The diagnostic value of PET/CT for the lymph node metastasis in Asian patients with non-small cell lung cancer: A meta-analysis

Jiangming[1] Sun MD,
Yufeng[2] Li MD,
Fakuo Gong[1] BD,
Shengyang[1] Xu BD,
Jie Wu[1] BD,
Huan Wang[1] BD,
Tao He[1] MD

Jiangming Sun and Yufeng Li have contributed equally

1. Department of Nuclear Medicine, Panzhihua Central Hospital, Panzhihua, Sichuan, China
2. Department of UltraSound, Panzhihua Central Hospital, Panzhihua, Sichuan, China

Keywords: Non-small-cell lung cancer - Lymph node - PET - Meta-analysis

Corresponding author:
Tao He MD,
Department of Nuclear Medicine,Panzhihua Central Hospital, No.34 Yikang Street, Panzhihua,Sichuan 617067,China
Tel: +86-18096307922
hetao987@126.com

Received:
3 March 2022
Accepted revised:
29 June 2022

Abstract

Objective: To evaluate the accuracy of positron emission tomography/computed tomography (PET/CT) in the diagnosis of lymph node metastasis in non-small cell lung cancer (NSCLC) by a method of meta-analysis. **Materials and Methods:** A comprehensive research of PubMed, Cochrane Library, China National Knowledge Infrastructure (CNKI), and Embase data bases was conducted to collect literature about PET/CT diagnosing lymph node metastasis of NSCLC up to December 1, 2021. Stata 15.0 software was used for the calculation of sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR). The publication bias was evaluated by Deeks' funnel plot. **Results:** A total of 25 studies were enrolled, including 2,458 patients with NSCLC. The pooled sensitivity of PET/CT for diagnosing lymph node metastasis in NSCLC was 0.68 (95%CI: 0.61-0.75), the pooled specificity being 0.93 (95%CI: 0.89-0.95). Likelihood ratio syntheses gave an overall PLR of 9.4 (95%CI: 6.3-13.9), and NLR of 0.34 (95%CI: 0.28-0.41). The pooled DOR was 28 (95%CI: 19-40). The summary receiver operating characteristic curve showed the area under the curve of 0.88 (95%CI: 0.84-0.90). **Conclusions:** PET/CT has a good value in the diagnosis of lymph node metastasis of NSCLC, with specificity excellent. PET/CT can be used as one of the main imaging diagnosis methods for lymph node metastasis in patients with NSCLC.

Hell J Nucl Med 2022; 25(2): 196-204 *Epub ahead of print: 3 August 2022* *Published online: 29 August 2022*

Introduction

Lung cancer is one of the most common malignant tumors at present [1]. Regardless of gender differences, the incidence of lung cancer is increasing every year and is getting younger [1, 2]. Non-small cell lung cancer (NSCLC) occupies a large proportion in the classification of lung cancer, accounting for 85% of all types [3]. The metastatic pathways of non-small cell lung cancer include lymph node metastasis (LNM), blood type metastasis, local infiltration, and implantation metastasis, among which lymph node metastasis is the most common metastatic node of lung cancer [4]. Lymph node metastasis can occur in the early stage of non-small cell lung cancer, with high degree of malignancy and high recurrence rate [5].

At present, computed tomography (CT) or magnetic resonance (MR) is the most common imaging examination method to diagnose lymph node metastasis [6], while CT and MR are mostly judged by the change in lymph node shape, size, density, or signal, which have obvious limitations in the qualitative detection of lesions [3]. Compared to positron emission tomography (PET) for localization of lesions, CT or MR has disadvantages in qualitative aspects [7]. Positron emission tomography/CT combines the advantages of PET and CT, greatly improving the accuracy of detection and characterization of lesions [6, 8].

Comprehensive treatment of NSCLC cannot be separated from clinical staging. Determining the presence of lymph node metastases is helpful for directional lymph node dissection. Therefore, we aimed to use meta-analysis to evaluate the diagnostic value of PET/CT in lymph node metastasis of NSCLC.

Materials and Methods

Search strategy

The relevant studies on the diagnosis of lymph node metastasis in NSCLC were retri-

eved in PubMed, Cochrane Library, China National Knowledge Infrastructure (CNKI), and Embase up to December 1, 2021.The main retrieval strategies are as follows: ("PET-CT" OR"positron emission tomography") AND ("lung cancer"OR "NSCLC") AND ("lymph node metastasis"OR"lymphatic metastasis") AND ("specificity" OR "sensitivity" OR "diagnosis" OR"accuracy"). There are no restrictions on the retrieval language. Two researchers conducted the search independently, and finally cross-checked the results.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) The included studies were those evaluating the value of PET/CT in the diagnosis of lymph node metastasis of NSCLC; (2) Research is prospective or retrospective; (3) All subjects included should not only undergo PET/CT but also be supported by the golden criteria of diagnosis; (4) Literature can extract valuable results; (5) Studies with lymph nodes as samples.

The exclusion criteria were as follows:(1) Review, abstract, case report, and editorial; (2) Basic experimental research, such as animal experiments, and cell experiments; (3) There are obvious errors in the extraction of information, or the data is incomplete.

