



# Head-to-head comparison of $^{18}\text{F}$ -FDG PET/CT and $^{18}\text{F}$ -FDG PET/MRI for lymph node metastasis staging in non-small cell lung cancer: a meta-analysis

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## PURPOSE

The current meta-analysis aimed to compare the diagnostic performance of  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography/computed tomography ( $^{18}\text{F}$ -FDG PET/CT) with  $^{18}\text{F}$ -FDG PET/magnetic resonance imaging (MRI) in non-small cell lung cancer (NSCLC) lymph node metastasis staging.

## METHODS

We searched the PubMed, Web of Science, and Embase databases for relevant articles between November 1992 and September 2022. Studies evaluating the head-to-head comparison of  $^{18}\text{F}$ -FDG PET/CT and  $^{18}\text{F}$ -FDG PET/MRI for lymph node metastasis in patients with NSCLC were included. The quality of each study was assessed using the Quality Assessment of Diagnostic Performance Studies-2 tool.

## RESULTS

The analysis includes six studies with a total of 434 patients. The pooled sensitivity of  $^{18}\text{F}$ -FDG PET/CT and  $^{18}\text{F}$ -FDG PET/MRI was 0.78 [95% confidence interval (CI): 0.59–0.90] and 0.84 (95% CI: 0.68–0.93), and the pooled specificity was 0.87 (95% CI: 0.72–0.94) and 0.87 (95% CI: 0.80–0.92), respectively. The accuracy of  $^{18}\text{F}$ -FDG PET/CT and  $^{18}\text{F}$ -FDG PET/MRI was 0.81 (95% CI: 0.71–0.90) and 0.84 (95% CI: 0.75–0.92), respectively. When the pre-test probability was set at 50%, the post-test probability for  $^{18}\text{F}$ -FDG PET/CT could increase to 85%, and the post-test probability for  $^{18}\text{F}$ -FDG PET/MRI could increase to 87%.

## CONCLUSION

$^{18}\text{F}$ -FDG PET/CT and  $^{18}\text{F}$ -FDG PET/MRI have similar diagnostic performance in detecting lymph node metastasis in NSCLC. However, the results of this study were from a small sample study, and further studies with larger sample sizes are needed.

## KEYWORDS

$^{18}\text{F}$ -FDG PET/CT,  $^{18}\text{F}$ -FDG PET/MRI, lymph node metastasis, non-small cell lung cancer, meta-analysis

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Received 27 April 2023; revision requested 05 June 2023; last revision received 31 July 2023; accepted 16 October 2023.



Epub: 31.01.2024

Publication date: 05.03.2024

DOI: 10.4274/dir.2023.232280

According to the 2020 global cancer incidence and mortality statistics of the Global Cancer Observatory database, lung cancer has the highest mortality rate (approximately 18% of all cancer deaths) and the second highest incidence rate (approximately 11.4% of all new cancer cases).<sup>1</sup> The most common type of lung cancer is non-small cell lung cancer (NSCLC), which accounts for approximately 80% of all lung cancers.<sup>2,3</sup> The assessment of distant metastases and metastases to mediastinal lymph nodes in patients with NSCLC is critical not only for providing information about the staging of the disease but also for guiding treatment options and determining the patient's prognosis.<sup>4,5</sup>

Although computed tomography (CT) is the most-used non-invasive modality for assessing mediastinal staging in NSCLC, numerous studies have shown that CT has limited sensi-

tivity and reliability in lymph node staging.<sup>6-8</sup> <sup>18</sup>F-fluorodeoxyglucose positron emission tomography/CT (<sup>18</sup>F-FDG-PET) has been widely used to evaluate NSCLC over the last decade, as it can distinguish malignant isolated pulmonary nodules from benign lesions, improve staging accuracy, and anticipate histology, treatment response, and prognosis.<sup>9</sup> <sup>18</sup>F-FDG PET/magnetic resonance imaging (MRI) is a hybrid imaging modality. It provides useful information about metabolic activity as well as tumor cells while reducing radiation exposure and is now increasingly used in the diagnosis of NSCLC.<sup>10</sup> Kajiyama et al.<sup>11,12</sup> showed that both <sup>18</sup>F-FDG PET/CT and <sup>18</sup>F-FDG PET/MRI had more accurate pathological staging results than CT in the diagnosis of hilar and mediastinal lymph node metastases in NSCLC.

Over the past decade, radionuclide imaging techniques, including PET/CT and PET/MRI, have been widely used in the diagnosis of NSCLC and have gained much attention for their better diagnostic performance, compared with CT. However, which diagnostic tool has better diagnostic performance remains controversial. According to one report, PET/MRI may have advantages over PET/CT in terms of radiation dose management and local staging accuracy when evaluating thoracic tumors,<sup>10</sup> whereas another study demonstrated that PET/MRI and PET/CT have equivalent performance when it comes to evaluating the preoperative thoracic staging of NSCLC patients.<sup>13</sup>

Although many studies have reported that <sup>18</sup>F-FDG PET/CT performs well in assessing lymph node metastasis staging in NSCLC, few have quantified its performance in comparison with <sup>18</sup>F-FDG PET/MRI. The purpose

of the current study was to include head-to-head comparison articles comparing the diagnostic efficacy of the two diagnostic modalities for the staging of lymph node metastasis in NSCLC.

## Methods

### Search strategy

All available literature was searched in the PubMed, Embase, and Web of Science databases between November 1992 and September 2022. The keywords were based on the following: (Carcinoma, Non Small Cell Lung) OR (Carcinomas, Non-Small-Cell Lung) OR (Lung Carcinoma, Non-Small-Cell) OR (Lung Carcinomas, Non-Small-Cell) OR (Non-Small-Cell Lung Carcinomas) OR (Non-Small-Cell Lung Carcinoma) OR (Non Small Cell Lung Carcinoma) OR (Nonsmall Cell Lung Cancer) OR (Non-Small Cell Lung Cancer) OR (NSCLC) OR ("Carcinoma, Non-Small-Cell Lung"[Mesh]) AND (PET-MRI) OR (positron emission tomography/magnetic resonance imaging) OR (PET-MR) OR (positron emission tomography/magnetic resonance).

