.001	1.51 (0.28-8.10)	0.48	.628
1 Study	B vs D	**NA**	**NA**	**3.73 (3.05-4.56)**	**12.76**	**<.001**
1 Study	D vs A	NA	NA	1.20 (0.31-4.58)	0.27	.790

Abbreviations: 95% CI, 95% confidence interval; NA, not available; OR, odds ratios.
[a]A, magnetic resonance imaging; B, positron emission tomography; C, computer tomography; D, diffusion-weighted imaging; Bold means significant difference.

indicated that there was less likelihood of publication bias, which was confirmed by linear regression test (all $P > .05$; Figure 4). We conducted a direct paired comparison of the diagnostic value of 4 imaging methods in the diagnosis of LN metastasis in CC. The results revealed that positive likelihood ratio, negative likelihood ratio, and diagnostic OR of PET were relatively higher than MRI (Table 1).

Evidence Network of the Diagnostic Value of 4 Imaging Methods in the Diagnosis of LN Metastasis in CC

Four imaging methods were included in this NMA. In terms of positive likelihood ratio, negative likelihood ratio, and diagnostic OR, a large number of patients were diagnosed with MRI (as shown in Figure 5).

Inconsistency Tests of Positive Likelihood Ratio, Negative Likelihood Ratio, and Diagnostic OR

The inconsistency tests demonstrated that the results of the direct and indirect evidence on positive likelihood ratio, negative likelihood ratio, and diagnostic OR were consistent; thus, the consistency model was adopted (both $P > .05$; Figure 6).

Main Results of the NMA of the Diagnostic Value of 4 Imaging Methods in the Diagnosis of LN Metastasis in CC

The results of this NMA indicated that the positive likelihood ratio, negative likelihood ratio, and diagnostic OR of PET had a corresponding higher trend compared to MRI, DWI, and CT (Table 2).

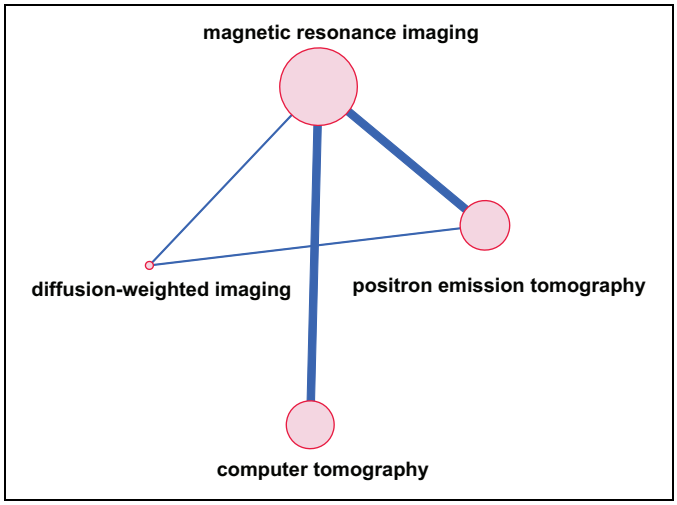

Figure 5. Network evidence of the diagnostic value of 4 imaging methods in the diagnosis of lymph node metastasis in patients with CC. CC indicates cervical cancer; CT, computer tomography; DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; PET, positron emission tomography.

The SUCRA Values of the Diagnostic Value of 4 Imaging Methods in the Diagnosis of LN Metastasis in CC

As shown in Table 3, the SUCRA values demonstrated that in terms of positive likelihood ratio and diagnostic OR, PET had a relatively higher diagnostic value for LN metastases in patients with CC.

Sensitivity Analysis of the Diagnostic Value of 4 Imaging Methods in the Diagnosis of LN Metastasis in CC

As shown in Supplemental Figure 2, the SROC curves of CT, MRI, and PET had no significant change after rejecting an