Data extraction and quality assessment

Study inclusion and exclusion criteria were followed. First, use Endnote software to eliminate duplicate research, and then preliminarily eliminate unqualified documents by reading the titles and abstracts. For those studies that cannot be confirmed, the decision should be made after reading the full text. If the article still cannot be determined, more than two people should discuss and decide whether to include it. The extraction of the included literature information was carried out by two researchers, respectively. If the opinions were not unanimous, they would discuss them together or seek the help of the relevant third-party experts. The basic research information to be collected was as follows: author, country and publication time, sample size, and original data (true positive, false positive, true negative, false negative, sensitivity, and specificity) [9].

The literature quality evaluation was strictly assessed based on the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) [10]. This tool mainly evaluates the risk bias of literature from four aspects: patient selection, index test, reference standard, and flow of patients through the study and timing of the index tests and reference standard.

Statistical analysis

Statistical analyses were performed with commercial software programs (STATA, version15.0; College Station, TX, USA). The risk bias of the literature was assessed by Review Manager 5.3 (The Cochrane Collaboration, Copenhagen, Denmark).The corresponding data were combined by software programs, including the sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR). The area under the summary receiver operating characteristic (SROC) curve (AUC) is obtained to reveal pooled diagnostic accuracy [11]. The I^2 test was used to evaluate the heterogeneity among the included studies. We used the binary mixed-effect models to evaluate the diagnostic performance indicators. Publication Bias was performed by Deeks' funnel plot [12].$P<0.05$ was considered statistically significant.

Results

Study selection and characteristics of eligible studies

The detailed process of study selection was performed for this meta-analysis (Figure 1). A total of 3,544 studies were retrieved in the primary literature search, of which 466 records of duplicated studies were excluded after reviewing abstracts. After 2,503 non-relevant studies, 152 conference abstracts, 125 review articles, 121 case reports, 11 notes, 97 editorials, 73 letters, and so on were excluded, the rest of the 28 full-text studies were assessed for eligibility. After inclusion and exclusion,13 studies with insufficient data for calculation of sensitivity and specificity were excluded and finally, 25 studies were selected in qualitative synthesis [13-38]. The characteristics of eligible studies are presented in Table 1. A total of 2,458 patients with an average of 4.28 lesion yields per patient were involved in this study.

Quality assessment of eligible studies

We evaluated the study quality by using the Quality Assessment of Diagnostic Accuracy Studies included in Systematic Reviews (QUADAS-2) (Figure 2A, B). Among the 25 included studies, there were 7 prospective studies [13-19] and 18 retrospective studies [20-38]. All trials scan were performed at breath holding with the same reconstruction algorithm. All of the studies were supported by the pathological examination. The reviewers carried out the PET/CT image reading without knowing the result of the pathological examination in 20 studies. All trials reported the gender ratio, age range, or average age of patients, as well as the type of primary lesion.

In 11 studies, patient selection was judged to have a high bias risk, and the bias risk of the remaining 14 studies was low or unclear. Most of the selected studies did not provide information on continuous enrolment. For the index test, 8 articles displayed high risk, and 17 articles presented moderate or low risk. For reference standards, common weaknesses focused on the fact that there is no blind method in interpreting the results. With regard to the flow and timing, 16 articles displayed low risk of bias. Overall, the quality of the included studies was satisfactory.

Diagnostic accuracy of PET/CT in NSCLC

The forest plot was conducted for the diagnostic performance of PET/CT in predicting lymph node metastasis of NSCLC patients (Figure 3). The pooled sensitivity of PET/CT was 0.68 (95%CI: 0.61-0.75), with heterogeneity significant (I^2=88.88, $P<0.05$). The combined specificity was 0.93 (95% CI: 0.89-0.95), with heterogeneity obvious (I^2=97.36, $P<0.05$). The combined DOR was 28 (95%CI: 19-40), the SROC

curve showing an AUC of 0.88 (95%CI: 0.84-0.90) (Figure 4).

Evaluation of the clinical utility

The likelihood ratio scatter gram was constructed for the diagnostic utility of PET/CT in NSCLC (Figure 5). The result displayed the summary likelihood ratio (LR) for PET/CT test was located in the lower right quadrant. Likelihood ratio synthesis gave an overall PLR of 9.4 (95%CI: 56.3-13.9), and NLR of 0.34 (95%CI: 0.28-0.41).

Publication bias

We performed Deeks' funnel plot asymmetry tests to evaluate potential publication bias (Figure 6). The funnel plot showed that the graph was symmetric (P>0.05), indicating no significant publication bias.

Discussion

Surgical resection of the lesion is the preferred treatment method for patients with NSCLC at the present stage [39]. However, this kind of patient is prone to mediastinal lymph node metastasis. Therefore, accurate preoperative determination of metastases is important for accurate staging and rational surgical planning [40]. At present, the main non-invasive imaging diagnostic method for patients with NSCLC with mediastinal lymph node metastasis is chest CT, usually when the short diameter of the lymph node is more than 10mm [41]. Positron emission tomography/CT is an advanced imaging technology applied in clinics in recent years, which can realize the functional imaging of lesions [42], which enables functional imaging of lesions and integration of anatomical structural, and metabolic information of lesions [43]. At the same time, PET/CT can also provide the correlation between the size, density, and diameter of the patient's lymph nodes for clinical diagnosis [44], and clarify the specific metabolic status and accurate location of the lymph nodes. In the diagnosis of mediastinal lymph node metastasis, PET/CT is superior to CT or PET alone [45].Therefore, evidence-based data to predict the diagnosis of lymph node metastasis is expected to provide enough information before deciding whether to carry out lung function protection therapy.