### Inclusion and exclusion criteria

Studies were considered for inclusion if all the following criteria were satisfied: (a) patients with NSCLC who were evaluated for N-stage cancer before starting treatment; (b) head-to-head comparison of <sup>18</sup>F-FDG PET/CT and <sup>18</sup>F-FDG PET/MRI; (c) retrospective or prospective original research.

The exclusion criteria were (a) duplicated articles; (b) abstract, case reports, letters, reviews, or meta-analyses; (c) non-English full-text articles; (d) irrelevant titles and abstracts; (e) data unavailable; (d) lesion-based studies.

Two researchers independently reviewed the remaining texts' titles and abstracts, as well as the full-text versions, to determine their eligibility for inclusion in the next stage using the aforementioned inclusion and exclusion criteria. The two researchers resolved disagreements by reaching a consensus.

### Quality assessment

The two researchers independently used the Quality Assessment of Diagnostic Performance Studies-2 (QUADAS-2) tool to evaluate the quality of each study.<sup>14</sup> The following criteria were used to evaluate each study: patient selection, index test, reference standard, flow, and timing. Based on the bias risk, these domains were then classified as high, low, or uncertain in terms of applicability. Disagreements that arose during the evalu-

ation process were resolved by a third-party researcher.

### Data extraction

Data extracted for all included articles included first author, year, country, study design (retrospective or prospective study), patient characteristics (sample size, mean age), study period, interval between the <sup>18</sup>F-FDG PET/CT and <sup>18</sup>F-FDG PET/MRI scans, and reference for lymph node metastasis of NSCLC. The numbers of true-positive, true-negative, false-positive, and false-negative results for <sup>18</sup>F-FDG PET/CT and <sup>18</sup>F-FDG PET/MRI on a patient-by-patient basis were also extracted for each study. In addition, data were extracted on technical aspects of each study including scanner modality, ligand dose, and image analysis. All the above data extraction was done independently by two researchers, and any differences were resolved through consensus. This analysis did not require ethics committee or patient approval.

### Statistical analysis

The heterogeneity of the threshold effect among pooled studies was assessed using the Spearman correlation coefficient. A value of  $P < 0.05$  indicated a statistically significant threshold effect. A bivariate random effects model was used to calculate pooled estimates of sensitivity and specificity. A Fagan diagram was used to evaluate the pre-test and post-test probabilities of the testing tool.

The heterogeneity of non-threshold effects among pooled studies was assessed using inconsistency index ( $I^2$ ) statistics and the Cochran Q test. A value of  $I^2 > 50\%$  or  $P < 0.1$  for the Cochran Q test indicated a statistically significant non-threshold effect. Due to the small number of included studies, sensitivity analysis was performed, rather than meta-regression or subgroup analysis.

A Deeks' funnel plot was used to evaluate the publication bias of the included studies. A  $P$  value of  $< 0.05$  was deemed to indicate publication bias. The statistical analysis was performed using STATA v15.1 (Stata-Corp, College Station, TX, USA, Review Manager v5.4 (the Nordic Cochrane Centre, Copenhagen, Denmark) and MetaDisc v1.4.

## Results

### Literature search and study selection

The literature search led to the initial identification of 460 publications. Ninety-three duplicate studies were excluded, 281 studies were excluded by title and abstract, and

### Main points

- Our meta-analysis showed that <sup>18</sup>F-fluorodeoxyglucose positron emission tomography/computed tomography (<sup>18</sup>F-FDG PET/CT) has good diagnostic potential for non-small cell lung cancer (NSCLC) lymph node metastases, with a pooled sensitivity of 0.78 [95% confidence interval (CI): 0.59–0.90] and a pooled specificity of 0.87 (95% CI: 0.72–0.94).
- <sup>18</sup>F-FDG PET/magnetic resonance imaging (MRI) had a pooled sensitivity of 0.84 (95% CI: 0.68–0.93) and a pooled specificity of 0.87 (95% CI: 0.80–0.92), which had better diagnostic ability for lymph node metastasis in NSCLC.
- <sup>18</sup>F-FDG PET/CT and <sup>18</sup>F-FDG PET/MRI have similar diagnostic performance in detecting lymph node metastasis in NSCLC.

72 studies were excluded by article category (review, abstract, case report, meta-analysis). The remaining 14 studies were carefully assessed by full text, and were excluded for the following reasons: not meeting the inclusion criteria (n = 5); data unavailable (n = 3). Finally, 6 articles evaluating head-to-head comparison of <sup>18</sup>F-FDG PET/CT and <sup>18</sup>F-FDG PET/MRI for lymph node metastasis in patients with NSCLC were qualified for meta-analysis.<sup>15-20</sup> A PRISMA flow diagram of the study selection process is shown in Figure 1.

### Study description and quality assessment

The 6 eligible studies contained a total of 434 patients with NSCLC who were evaluated for N-stage cancer before starting treatment, were published between 2014 and 2020, and had a sample size ranging from 22 to 140. Table 1 summarizes the study and patient characteristics. The technical aspects of <sup>18</sup>F-FDG PET/CT and <sup>18</sup>F-FDG PET/MRI are shown in Table 2. The QUADAS-2 tool was used to assess the risk of bias in these studies, as shown in Figure 2. None of the studies had a “high” risk of bias, according to the QUADAS-2 suggestions. The included studies were deemed to be of adequate quality.