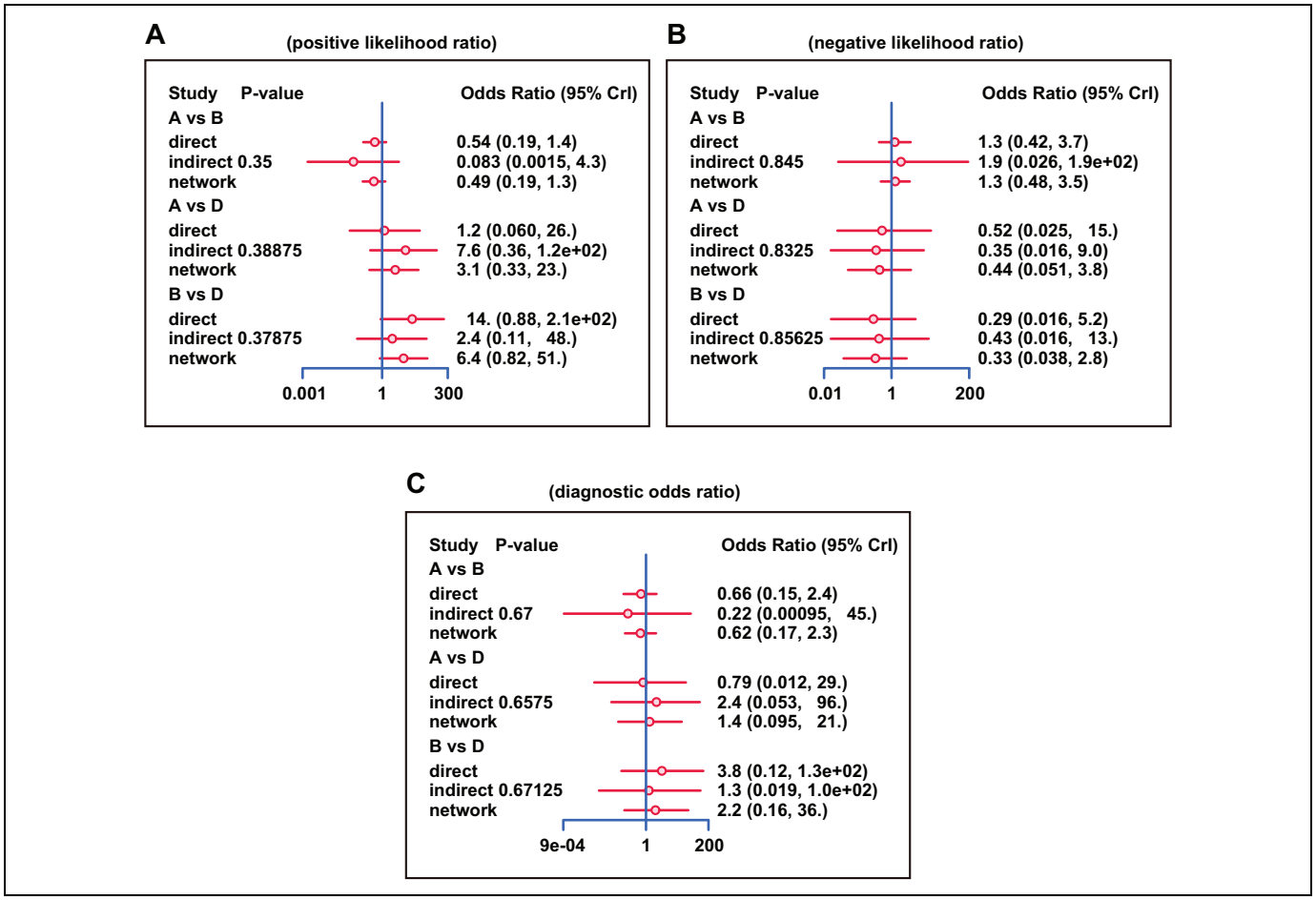

Figure 6. Node splitting plot of the diagnostic value of 4 imaging methods in the diagnosis of lymph node metastasis in patients with CC. A, Magnetic resonance imaging. B, Positron emission tomography. C, Computer tomography; D, diffusion-weighted imaging. CC indicates cervical cancer.

Table 2. Odds Ratios and 95% Confidence Intervals of 4 Modalities for the Diagnosis of Cervical Cancer Under 2 End Indicators Based on the Network Meta-Analysis.[a]

Odds Ratio (95% Confidence Interval)			
Positive likelihood ratio			
A	2.1 (0.78-5.6)	0.96 (0.35-2.5)	0.31 (0.043-2.5)
0.49 (0.18-1.3)	B	0.46 (0.12-1.9)	0.15 (0.021-1.1)
1.0 (0.40-2.9)	2.2 (0.54-8.5)	C	0.33 (0.035-3.2)
3.2 (0.40-23.0)	6.6 (0.92-48.0)	3.1 (0.31-29.0)	D
Negative likelihood ratio			
A	1.3 (0.47-3.6)	0.99 (0.33-2.9)	0.99 (0.33-2.9)
0.77 (0.27-2.1)	B	0.75 (0.18-3.2)	0.32 (0.038-2.7)
1.0 (0.34-3.0)	1.3 (0.31-5.5)	C	0.42 (0.040-4.5)
2.4 (0.28-19.0)	3.1 (0.37-26.0)	0.42 (0.040-4.5)	D
Diagnostic odds ratio			
A	1.6 (0.46-6.4)	0.90 (0.23-3.5)	0.71 (0.049-11.0)
0.61 (0.16-2.2)	B	0.55 (0.077-3.5)	0.43 (0.031-6.7)
1.1 (0.29-4.4)	1.8 (0.28-13.0)	C	0.78 (0.039-18.0)
1.4 (0.092-20.0)	2.3 (0.15-32.0)	1.3 (0.055-26.0)	D