In this study, a meta-analysis was used to summarize the results of PET/CT in the diagnosis of lymph node metastasis of NSCLC. A total of 25 studies with 2,458 patients were included. The pooled sensitivity, specificity, and 95%CI of the total effect size were 0.68 (95%CI; 0.6-0.75) and 0.93 (95%CI;

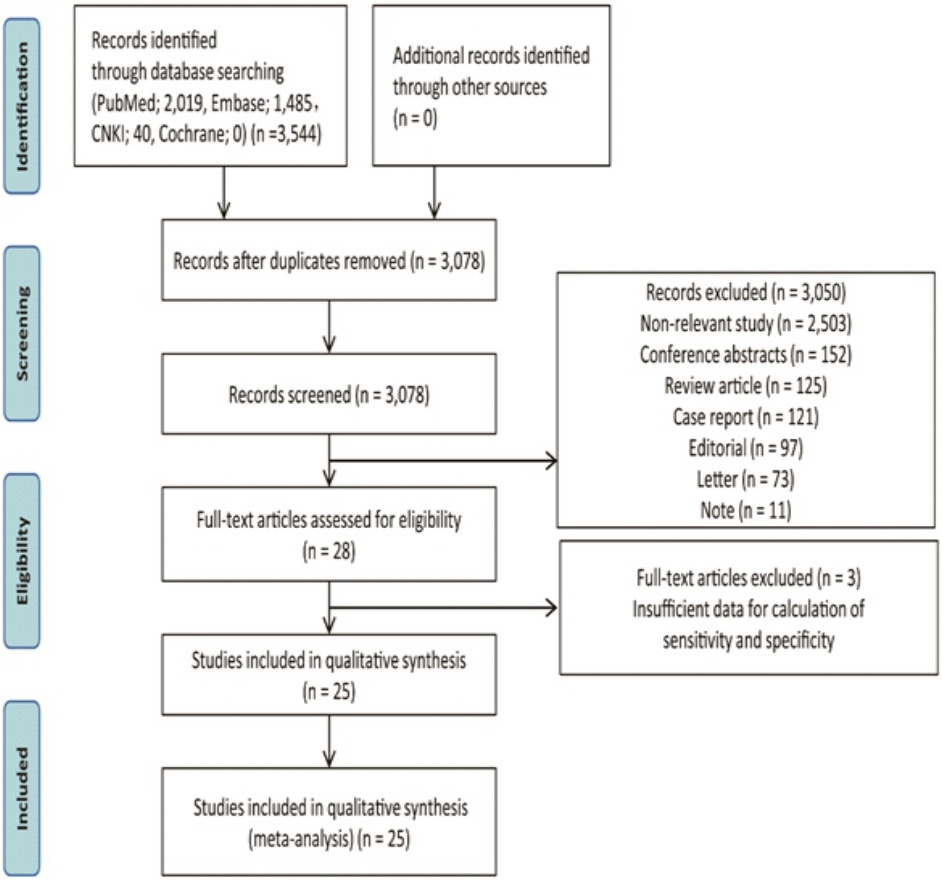


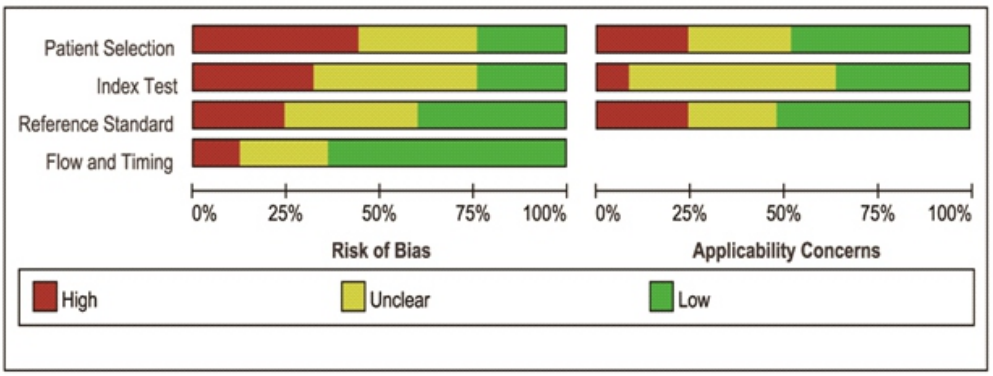
Figure 1. Flow chart of studies identified and included in the present meta-analysis.