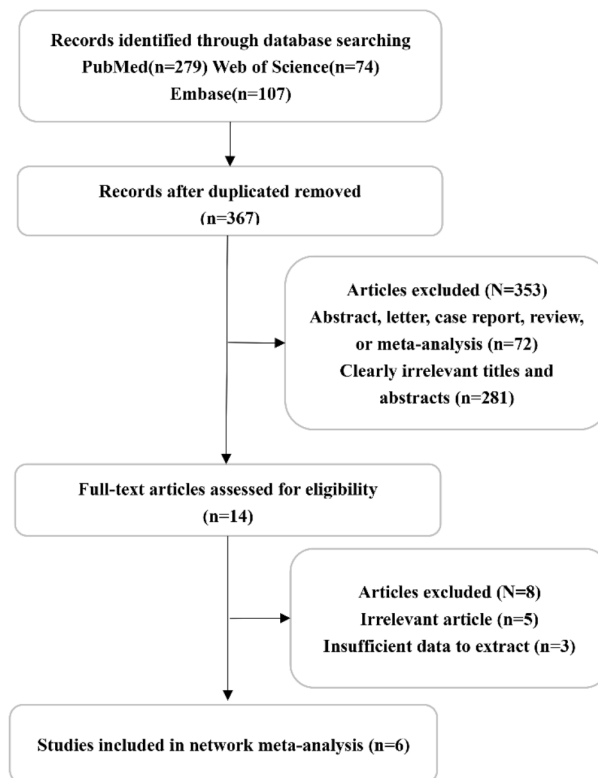


Figure 1. PRISMA flow diagram for study selection.

**Table 1.** Study characteristics and patient characteristics of the included studies

First author	Year	Country	Study design	Sample size (n)	Age (y) <sup>a</sup>	Study period	Interval between the two imaging tests	Reference standard	<sup>18</sup> F-FDG PET/CT				<sup>18</sup> F-FDG PET/MRI			
									TP	FP	FN	TN	TP	FP	FN	TN
Ohno et al. <sup>20</sup>	2020	Japan	Retro	104	71 ± 6.3 (43–85)	2014–2015	<3 wk	PA	23	3	18	60	33	8	8	55
Kirchner et al. <sup>19</sup>	2018	Germany	Pro	84	62.5 ± 9.1	NA	<1 d	PA	42	1	5	36	42	2	5	35
Lee et al. <sup>18</sup>	2016	Korea	Pro	42	62.9 ± 9.9 (35–79)	2013–2014	<1 h	PA	10	9	11	12	8	5	13	16
Huellner et al. <sup>17</sup>	2016	Switzerland	Retro	42	65 (35–89)	2012–2014	<1 h	PA	31	3	1	7	28	4	4	6
Ohno et al. <sup>16</sup>	2015	Japan	Retro	140	72 ± 7.4 (47–83)	2012–2013	<3 wk	PA	48	13	14	65	58	8	4	70
Heusch et al. <sup>15</sup>	2014	Germany	Pro	22	65 ± 9.1	NA	NA	PA	6	2	2	12	7	1	1	13

n, the numbers of patients included in the study; Retro, retrospective; Pro, prospective; <sup>a</sup>data are mean (range) or mean ± standard deviation (range); NA, not available; PA, pathology; TP, true positive; FP, false positive; FN, false negative; TN, true negative; <sup>18</sup>F-FDG PET/CT, <sup>18</sup>F-fluorodeoxyglucose positron emission tomography/computed tomography; MRI, magnetic resonance imaging.

**Table 2.** Technical aspects of included studies

First author	Year	Scanner modality (PET/CT)	Scanner modality (PET/MRI)	Ligand dose	Image analysis
Ohno et al. <sup>20</sup>	2020	GE Healthcare	Canon Medical Systems	3.3 MBq/kg	Quantitative
Kirchner et al. <sup>19</sup>	2018	Siemens, Healthcare GmbH, Erlangen, Germany	Siemens Healthcare GmbH, Erlangen, Germany	275.7 ± 47.4 MBq	Quantitative
Lee et al. <sup>18</sup>	2016	Siemens Healthcare, Erlangen, Germany	Siemens Medical Solutions, Knoxville, TN	5.2 MBq/kg	Quantitative
Huellner et al. <sup>17</sup>	2016	GE Healthcare, Waukesha, WI, USA	GE Healthcare, Waukesha, WI, USA	350 MBq	Quantitative
Ohno et al. <sup>16</sup>	2015	GE Healthcare, Milwaukee, Wis	Toshiba Medical Systems, Otawara, Japan	132–300 MBq	Quantitative
Heusch et al. <sup>15</sup>	2014	Siemens Molecular Imaging	Siemens Healthcare	300 ± 45 MBq	Quantitative

PET/CT, positron emission tomography/computed tomography; MRI, magnetic resonance imaging.

Quantitative synthesis

The analysis includes six studies with a total of 434 patients. For <sup>18</sup>F-FDG PET/CT, the results of the Spearman correlation coefficient demonstrated no threshold effect heterogeneity (Spearman correlation coefficient: -0.200; *P* = 0.704); the forest plot demonstrated a pooled sensitivity of 0.78 (95% CI: 0.59–0.90) and a pooled specificity of 0.87 (95% CI: 0.72–0.94); the heterogeneity results obtained by *I*<sup>2</sup> were 83.6% for sensitivity and 83.4% for specificity (Figure 3), which was statistically significant in both sensitivity and specificity (*I*<sup>2</sup> > 50%). The accuracy of <sup>18</sup>F-FDG PET/CT in diagnosing NSCLC lymph node metastasis was 0.81 (95% CI: 0.71–0.90). Furthermore, the Deeks' funnel plot of <sup>18</sup>F-FDG PET/CT revealed no publication bias in the included studies (*P* = 0.802) (Figure 4). The Fagan nomogram indicated that when the pre-test probability was set at 50%, the post-test probability for <sup>18</sup>F-FDG PET/CT could increase to 85% (Figure 5).

For <sup>18</sup>F-FDG PET/MRI, the results of the Spearman correlation coefficient demonstrated no threshold effect heterogeneity (Spearman correlation coefficient: -0.551; *P* = 0.257); the forest plot demonstrated a pooled sensitivity of 0.84 (95% CI: 0.68–0.93) and a pooled specificity of 0.87 (95% CI: 0.80–0.92); the heterogeneity results obtained by *I*<sup>2</sup> were 86.6% for sensitivity and 56.6% for specificity (Figure 6), which was statistically significant in both sensitivity and specificity (*I*<sup>2</sup> > 50%). The accuracy of <sup>18</sup>F-FDG PET/MRI in diagnosing NSCLC lymph node metastasis was 0.84 (95% CI: 0.75–0.92). Moreover, the Deeks' funnel plot of <sup>18</sup>F-FDG PET/MRI revealed no publication bias in the included studies (*P* = 0.310) (Figure 7). The Fagan nomogram indicated that when the pre-test probability was set at 50%, the post-test probability for <sup>18</sup>F-FDG PET/MRI could increase to 87% (Figure 8).