[a]A, magnetic resonance imaging; B, positron emission tomography; C, computer tomography; D, diffusion-weighted imaging.

arbitrary research, which demonstrated that all including researches less affected the outcomes. In Supplemental Figures 3 to 11, the SUCRA values of others had no significant change after rejecting an arbitrary research, which demonstrated that the conclusion was convincing.

Discussion

The lymphatic system is the most important pathway for the spread of CC.[39] A noninvasive technique that could accurately identify LN metastasis in malignant tumors would be strongly beneficial for improving treatment management.[40] This NMA compared 4 imaging methods using 16 diagnostic tests involving 1172 patients with CC. The results of NMA demonstrated that in comparison with the DWI, positive likelihood ratio, negative likelihood ratio, and diagnostic OR of PET were relative higher. The SUCRA results indicated that in terms of positive likelihood ratio and diagnostic OR, PET had a relatively higher diagnostic value for LN metastases in patients with CC.

Firstly, we conducted a direct paired comparison of the diagnostic value of 4 imaging methods in the diagnosis of LN metastasis in CC. The results revealed that positive

Table 3. The SUCRA Values of 4 Diagnostic Modalities Under 3 End Point Outcomes.[a]

Diagnostic Tests	SUCRA Values		
	Positive Likelihood Ratio	Negative Likelihood Ratio	Diagnostic Odds Ratio
A	0.616	0.604	0.598
B	0.943	0.443	0.821
C	0.608	0.601	0.570
D	0.333	0.851	0.512

Abbreviation: SUCRA, surface under the cumulative ranking curves.
[a]A, magnetic resonance imaging; B, positron emission tomography; C, computer tomography; D, diffusion-weighted imaging.

likelihood ratio, negative likelihood ratio, and diagnostic OR of PET were relatively higher than DWI. Extracapsular spread of LN metastasis has been shown as a negative prognostic factor in cancers of several organs.[41] Positron emission tomography may be a useful follow-up method for CC, thereby providing the patients with early opportunities for sophisticated treatments.[42] Positron emission tomography proved to be valuable for LN staging in patients with early-stage CC, with short-axis diameter greater than 0.5 cm being the size threshold for accurate depiction of metastatic nodes.[43] Positron emission tomography appears useful in the management of CC, in particular for staging extrapelvic metastases or optimally detecting a recurrence.[44]

Secondly, the SUCRA values demonstrated that in terms of positive likelihood ratio and diagnostic OR, PET had a relatively higher diagnostic value for LN metastases in patients with CC. Positron emission tomography scan is a sensitive imaging modality for the detection of recurrent cervical carcinoma in both symptomatic and asymptomatic women.[45] Using this modality may reduce unnecessary surgical interventions, help modify radiation fields, and change therapeutic approaches.[46] Therefore, PET in conjunction with MRI can improve the detection of extrapelvic metastasis.[47] Diffusion-weighted imaging is a technique which evaluates the rate of microscopic water diffusion in tissues.[48] It has recently been used in oncologic imaging to depict and characterize tumors and to differentiate benign lesions from malignant lesions in various tumors such as uterine cancer.[49,50] A previous study evaluated its potential in detecting and evaluating pelvic LN metastases via body DWIs in patients with gynecologic malignancies. It showed that body DWI is useful in detecting pelvic LNs in patients with gynecologic malignancy.[51] However, the results of this study were controversial due to the quantitative apparent diffusion coefficient value for differentiation of malignant from benign LNs in uterine cancer. Shen *et al* evaluated the diagnostic performance of DWI in CC metastasis with a sensitivity, specificity, and AUC of 86%, 84%, and 0.9384, respectively. The results showed a strong diagnostic performance of DWI in relation to sensitivity, specificity, and AUC in comparison with other imaging methods.[52]