Table 1. *The principal characteristics of included studies.*

Study	Year	Country	Study design	Conse-cutive	No. of patients and lesions	Tp	Fp	Fn	Tn	Sensi-tivity	Speci-ficity
Lee	2012	Korea	P	C	160/756	22	23	13	698	0.97	0.63
Ohno	2007	Japan	P	C	115/891	60	31	13	787	0.82	0.96
Sit, A	2010	China	R	ND	107/249	18	31	34	166	0.84	0.35
Tabo	2010	Japan	R	C	42/217	17	15	4	181	0.92	0.81
Hu	2008	China	R	ND	46/584	117	72	17	378	0.84	0.87
Yi	2007	Korea	R	ND	143/453	22	4	28	399	0.99	0.44
Shim	2005	Korea	P	C	106/393	28	58	5	302	0.84	0.85
Nomorl	2008	Japan	P	C	88/734	24	3	10	680	0.72	0.97
Tasci	2010	Turkey	R	ND	127/826	41	50	24	711	0.93	0.63
Jeon	2010	Korea	R	C	168/617	30	10	30	547	0.98	0.50
Morikawa	2009	Japan	P	C	93/137	74	19	8	36	0.65	0.90
Liu	2009	China	R	ND	39/208	40	24	26	120	0.83	0.61
Li	2012	China	R	C	80/265	33	7	18	207	0.97	0.65
Kuo	2012	China	R	C	102/118	12	25	9	72	0.74	0.57
Kim	2012	Korea	P	C	49/206	18	6	21	161	0.81	0.39
Usuda	2013	Japan	P	C	158/705	24	3	37	641	0.39	0.99
Xu	2014	China	R	C	101/528	52	18	49	409	0.96	0.51
Lee	2014	Korea	R	C	104/372	23	31	26	292	0.90	0.47
Zhou	2014	China	R	ND	64/280	25	9	9	237	0.96	0.74
Zhang	2016	China	R	C	167/731	143	26	61	501	0.95	0.70
Zhai	2020	China	R	C	41/93	37	4	19	18	0.66	0.82
Shi	2020	China	R	C	80/124	17	41	2	64	0.90	0.61
Wang	2020	China	R	C	160/670	58	138	14	460	0.80	0.77
Zhang	2018	China	R	C	46/92	17	13	6	56	0.74	0.81
Li	2018	China	R	C	72/280	130	42	16	92	0.89	0.82

ND: no documented; No.: number; TP: true positive; FP: false positive; FN: false negative; TN: true negative. P: prospective; R: retrospective; C: consecutive

A



B

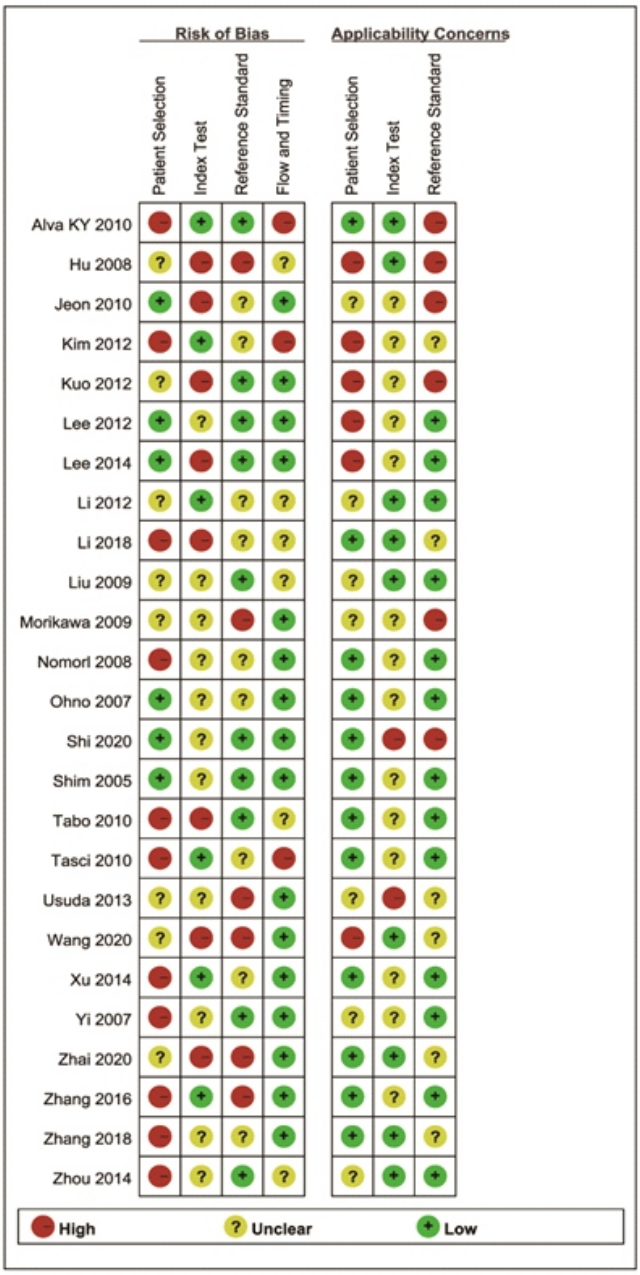


Figure 2. Literature quality assessment. A, Proportion of studies with low, high and moderate risks of bias and applicability concerns; B, Risk of bias and applicability concerns summary.?, represents moderate risk of bias.