Heterogeneity analysis

For <sup>18</sup>F-FDG PET/CT and <sup>18</sup>F-FDG PET/MRI, the *I*<sup>2</sup> for their pooled sensitivity were 83.6% (*P* < 0.001) and 86.6% (*P* < 0.001), and for their pooled specificity were 83.4% (*P* < 0.001) and 56.6% (*P* = 0.042), respectively. This demonstrated that both <sup>18</sup>F-FDG PET/CT and <sup>18</sup>F-FDG PET/MRI had high heterogeneity. For <sup>18</sup>F-FDG PET/MRI, sensitivity analysis by excluding data from Lee et al.<sup>18</sup> demonstrated a pooled sensitivity of 0.88 (95% CI: 0.82–0.93), with acceptable heterogeneity (*I*<sup>2</sup> = 4.3%), and excluding data from Huellner et al.<sup>17</sup> showed a pooled specificity of 0.88 (95%

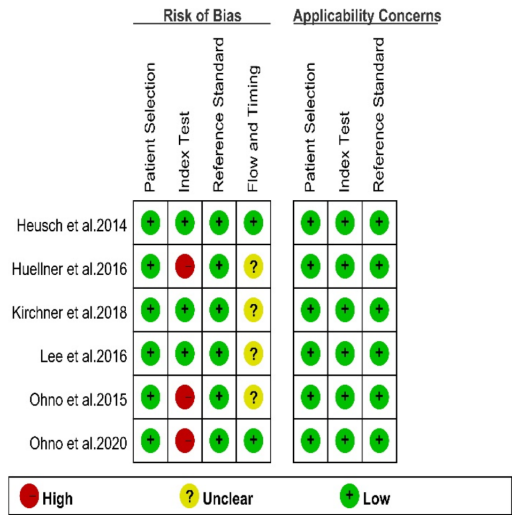


Figure 2. Summary risk of bias and applicability concerns of the included studies.

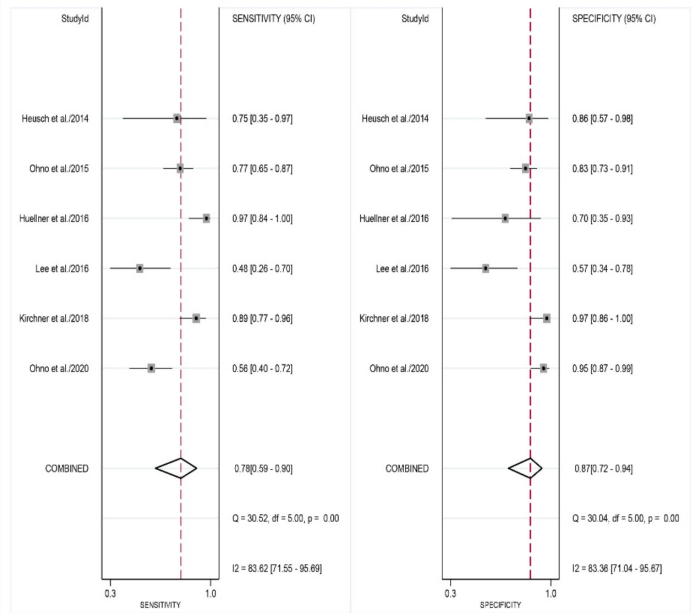


Figure 3. Forest plot showing the pooled sensitivity and specificity of <sup>18</sup>F-fluorodeoxyglucose positron emission tomography/computed tomography.

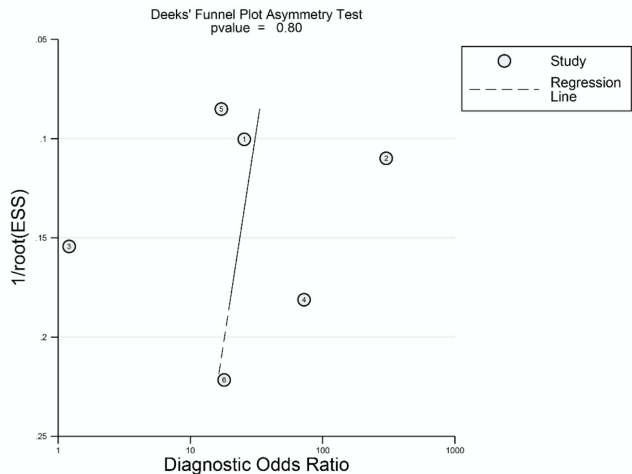


Figure 4. Deeks' funnel plot showing the publication bias of the included studies <sup>18</sup>F-fluorodeoxyglucose positron emission tomography/computed tomography.



CI: 0.81–0.93) with reasonable heterogeneity ( $I^2 = 20.8\%$ ). For  $^{18}\text{F}$ -FDG PET/CT, sensitivity analysis was unable to identify the source of heterogeneity. Table 3 shows all the results of the sensitivity analysis.

### Discussion

NSCLC has long been an issue of great importance to surgeons, as it is an important factor affecting and determining staging and prognosis.<sup>21</sup>  $^{18}\text{F}$ -FDG PET/CT is increasingly being used to diagnose NSCLC. Since CT can obtain anatomical information about tumor size and location, and FDG-PET can obtain metabolic information about the tissue, this gives  $^{18}\text{F}$ -FDG PET/CT a unique advantage in detecting lymph node metastases.<sup>22,23</sup> MRI has a greater ability to detect pleural and mediastinal involvement and a higher sensitivity to detect brain, liver, and bone metastases. Therefore,  $^{18}\text{F}$ -FDG-PET combined with  $^{18}\text{F}$ -FDG PET/MRI has also become the mainstream diagnostic tool for chest tumors in the past decade.<sup>24-26</sup>

To our knowledge, this is one of the few meta-analyses of a head-to-head comparison of  $^{18}\text{F}$ -FDG PET/CT and  $^{18}\text{F}$ -FDG PET/MRI to determine their performance in the diagnosis of lymph node metastasis in NSCLC. According to Kirchner et al.<sup>19</sup>,  $^{18}\text{F}$ -FDG PET/MRI and  $^{18}\text{F}$ -FDG PET/CT have comparable diagnostic performance for T- and N-staging in patients with NSCLC.<sup>19</sup> However, Laffon and Marthan<sup>27</sup> suggested that the equivalence between the two imaging techniques reported in the previous study could be due to experimental design, and they concluded that  $^{18}\text{F}$ -FDG PET/MRI has greater value for NSCLC chest staging and may even replace  $^{18}\text{F}$ -FDG PET/CT. Therefore, a meta-analysis was conducted to compare the performance of the two diagnostic modalities.