Conclusion

Our study evaluated the diagnostic performance of 4 different imaging techniques and concluded that DWI, PET, CT, and MRI are the optimal imaging methods for the diagnosis of LN metastases in CC. This may provide theoretical evidence for the diagnosis of patients with CC. However, there are some limitations of this study which should be mentioned. Firstly, because of the limited number of documents and direct imaging method comparisons, our results may have been influenced. Secondly, patients in different stages of CC have different LN metastasis levels, which can affect the preference of imaging method. Thirdly, limited data on the diagnostic efficacy of a single criterion were corresponding, thus may have influenced data pooling with a single criterion. Finally, there were only 2 studies about DWI, so a threshold and SROC curve could not be conducted about it. And we did not obtain the effective methodology applied from the included study of Bellomi *et al*, which might cause bias for our final results. A well-designed prospective, randomized, multicentered clinical trial is required to evaluate the diagnostic value of these imaging methods in the diagnosis of LN metastases in CC.

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Declaration of Conflicting Interests

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Supplemental Material

Supplementary material for this article is available online.

References

1. Nowakowski A, Sliwczynski A, Seroczynski P, Cybulski M, Teter Z. Reimbursed costs of management of uterine cervical lesions in Poland—a descriptive analysis of data from the National Health Fund and the Ministry of Health. *Cent Eur J Public Health*. 2016;24(2):163-168.
2. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136(5):E359-E386.
3. Chang B, Kim J, Jeong D, et al. Klotho inhibits the capacity of cell migration and invasion in cervical cancer. *Oncol Rep*. 2012;28(3): 1022-1028.
4. Cheng YM, Chou CY, Hsu Y.C, Chen MJ, Wing LY. The role of human papillomavirus type 16 E6/E7 oncoproteins in cervical epithelial-mesenchymal transition and carcinogenesis. *Oncol Lett*. 2012;3(3):667-671.
5. Luhn P, Walker J, Schiffman M, et al. The role of co-factors in the progression from human papillomavirus infection to cervical cancer. *Gynecol Oncol*. 2013;128(2):265-270.