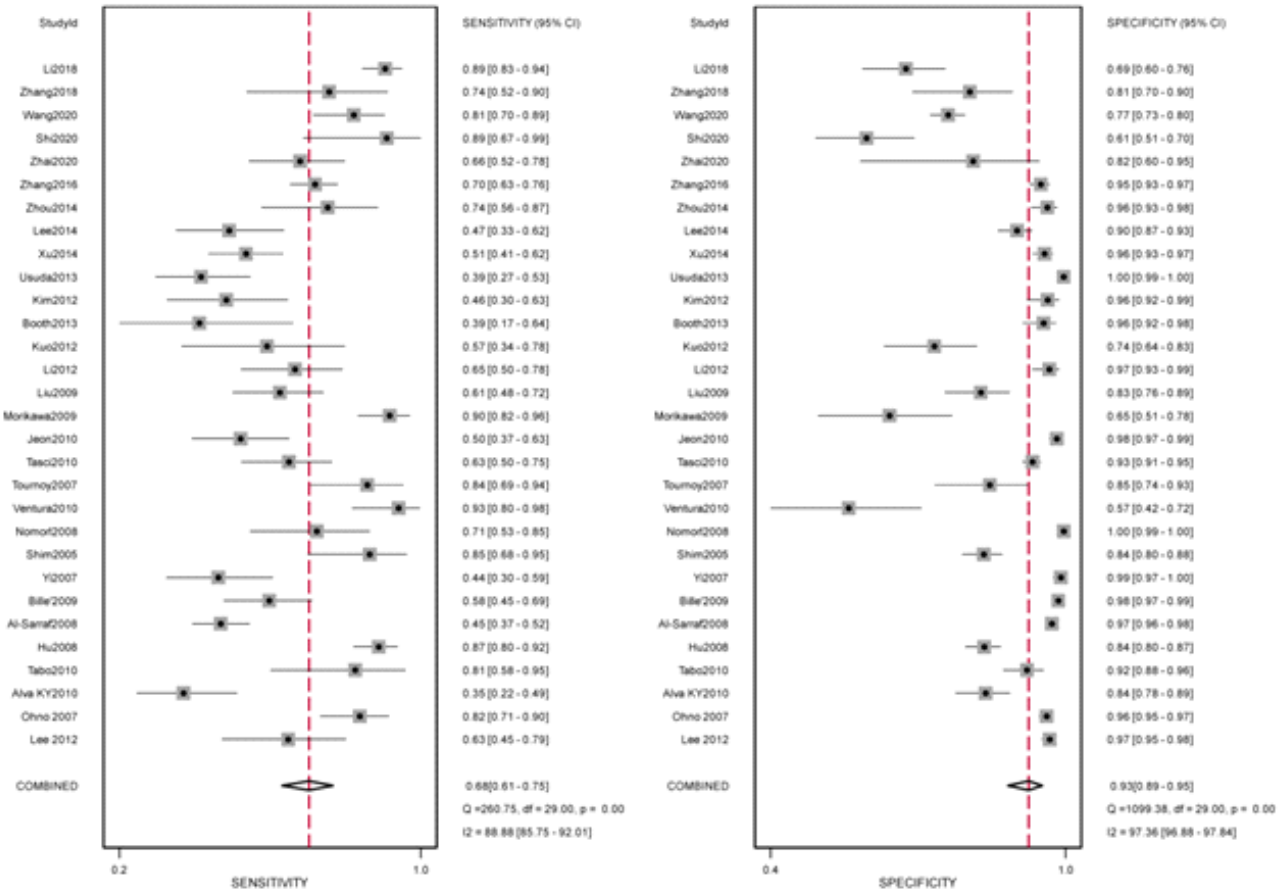


Figure 3. Forest plot of sensitivity and specificity for PET/CT. Each solid circle represents sensitivity and specificity of individual studies.

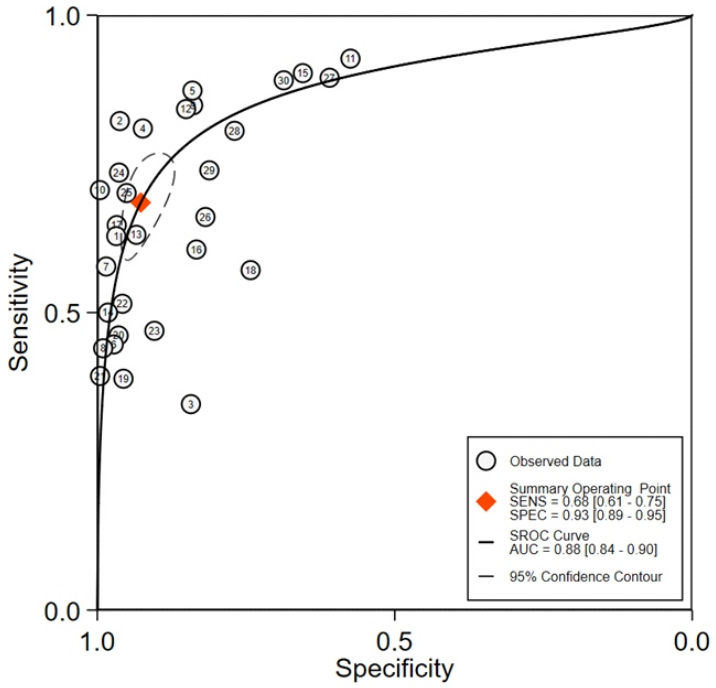


Figure 4. Hierarchical SROC curves of PET/CT for theprediction of lymph node metastasis in NSCLC patients.