In this meta-analysis, we systematically reviewed and compared the ability of two imaging modalities in the detection of lymph node metastases in NSCLC. In the detection of lymph node metastasis in NSCLC, the pooled sensitivity of  $^{18}\text{F}$ -FDG PET/CT and  $^{18}\text{F}$ -FDG PET/MRI were 0.78 (95% CI: 0.59–0.90) and 0.84 (95% CI: 0.68–0.93), respectively. Sun et al.<sup>28</sup> reported a pooled sensitivity of 0.68 (95% CI: 0.61–0.75) and a pooled specificity of 0.93 (95% CI: 0.89–0.95) for PET/CT to diagnose lymph node metastasis in NSCLC in a current study. Furthermore, Seol et al.<sup>29</sup> showed the pooled sensitivity for  $^{18}\text{F}$ -FDG PET was 0.79 (95% CI: 0.70–0.86) and

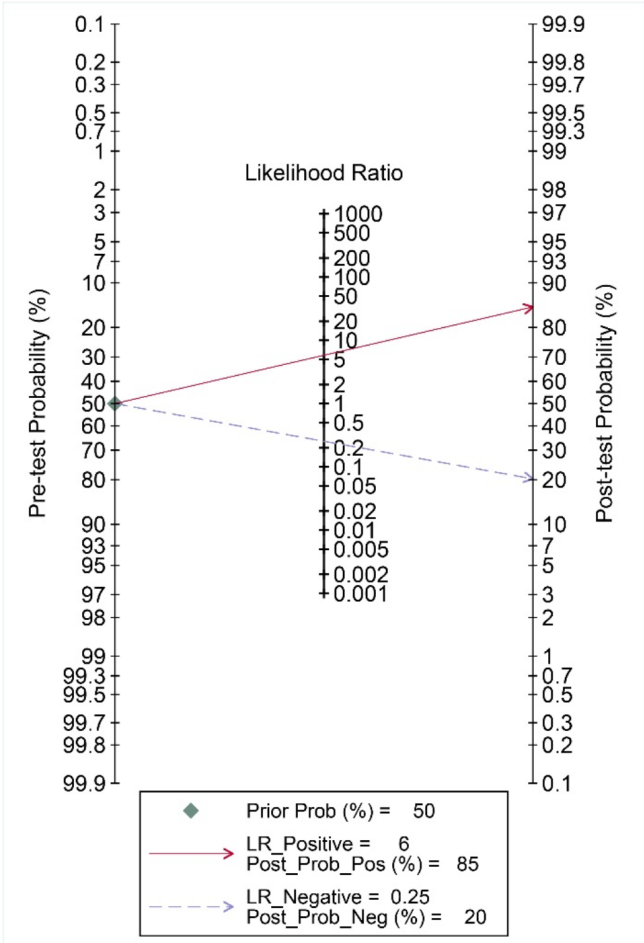


Figure 5. Fagan diagrams showing the pre-test and post-test probabilities of  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography/computed tomography.

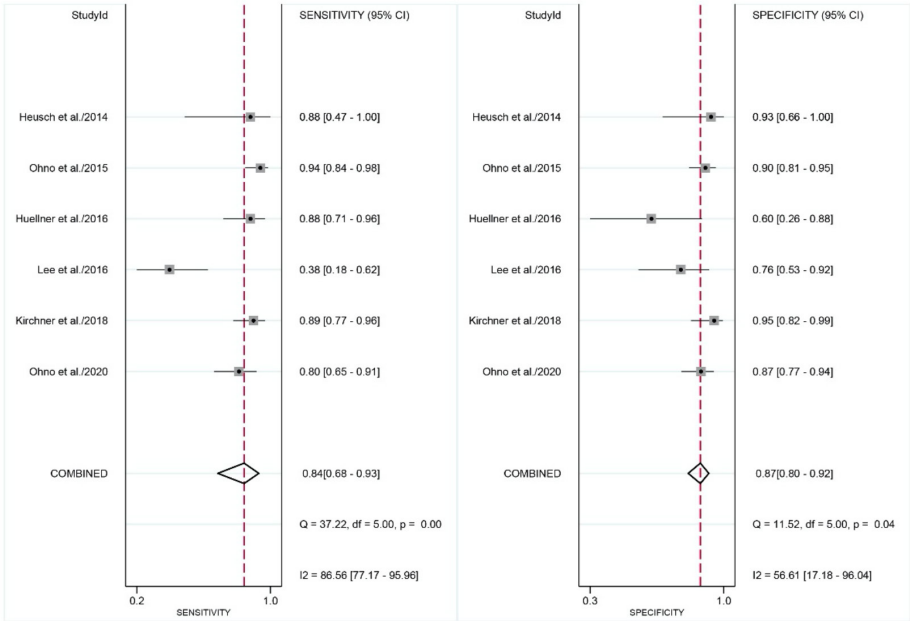
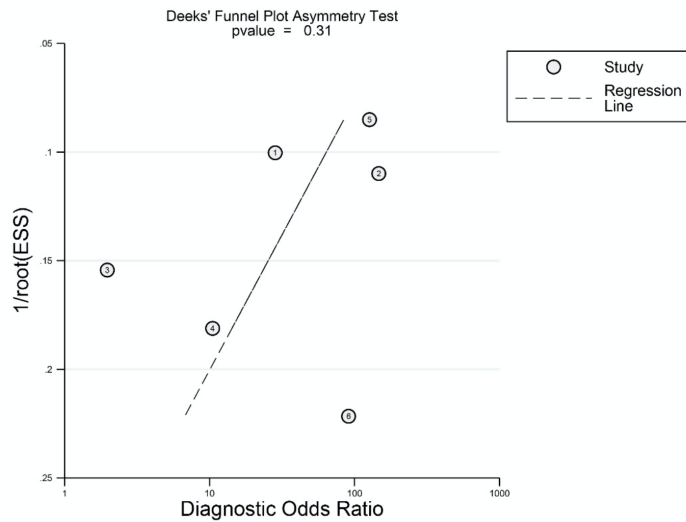
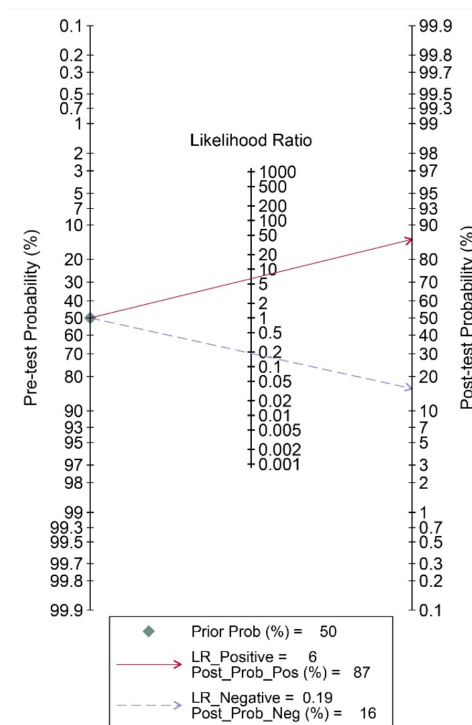