6. Asgarlou Z, Tehrani S, Asghari E, et al. Cervical cancer prevention knowledge and attitudes among female university students and hospital staff in Iran. *Asian Pac J Cancer Prev*. 2016;17(11): 4921-4927.
7. Thongsak N, Chitapanarux I, Suprasert P, et al. Spatial and temporal analyses of cervical cancer patients in Upper Northern Thailand. *Asian Pac J Cancer Prev*. 2016;17(11);5011-5017.
8. Ferns DM, Heeren AM, Samuels S, et al. Classical and non-classical HLA class I aberrations in primary cervical squamous- and adenocarcinomas and paired lymph node metastases. *J Immunother Cancer*. 2016;4:78.
9. Sakuragi N, Satoh C, Takeda N, et al. Incidence and distribution pattern of pelvic and paraaortic lymph node metastasis in patients with Stages IB, IIA, and IIB cervical carcinoma treated with radical hysterectomy. *Cancer*. 1999;85(7):1547-1554.
10. Hong JH, Min KJ, Lee JK, et al. Prognostic value of the sum of metabolic tumor volume of primary tumor and lymph nodes using ^{18}F-FDG PET/CT in patients with cervical cancer. *Medicine (Baltimore)*.2016;95(9):e2992.
11. Park JJ, Kim CK, Park SY, Park Lee HM, Cho SW. Prostate cancer: role of pretreatment multiparametric 3-T MRI in predicting biochemical recurrence after radical prostatectomy. *AJR Am J Roentgeno*. 2014; 202(5):W459-W465.
12. Chong Y, Kim CK, Park SY, Park BK, Kwon GY, Park JJ. Value of diffusion-weighted imaging at 3 T for prediction of extracapsular extension in patients with prostate cancer: a preliminary study. *AJR Am J Roentgenol*. 2014;202(4):772-777.
13. Miller TR, Grigsby PW. Measurement of tumor volume by PET to evaluate prognosis in patients with advanced cervical cancer treated by radiation therapy. *Int J Radiat Oncol Biol Phys*. 2002; 53(2):353-359.
14. Grosu AL, Piert M, Weber WA, et al. Positron emission tomography for radiation treatment planning. *Strahlenther Onkol*. 2005;181(8):483-499.
15. Hancke K, Heilmann V, Straka P, Kreienberg R, Kurzeder C. Pretreatment staging of cervical cancer: is imaging better than palpation?: role of CT and MRI in preoperative staging of cervical cancer: single institution results for 255 patients. *Ann Surg Oncol*. 2008;15(10):2856-2861.
16. Narayan K, Hicks RJ, Jobling T, Bernshaw D, McKenzie AF. A comparison of MRI and PET scanning in surgically staged loco-regionally advanced cervical cancer: potential impact on treatment. *Int J Gynecol Cancer*. 2001;11(4):263-271.
17. Exner M, Kuhn A, Stumpp P, et al. Value of diffusion-weighted MRI in diagnosis of uterine cervical cancer: a prospective study evaluating the benefits of DWI compared to conventional MR sequences in a 3 T environment. *Acta Radiol*. 2016;57(7): 869-877.
18. Havrilesky LJ, Wong TZ, Secord AA, Berchuck A, Clarke-Pearson DL, Jones EL. The role of PET scanning in the detection of recurrent cervical cancer. *Gynecol Oncol*. 2003;90(1): 186-190.
19. Whiting PF, Rutjes AW, Westwood ME, et al; QUADAS-2 Group. QUADAS-2: a revised tool for the Quality Assessment of Diagnostic Accuracy Studies. *Ann Intern Med*. 2011;155(8): 529-536.
20. Deeks JJ, Macaskill P, Irwig L. The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. *J Clin Epidemiol*. 2005; 58(9):882-893.
21. Chen LX, Li YL, Ning GZ, et al. Comparative efficacy and tolerability of three treatments in old people with osteoporotic vertebral compression fracture: a network meta-analysis and systematic review. *PLoS One*. 2015;10(4):e0123153.
22. Tu YK, Needleman I, Chambrone L, Lu HK, Faggion CM Jr. A Bayesian network meta-analysis on comparisons of enamel matrix derivatives, guided tissue regeneration and their combination therapies. *J Clin Periodontol*. 2012;39(3):303-314.
23. Zhu GQ, Shi KQ, Huang S, et al. Systematic review with network meta-analysis: the comparative effectiveness and safety of interventions in patients with overt hepatic encephalopathy. *Aliment Pharmacol Ther*. 2015;41(7):624-635.
24. Chaimani A, Higgins JP, Mavridis D, Spyridonos P, Salanti G. Graphical tools for network meta-analysis in STATA. *PLoS One*. 2013;8(10):e76654.
25. Salanti G, Ades AE, Ioannidis JP. Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial. *J Clin Epidemiol*. 2011;64(2):163-171.
26. Choi HJ, Roh JW, Seo SS, et al. Comparison of the accuracy of magnetic resonance imaging and positron emission tomography/computed tomography in the presurgical detection of lymph node metastases in patients with uterine cervical carcinoma: a prospective study. *Cancer*. 2006;106(4):914-922.
27. Park W, Park YJ, Huh SJ, et al. The usefulness of MRI and PET imaging for the detection of parametrial involvement and lymph node metastasis in patients with cervical cancer. *Jpn J Clin Oncol*. 2005;35(5):260-264.
28. Kim SH, Choi BI, Lee HP, et al. Uterine cervical carcinoma: comparison of CT and MR findings. *Radiology*. 1990;175(1): 45-51.
29. Kim SH, Choi BI, Han JK, et al. Preoperative staging of uterine cervical carcinoma: comparison of CT and MRI in 99 patients. *J Comput Assist Tomogr*. 1993;17(4):633-640.
30. Subak LL, Hricak H, Powell CB, Azizi L, Stern JL. Cervical carcinoma: computed tomography and magnetic resonance imaging for preoperative staging. *Obstet Gynecol*. 1995;86(1):43-50.
31. Yang WT, Lam WW, Yu MY, Cheung TH, Metreweli C. Comparison of dynamic helical CT and dynamic MR imaging in the evaluation of pelvic lymph nodes in cervical carcinoma. *AJR Am J Roentgenol*. 2000;175(3):759-766.
32. Reinhardt MJ, Ehritt-Braun C, Vogelgesang D, et al. Metastatic lymph nodes in patients with cervical cancer: detection with MR imaging and FDG PET. *Radiology*. 2001;218(3):776-782.
33. Bellomi M, Bonomo G, Landoni F, et al. Accuracy of computed tomography and magnetic resonance imaging in the detection of lymph node involvement in cervix carcinoma. *Eur Radiol*. 2005; 15(12):2469-2474.
34. Mitchell DG, Snyder B, Coakley F, et al. Early invasive cervical cancer: MRI and CT predictors of lymphatic metastases in the ACRIN 6651/GOG 183 intergroup study. *Gynecol Oncol*. 2009; 112(1):95-103.