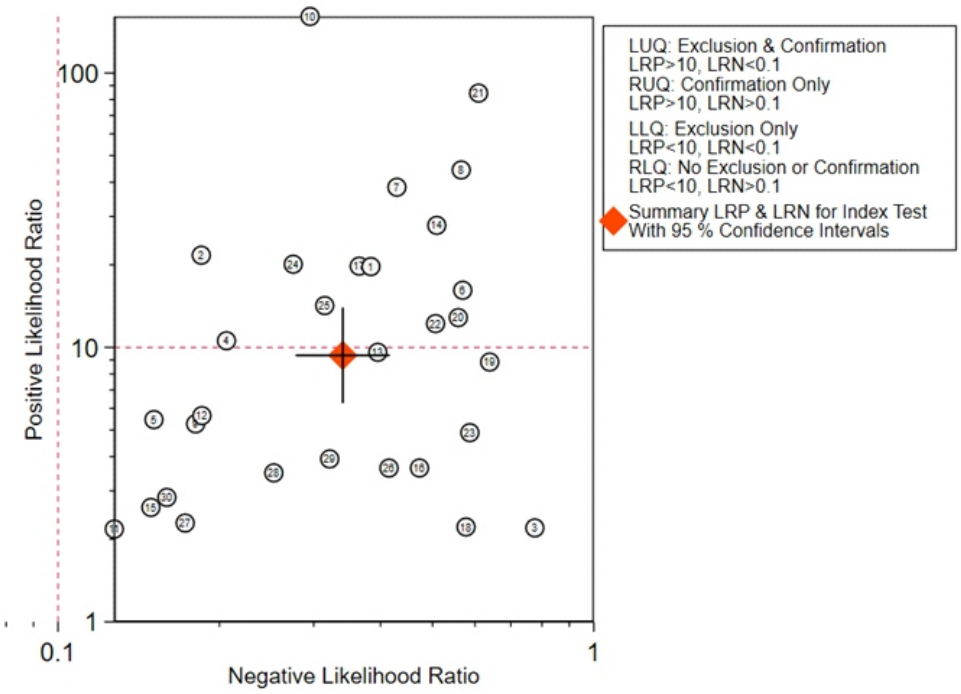


Figure 5. Likelihood ratio scattergram of PET/CT for the prediction of lymph node metastasis in NSCLC patients.

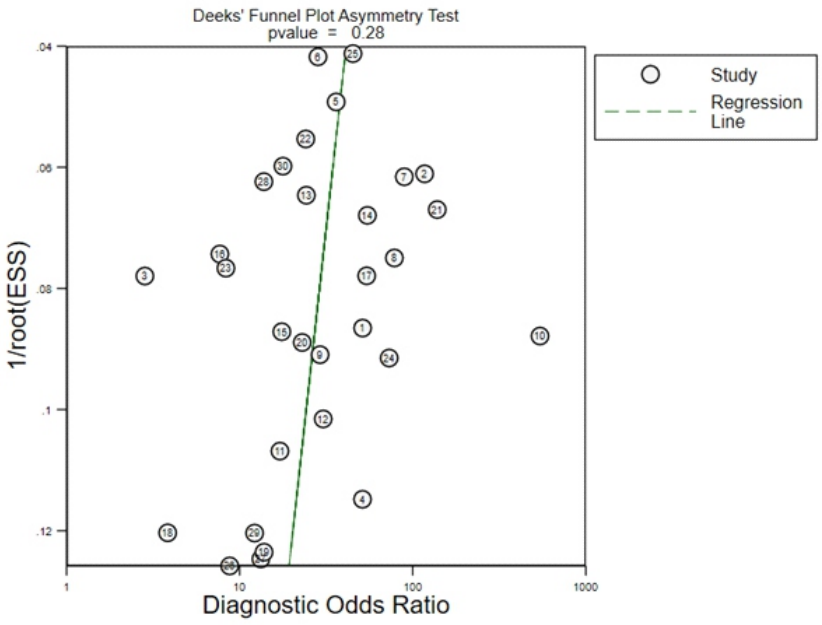


Figure 4. Hierarchical SROC curves of PET/CT for the prediction of lymph node metastasis in NSCLC patients.

(95%CI; 0.89-0.95) for lymphatic subjects, respectively, which meaning that PET/CT were helped detect lymph nodes metastases in NSCLC. Positron emission tomography/CT for the prediction performance of lymph node metastasis in NSCLC patients showed that the positive and negative likelihood ratios were 9.4 (95%CI; 6.3-13.9) and 0.34 (95%CI; 0.28-0.41), respectively. Since the AUC value is not affected by the prevalence rate, it can objectively and comprehensively reflect the relationship between sensitivity and specificity, truly reflect the value of diagnostic experiments, and comprehensively evaluate the accuracy of diagnostic experiments [11]. In this study, lymph node as the study object, AUC value and 95%CI were 0.88 (95%CI; 0.84-0.90), suggesting that PET/CT has high efficiency in the diagnosis of mediastinal lymph node metastasis of NSCLC.

Publication bias is another important factor affecting the results of meta-analysis, because positive or significant results are easier to publish, while insignificant or negative re-

sults are usually rejected [46]. In this study, Deeks' Funnel Plot test showed no publication bias, which further indicated that the results of this study were highly reliable.

However, there are still some limitations to this meta-analysis. Firstly, the design methods used in the study are not uniform, with both retrospective and prospective studies. Secondly, equipment models and processing software are different. Thirdly, the sampling method of positive lymphatic biopsy. Fourthly, the SUV values of PET/CT are different in imaging diagnosis standards. Given the above influencing factors, the random effect model was selected in the statistical method of this study, and the influence of variance inhomogeneity among studies was considered to improve the credibility of the summary results.

In conclusion, PET/CT has a good diagnostic value for the lymph node metastasis of NSCLC, which can be used as one of the main imaging diagnosis methods for lymph node metastasis in patients with NSCLC. Positron emission tomography/CT provides an important basis for the diagnosis of lymph node metastasis of NSCLC, and also provides a basis for the choice of the treatment scheme, which has high clinical application value.