Figure 6. Forest plot showing the pooled sensitivity and specificity of  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography/magnetic resonance imaging.



**Figure 7.** Deeks' funnel plot showing the publication bias of the included studies of  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography/magnetic resonance imaging.



**Figure 8.** Fagan diagrams showing the pre-test and post-test probabilities of  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography/magnetic resonance imaging.

a pooled specificity of 0.65 (95% CI: 0.57–0.72) in their study. In terms of sensitivity, our meta-analysis did not differ significantly from previous studies, but it did show higher results in terms of specificity, which could be attributed to the small sample size of our included studies, which required the use of both detection tools in the same patient cohort.

Our meta-analysis showed that both  $^{18}\text{F}$ -FDG PET/CT and  $^{18}\text{F}$ -FDG PET/MRI have high diagnostic performance for lymph node metastases of NSCLC, and we believe that both diagnostic tools have the potential to be used more often in the clinic in the future. However, by reviewing other related studies, we also found that these two diagnostic tools have their shortcomings. There are two key limitations to PET CT: first, it involves a relatively high radiation exposure; second, it has relatively low spatial resolution.<sup>30</sup> The following are the primary drawbacks of PET MRI: compared with PET/CT, it needs a specific lung imaging procedure, and the examination is significantly more time-consuming;<sup>15</sup> however, it was introduced relatively recently and has not been studied extensively, and numerous pertinent studies and clinical trials will be required in the future to incorporate it into clinical practice.<sup>26</sup> In addition, it has been shown that both diagnostic tools have limited evaluation in the detection of microscopic nodules in the lung.<sup>31</sup> To produce novel and promising findings, more research comparing these two models head-to-head is required in the future.

In addition,  $^{18}\text{F}$ -FDG PET/MRI has been studied extensively as a novel diagnostic tool for applications in other diseases. A study of  $^{18}\text{F}$ FDG PET/MRI for the diagnosis of bladder cancer showed that it has a better ability to detect metastatic lesions as well as soft tissue lesions compared with conventional CT, thus allowing better differentiation between primary bladder tumors and pelvic metastases.<sup>32</sup> Another review of rectal cancer

**Table 3.** Sensitivity analysis of overall detection rate for  $^{18}\text{F}$ -FDG PET/CT and  $^{18}\text{F}$ -FDG PET/MRI

	$^{18}\text{F}$ -FDG PET/CT			$^{18}\text{F}$ -FDG PET/MRI				
	Sensitivity (95% CI)	$I^2$	Specificity (95% CI)	$I^2$	Sensitivity (95% CI)	$I^2$	Specificity (95% CI)	$I^2$
Omitting Ohno et al.	0.81 (0.63–0.91)	82.8%	0.84 (0.70–0.93)	78.5%	0.84 (0.64–0.94)	89.5%	0.87 (0.78–0.92)	64.8%
Omitting Kirchner et al. <sup>19</sup>	0.75 (0.52–0.89)	81.8%	0.82 (0.66–0.92)	79.9%	0.82 (0.61–0.93)	87.8%	0.85 (0.78–0.91)	53.0%
Omitting Lee et al. <sup>18</sup>	0.83 (0.65–0.92)	83.0%	0.89 (0.78–0.95)	72.7%	0.88 (0.82–0.93)	4.3%	0.89 (0.83–0.92)	59.4%
Omitting Huellner et al. <sup>17</sup>	0.71 (0.54–0.84)	78.9%	0.88 (0.72–0.96)	84.4%	0.83 (0.62–0.93)	88.7%	0.88 (0.81–0.93)	20.8%
Omitting Ohno et al. <sup>16</sup>	0.79 (0.54–0.92)	86.4%	0.87 (0.69–0.96)	88.7%	0.80 (0.61–0.91)	84.9%	0.86 (0.78–0.92)	63.4%
Omitting Heusch et al. <sup>15</sup>	0.78 (0.56–0.91)	87.0%	0.87 (0.69–0.95)	87.1%	0.83 (0.64–0.93)	88.8%	0.86 (0.79–0.91)	62.3%

$I^2$ , inconsistency index;  $^{18}\text{F}$ -FDG PET/CT,  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography/computed tomography; MRI, magnetic resonance imaging; CI, confidence interval.

indicated that  $^{18}\text{F}$ FDG PET/MRI could be utilized to restage rectal cancer after preoperative chemoradiotherapy or to detect recurrence. Furthermore, because it is more accurate in T-staging and N-staging than PET/CT or MRI, it can be a precise tool for determining which patients to use for rectal preservation rather than standard surgery.<sup>33</sup> In addition, we focused on the concordance between  $^{18}\text{F}$ FDG semiquantitative metrics from PET/MRI and PET/CT in the included studies. One of the studies we included showed that the mean difference in standardized uptake value ( $\text{SUV}_{\text{mean}}$  and  $\text{SUV}_{\text{max}}$  for NSCLC from  $^{18}\text{F}$ FDG PET/MR imaging and  $^{18}\text{F}$ FDG-PET/CT was not statistically significant and showed a high correlation.<sup>15</sup> In contrast, another study showed that the  $\text{SUV}_{\text{max}}$  of PET/CT was significantly higher than that of PET/MR in primary foci,<sup>18</sup> which may be due to the differences in the hardware of PET/CT and PET/MRI devices and the reconstruction software methods used.