35. Chung HH, Kang KW, Cho JY, et al. Role of magnetic resonance imaging and positron emission tomography/computed tomography in preoperative lymph node detection of uterine cervical cancer. *Am J Obstet Gynecol*. 2010;203(2):156.e151-e155.
36. Monteil J, Maubon A, Leobon S, et al. Lymph node assessment with (18)F-FDG-PET and MRI in uterine cervical cancer. *Anticancer Res*. 2011;31(11):3865-3871.
37. Kitajima K, Yamasaki E, Kaji Y, Murakami K, Sugimura K. Comparison of DWI and PET/CT in evaluation of lymph node metastasis in uterine cancer. *World J Radiol*. 2012;4(5):207-214.
38. Lv K, Guo HM, Lu YJ, et al. Role of 18F-FDG PET/CT in detecting pelvic lymph-node metastases in patients with early-stage uterine cervical cancer: comparison with MRI findings. *Nucl Med Commun*. 2014;35(12):1204-1211.
39. Burghardt E, Pickel H. Local spread and lymph node involvement in cervical cancer. *Obstet Gynecol*. 1978;52(2):138-145.
40. Rockall AG, Sohaib SA, Harisinghani MG, et al. Diagnostic performance of nanoparticle-enhanced magnetic resonance imaging in the diagnosis of lymph node metastases in patients with endometrial and cervical cancer. *J Clin Oncol*. 2005;23(12):2813-2821.
41. Metindir J, Bilir Dilek G. Evaluation of prognostic significance in extracapsular spread of pelvic lymph node metastasis in patients with cervical cancer. *Eur J Gynaecol Oncol*. 2008;29(5):476-478.
42. Ryu SY, Kim MH, Choi SC, Choi CW, Lee KH. Detection of early recurrence with 18F-FDG PET in patients with cervical cancer. *J Nucl Med*. 2003;44(3):347-352.
43. Sironi S, Buda A, Picchio M, et al. Lymph node metastasis in patients with clinical early-stage cervical cancer: detection with integrated FDG PET/CT. *Radiology*. 2006;238(1):272-279.
44. Belhocine T, Thille A, Fridman V, et al. Contribution of whole-body 18FDG PET imaging in the management of cervical cancer. *Gynecol Oncol*. 2002;87(1):90-97.
45. Unger JB, Ivy JJ, Connor P, et al. Detection of recurrent cervical cancer by whole-body FDG PET scan in asymptomatic and symptomatic women. *Gynecol Oncol*. 2004;94(1):212-216.
46. Amit A, Beck D, Lowenstein L, et al. The role of hybrid PET/CT in the evaluation of patients with cervical cancer. *Gynecol Oncol*. 2006;100(1):65-69.
47. Tsai CS, Lai CH, Chang TC, et al. A prospective randomized trial to study the impact of pretreatment FDG-PET for cervical cancer patients with MRI-detected positive pelvic but negative para-aortic lymphadenopathy. *Int J Radiat Oncol Biol Phys*. 2010;76(2):477-484.
48. Kwee TC, Takahara T, Ochiai R, Nievelstein RA, Luijten PR. Diffusion-weighted whole-body imaging with background body signal suppression (DWIBS): features and potential applications in oncology. *Eur Radiol*. 2008;18(9):1937-1952.
49. Naganawa S, Sato C, Kumada H, Ishigaki T, Miura S, Takizawa O. Apparent diffusion coefficient in cervical cancer of the uterus: comparison with the normal uterine cervix. *Eur Radiol*. 2005;15(1):71-78.
50. Fujii S, Matsusue E, Kigawa J, et al. Diagnostic accuracy of the apparent diffusion coefficient in differentiating benign from malignant uterine endometrial cavity lesions: initial results. *Eur Radiol*. 2008;18(2):384-389.
51. Nakai G, Matsuki M, Inada Y, et al. Detection and evaluation of pelvic lymph nodes in patients with gynecologic malignancies using body diffusion-weighted magnetic resonance imaging. *J Comput Assist Tomogr*. 2008;32(5):764-768.
52. Shen G, Zhou H, Jia Z, Deng H. Diagnostic performance of diffusion-weighted MRI for detection of pelvic metastatic lymph nodes in patients with cervical cancer: a systematic review and meta-analysis. *Br J Radiol*. 2015;88(1052):20150063.