The authors declare that they have no conflicts of interest.

Bibliography

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin* 2020; 70: 7-30.
2. Seol HY, Kim YS, Kim SJ. Predictive Value of ^{18}F-Fluorodeoxyglucose Positron Emission Tomography or Positron Emission Tomography/Computed Tomography for Assessment of Occult Lymph Node Metastasis in Non-Small Cell Lung Cancer. *Oncology* 2021; 99: 96-104.
3. Pak K, Park S, Cheon GJ et al. Update on nodal staging in non-small cell lung cancer with integrated positron emission tomography/computed tomography: a meta-analysis. *Ann Nucl Med* 2015; 29: 409-19.
4. Schmoll HJ, Jordan K, Huddart R et al. Testicular seminoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2010; 21 Suppl 5: v140-6.
5. Field JK, Oudkerk M, Pedersen JH, Duffy SW. Prospects for population screening and diagnosis of lung cancer. *Lancet* 2013; 382: 732-41.
6. Wu LM, Xu JR, Gu HY et al. Preoperative mediastinal and hilar nodal staging with diffusion-weighted magnetic resonance imaging and fluorodeoxyglucose positron emission tomography/computed tomography in patients with non-small-cell lung cancer: which is better? *J Surg Res* 2012; 178: 304-14.
7. Matoba M, Tonami H, Kondou T et al. Lung carcinoma: diffusion-weighted mr imaging--preliminary evaluation with apparent diffusion coefficient. *Radiology* 2007; 243: 570-7.
8. 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: 882-93.
9. Reitsma JB, Glas AS, Rutjes AW et al. Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *J Clin Epidemiol* 2005; 58: 982-90.
10. Whiting PF, Rutjes AW, Westwood ME et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011; 155: 529-36.
11. Rutter CM, Gatsonis CA. A hierarchical regression approach to meta-analysis of diagnostic test accuracy evaluations. *Stat Med* 2001; 20: 2865-84.
12 Lijmer JG, Mol BW, Heisterkamp S et al. Empirical evidence of design-related bias in studies of diagnostic tests. *JAMA* 1999; 282: 1061-6.
13 Lee SM, Park CM, Paeng JC et al. Accuracy and predictive features of ^{18}F-FDG-PET/CT and CT for diagnosis of lymph node metastasis of T1 non-small-cell lung cancer manifesting as a subsolid nodule. *Eur Radiol* 2012; 22: 1556-63.
14. Ohno Y, Koyama H, Nogami M et al. STIR turbo SE MR imaging vs. co-registered ^{18}F-FDG-PET/CT: quantitative and qualitative assessment of N-stage in non-small-cell lung cancer patients. *J Magn Reson Imaging* 2007; 26: 1071-80.
15 Shim SS, Lee KS, Kim BT. Non-small cell lung cancer prospective comparison of integrated ^{18}F-FDG PET/CT and CT alone for preoperative staging. *Radiology* 2005; 236: 1011-9.
16. Nomori H, Mori T, Ikeda K et al. Diffusion-weighted magnetic resonance imaging can be used in place of positron emission tomography for N staging of non-small cell lung cancer with fewer false-positive results. *J Thorac Cardiovasc Surg* 2008; 135: 816-22.
17. Usuda K, Sagawa M, Motono N et al. Advantages of diffusion-weighted imaging over positron emission tomography-computed tomography in assessment of hilar and mediastinal lymph node in lung cancer. *Ann Surg Oncol* 2013; 20: 1676-83.
18. Morikawa M, Demura Y, Ishizaki T et al. The effectiveness of ^{18}F-FDG PET/CT combined with STIR MRI for diagnosing nodal involvement in the thorax. *J Nucl Med* 2009; 50: 81-7.
19. Kim YN, Yi CA, Lee KS et al. A proposal for combined MRI and PET/CT interpretation criteria for preoperative nodal staging in non-small-cell lung cancer. *Eur Radiol* 2012; 22: 1537-46.
20. Sit AK, Sihoe AD, Suen WS, Cheng LC. Positron-emission tomography for lung cancer in a tuberculosis-endemic region. *Asian Cardiovasc Thorac Ann* 2010; 18: 33-8.
21. Hu M, Yu J, Sun X et al. Significance of Dual-time-point ^{18}F-FDG PET/CT Imaging in Evaluation of Hilar and Mediastinal Lymph Node Metastasis in Non-small Cell Lung Cancer. *Intern J Radiat Oncol Biol Phys* 2008; 72: S436-S7.
22. Kuo WH, Wu YC, Wu CY et al. Node/aorta and node/liver SUV ratios from ^{18}F-FDG PET/CT may improve the detection of occult mediastinal lymph node metastases in patients with non-small cell lung carcinoma. *Acad Radiol* 2012; 19: 685-92.
23. Lee AY, Choi SJ, Jung KP et al. Characteristics of Metastatic Mediastinal Lymph Nodes of Non-Small Cell Lung Cancer on Preoperative ^{18}F-FDG PET/CT. *Nucl Med Mol Imaging* 2014; 48: 41-6.
24. Li H. The differential value of ^{18}F-FDG PET /CT to N2 mediastinal lymph nodes in NSCLC. *Mod Oncol* 2018; 27: 1093-43.
25. Li M, Wu N, Liu Y et al. Regional nodal staging with ^{18}F-FDG PET/CT in non-small cell lung cancer: Additional diagnostic value of CT attenuation and dual-time-point imaging. *Eur J Radiol* 2012; 81: 1886-90.
26. Liu B, Dong J. Accuracy of ^{18}F-FDG PET/CT for lymph mode metastasis in non-small-cell lung cancers. *Chin Med J* 2009; 122: 1749-54.
27. Shi YM, Niu R, Shao XL et al. Tumor-to-liver standard uptake ratio using fluorine-18 fluorodeoxyglucose positron emission tomography computed tomography effectively predict occult lymph node metastasis of non-small cell lung cancer patients. *Nucl Med Commun* 2020; 41: 459-68.
28. Tasci E, Tezel C, Orki A et al. The role of integrated positron emission tomography and computed tomography in the assessment of nodal spread in cases with non-small cell lung cancer. *Interact Cardiovasc Thorac Surg* 2010; 10: 200-3.
29. Toba H, Kondo K, Otsuka H. Diagnosis of the presence of lymph node metastasis and decision of operative indication using fluorodeoxyglucose-positron emission tomography and computed tomography in patients with primary lung cancer. *J Med Invest* 2010; 57: 305-10.
30. Tournoy KG, Maddens S, Gosselin R et al. Integrated ^{18}F-FDG-PET/CT does not make invasive staging of the intrathoracic lymph nodes in non-small cell lung cancer redundant: a prospective study. *Thorax* 2007; 62: 696-701.
31. Ventura E, Islam T, Gee MS et al. Detection of nodal metastatic disease in patients with non-small cell lung cancer: comparison of positron emission tomography (PET), contrast-enhanced computed tomography (CT), and combined PET-CT. *Clin Imaging* 2010; 34: 20-8.
32. Wang S, Lin D, Yang X et al. Clinical significance of PET/CT uptake for peripheral clinical N0 non-small cell lung cancer. *Cancer Med* 2020; 9: 2445-53.
33. Xu., Wang M. Integrated positron emission tomography and computed tomography in preoperative lymph mode metastasis of non-small cell lung cancer. *Chin Med J (Engl)* 2014; 124: 607-13.
34. Yi CA, Lee KS, Kim BT et al. Efficacy of helical dynamic CT versus integrated PET/CT for detection of mediastinal nodal metastasis in non-