According to our meta-analysis, there was a high heterogeneity in the pooled sensitivity and specificity of  $^{18}\text{F}$ FDG PET/CT and  $^{18}\text{F}$ FDG PET/MRI, and we explored the sources of heterogeneity that would result from the inclusion of studies through sensitivity analysis. For  $^{18}\text{F}$ FDG PET/MRI, we discovered that by omitting the data from Lee et al.<sup>18</sup>, a reasonable heterogeneity in pooled sensitivity was obtained, and an acceptable heterogeneity in pooled specificity was obtained by excluding the data from Huellner et al.<sup>17</sup>, which could be explained by different cut-off thresholds. This may be related to the fact that these two articles included patients with suspected NSCLC, whereas several other studies included patients with NSCLC confirmed by pathologic examination. Nevertheless, other causes, such as changes in the patients, method, and research design, are also possible. Regrettably, we were unable to identify a source of heterogeneity in  $^{18}\text{F}$ FDG PET/CT.

However, our meta-analysis has limitations that cannot be ignored. First, we searched only three databases, which may have caused us to omit some studies that were consistent with this study. Second, the number of included studies was too small and they were all small sample size studies, which may be related to the included articles all required the use of  $^{18}\text{F}$ FDG PET/CT and  $^{18}\text{F}$ FDG PET/MRI in the same patient cohort. Third, half of the included articles were retrospective studies, and more prospective studies are needed in the future. Finally, no consistent source of  $^{18}\text{F}$ FDG PET/CT pooled

sensitivity and specificity was found by sensitivity analysis. We must interpret these results cautiously due to these limitations.

Based on the results pooled in the meta-analysis,  $^{18}\text{F}$ FDG PET/CT has good diagnostic potential for NSCLC lymph node metastases with a pooled sensitivity of 0.78 (95% CI: 0.59–0.90) and a pooled specificity of 0.87 (95% CI: 0.72–0.94), and  $^{18}\text{F}$ FDG PET/MRI had a pooled sensitivity of 0.84 (95% CI: 0.68–0.93) and a pooled specificity of 0.87 (95% CI: 0.80–0.92), which also had better diagnostic ability for lymph node metastasis in NSCLC. Therefore, we conclude that  $^{18}\text{F}$ FDG PET/CT and  $^{18}\text{F}$ FDG PET/MRI have similar diagnostic performance in detecting lymph node metastasis in NSCLC. Nevertheless, the results of this analysis were from a small sample study, and further studies with larger sample sizes are needed to draw more convincing conclusions.

$^{18}\text{F}$ FDG PET/CT and  $^{18}\text{F}$ FDG PET/MRI have similar diagnostic performance in detecting lymph node metastasis in NSCLC. Nevertheless, the results of this study were from a small sample study, and further studies with larger sample sizes are needed.

### Conflict of interest disclosure

The authors declared no conflicts of interest.

### Funding

Supported by Education Science and Technology Innovation Project of Gan-su Province (2022B-014) and First Hospital of Lanzhou University Intramural Fund (Idyyyn2021-66).

## References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: Cancer J Clin.* 2021;71(3):209–249. [\[CrossRef\]](#)
2. Molina JR, Yang P, Cassivi SD, Schild SE, Adjei AA. Non-small cell lung cancer: epidemiology, risk factors, treatment, and survivorship. *Mayo Clin Proc.* 2008;83(5):584–594. [\[CrossRef\]](#)
3. Zheng X, Cheng M, Fu B, et al. Targeting LUNX inhibits non-small cell lung cancer growth and metastasis. *Cancer Res.* 2015;75(6):1080–1090. [\[CrossRef\]](#)
4. Pieterman RM, van Putten JW, Meuzelaar JJ, et al. Preoperative staging of non-small-cell lung cancer with positron-emission tomography. *N Engl J Med.* 2000;343(4):254–261. [\[CrossRef\]](#)
5. De Leyn P, Doooms C, Kuzdzal J, et al. Revised ESTS guidelines for preoperative mediastinal

lymph node staging for non-small-cell lung cancer. *Eur J Cardiothorac Surg.* 2014;45(5):787–798. [\[CrossRef\]](#)

6. Gould MK, Kuschner WG, Rydzak CE, et al. Test performance of positron emission tomography and computed tomography for mediastinal staging in patients with non-small-cell lung cancer: a meta-analysis. *Ann Intern Med.* 2003;139(11):879–892. [\[CrossRef\]](#)
7. Alongi F, Ragusa P, Montemaggi P, Bona CM. Combining independent studies of diagnostic fluorodeoxyglucose positron-emission tomography and computed tomography in mediastinal lymph node staging for non-small cell lung cancer. *Tumori.* 2006;92(4):327–333. [\[CrossRef\]](#)
8. Silvestri GA, Gould MK, Margolis ML, et al. Noninvasive staging of non-small cell lung cancer: ACCP evidenced-based clinical practice guidelines (2nd edition). *Chest.* 2007;132(3 Suppl):178–201. [\[CrossRef\]](#)
9. Manafi-Farid R, Askari E, Shiri I, et al. (18)F]FDG-PET/CT radiomics and artificial intelligence in lung cancer: technical aspects and potential clinical applications. *Semin Nucl Med.* 2022;52(6):759–780. [\[CrossRef\]](#)
10. Kaseda K. Recent and current advances in FDG-PET imaging within the field of clinical oncology in NSCLC: a review of the literature. *Diagnostics (Basel).* 2020;10(8):561. [\[CrossRef\]](#)
11. Al-Ibraheem A, Hirmas N, Fanti S, et al. Impact of (18)F-FDG PET/CT, CT and EBUS/TBNA on preoperative mediastinal nodal staging of NSCLC. *BMC Med Imaging.* 2021;21(1):49. [\[CrossRef\]](#)
12. Kajiyama A, Ito K, Watanabe H, et al. Consistency and prognostic value of preoperative staging and postoperative pathological staging using (18)F-FDG PET/MRI in patients with non-small cell lung cancer. *Ann Nucl Med.* 2022;36:1059–1072. [\[CrossRef\]](#)
13. Wang ML, Zhang H, Yu HJ, et al. An initial study on the comparison of diagnostic performance of (18)F-FDG PET/MR and (18)F-FDG PET/CT for thoracic staging of non-small cell lung cancer: focus on pleural invasion. *Rev Esp Med Nucl Imagen Mol (Engl Ed).* 2023;42(1):16–23. [\[CrossRef\]](#)
14. 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(8):529–536. [\[CrossRef\]](#)
15. Heusch P, Buchbender C, Köhler J, et al. Thoracic staging in lung cancer: prospective comparison of  $^{18}\text{F}$ FDG PET/MR imaging and  $^{18}\text{F}$ FDG PET/CT. *J Nucl Med.* 2014;55(3):373–378. [\[CrossRef\]](#)
16. Ohno Y, Koyama H, Yoshikawa T, et al. Three-way comparison of whole-body MR, coregistered whole-body FDG PET/MR, and integrated whole-body FDG PET/CT imaging: TNM and stage assessment capability for non-small cell lung cancer patients. *Radiology.* 2015;275(3):849–861. [\[CrossRef\]](#)

17. Huellner MW, de Galiza Barbosa F, Husmann L, et al. TNM staging of non-small cell lung cancer: comparison of PET/MR and PET/CT. *J Nucl Med*. 2016;57(1):21-26. [\[CrossRef\]](#)
18. Lee SM, Goo JM, Park CM, et al. Preoperative staging of non-small cell lung cancer: prospective comparison of PET/MR and PET/CT. *Eur Radiol*. 2016;26(11):3850-3857. [\[CrossRef\]](#)
19. Kirchner J, Sawicki LM, Schaarschmidt BM, et al. Prospective comparison of 18F-FDG PET/MRI and 18F-FDG PET/CT for thoracic staging of non-small cell lung cancer. *Eur J Nucl Med Mol Imaging*. 2019;437-445. [\[CrossRef\]](#)
20. Ohno Y, Takeshi Y, Takenaka D, Koyama H, Aoyagi K, Yui M. Comparison of diagnostic accuracy for TNM stage among whole-body MRI and coregistered PET/MRI using 1.5-T and 3-T MRI systems and integrated PET/CT for non-small cell lung cancer. *AJR. Am J Roentgenol*. 2020;215(5):1191-1198. [\[CrossRef\]](#)
21. Asamura H, Chansky K, Crowley J, et al. The international association for the study of lung cancer lung cancer staging project: proposals for the revision of the N descriptors in the forthcoming 8th edition of the TNM classification for lung cancer. *J Thorac Oncol*. 2015;10(12):1675-1684. [\[CrossRef\]](#)
22. Gambhir SS. Molecular imaging of cancer with positron emission tomography. *Nat Rev Cancer*. 2002;2(9):683-693. [\[CrossRef\]](#)
23. Steinert HC. PET and PET-CT of lung cancer. *Methods Mol Biol*. 2011;727:33-51. [\[CrossRef\]](#)
24. Landwehr P, Schulte O, Lackner K. MR imaging of the chest: mediastinum and chest wall. *Eur Radiol*. 1999;9(9):1737-1744. [\[CrossRef\]](#)
25. Beiderwellen K, Huebner M, Heusch P, et al. Whole-body [<sup>18</sup>F]FDG PET/MRI vs. PET/CT in the assessment of bone lesions in oncological patients: initial results. *Eur Radiol*. 2014;24(8):2023-2030. [\[CrossRef\]](#)
26. Sotoudeh H, Sharma A, Fowler KJ, McConathy J, Dehdashti F. Clinical application of PET/MRI in oncology. *J Magn Reson Imaging*. 2016;44(2):265-276. [\[CrossRef\]](#)
27. Laffon E, Marthan R. Performance of <sup>18</sup>F-FDG PET/MRI and <sup>18</sup>F-FDG PET/CT for T and N staging in patients with non-small-cell lung cancer. *Eur J Nucl Med Mol Imaging*. 2019;46(2):522-523. [\[CrossRef\]](#)
28. Sun J, Li Y, Gong F, et al. The diagnostic value of PET/CT for the lymph node metastasis in Asian patients with non-small cell lung cancer: a meta-analysis. *Hell J Nucl Med*. 2022;25(2):196-204. [\[CrossRef\]](#)
29. Seol HY, Kim YS, Kim SJ. Predictive value of 18F-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(2):96-104. [\[CrossRef\]](#)
30. Czernin J, Ta L, Herrmann K. Does PET/MR imaging improve cancer assessments? Literature evidence from more than 900 patients. *J Nucl Med*. 2014;55(Suppl 2):59-62. [\[CrossRef\]](#)
31. Truong MT, Ko JP, Rossi SE, et al. Update in the evaluation of the solitary pulmonary nodule. *Radiographics*. 2014;34(6):1658-1679. [\[CrossRef\]](#)
32. Civelek AC, Niglio SA, Malayeri AA, et al. Clinical value of (18)FDG PET/MRI in muscle-invasive, locally advanced, and metastatic bladder cancer. *Urol Oncol*. 2021;39(11):787. [\[CrossRef\]](#)
33. Crimi F, Valeggia S, Baffoni L, et al. [18F] FDG PET/MRI in rectal cancer. *Ann Nucl Med*. 2021;35(3):281-290. [\[CrossRef\]](#)