small cell lung cancer. *Am J Roentgenol* 2007; 188: 318-25.
35. Zhai X, Guo Y, Qian X. Combination of Fluorine-18 Fluorodeoxyglucose Positron-Emission Tomography/Computed Tomography (^{18}F-FDG PET/CT) and Tumor Markers to Diagnose Lymph Node Metastasis in Non-Small Cell Lung Cancer (NSCLC): A Retrospective and Prospective Study. *Med Sci Monit* 2020; 26: e922675.
36. Zhang W, Deng B. Value of ^{18}F-FDG PET/CT for diagnosis of lymphatic metastasis in patients with non-small cell lung cancer. *J Reg Anat Oper Surg* 2016; 25: 184-7.
37. Zhang Y. Value of metabolism by using ^{18}F-FDG PET/CT of NSCLC primary tumor in prediction of lymph node metastasis. *Chin J Cancer Prevent Treatment* 2018; 25: 816-20.
38. Zhou Y. Clinical Value of ^{18}F-FDG PET-CT Imaging in the Preoperative Diagnosis and Staging of Regional Lymph Nodes in Non-small Cell Lung Cacer. *Chin J CT MRI* 2014; 12: 56-60.
39. Nasim F, Sabath BF, Eapen GA. Lung Cancer. *Med Clin North Am* 2019; 103: 463-73.
40. Fujikawa A, Takiguchi Y, Mizuno S et al. Lung cancer screening--comparison of computed tomography and X-ray. *Lung Cancer* 2008; 61: 195-201.
41. Kondo R, Yoshida K, Kawakami S et al. Efficacy of CT screening for lung cancer in never-smokers: analysis of Japanese cases detected using a low-dose CT screen. *Lung Cancer* 2011; 74: 426-32.
42. Groheux D, Quere G, Blanc E et al. ^{18}F-FDG PET-CT for solitary pulmonary nodule and lung cancer: Literature review. *Diagn Interv Imaging* 2016; 97: 1003-17.
43. Teramoto A, Yamada A, Tsukamoto T et al. Decision Support System for Lung Cancer Using PET/CT and Microscopic Images. *Adv Exp Med Biol* 2020; 1213: 73-94.
44. Kandathil A, Sibley RC, III, Subramaniam RM. Lung Cancer Recurrence: ^{18}F-FDG PET/CT in Clinical Practice. *Am J Roentgenol* 2019; 213: 1136-44.
45. Kandathil A, Kay FU, Butt YM et al. Role of ^{18}F-FDG PET/CT in the Eighth Edition of TNM Staging of Non-Small Cell Lung Cancer. *Radiographics* 2018; 38: 2134-49.
46. Lin L, Chu H. Quantifying publication bias in meta-analysis. *Biometrics* 2018; 74: 785-94.
47. Jeon TY, Lee KS, Yi CA et al. Incremental value of PET/CT Over CT for mediastinal nodal staging of non-small cell lung cancer: Comparison between patients with and without idiopathic pulmonary fibrosis. *Am J Roentgenol* 2010; 195: 370-6.