Clinical evaluation of contrast-enhanced CT combined with PET/CT in diagnosis of mediastinal lymph node metastasis of non-small-cell lung cancer

Xiaodong Li¹, Xiaomeng Zheng², Tianle Zhang³, Xi Dong⁴, Jian Su⁵

ABSTRACT
Objectives: To investigate the clinical value of contrast-enhanced CT combined with PET/CT in the differential diagnosis of mediastinal lymph node metastasis (MLNM) of non-small-cell lung cancer (NSCLC).
Methods: A total of 120 patients with NSCLC combined with mediastinal lymphadenopathy hospitalized in our hospital were selected. All the patients received radical resection of lung cancer and mediastinal lymphadenectomy. After pathological diagnosis, they were divided into MLNM group (malignant group, undergoing contrast-enhanced CT) and non-MLNM group (benign group, receiving contrast-enhanced CT combined with PET-CT). The results were judged by two senior radiologists independently. The results of different scanning methods and postoperative pathology were compared using the t test, χ² test and Pearson correlation coefficient test.
Results: Compared with the pathological results, contrast-enhanced CT diagnosed 31 cases, with a coincidence rate of 62%, and contrast-enhanced CT combined with PET-CT diagnosed 42 cases, with a coincidence rate of 84%, presenting a statistically significant difference (P = 0.02). Among the 120 patients with lung cancer, pathological examination confirmed MLNM in 50 patients and benign enlargement in 70 patients, contrast-enhanced CT alone detected metastasis in 40 patients and benign enlargement in 80 patients, and contrast-enhanced CT combined with PET-CT detected metastasis in 47 patients and benign enlargement in 73 patients. The sensitivity and accuracy of the latter were significantly higher than those of the former (sensitivity, P = 0.01; accuracy, P = 0.01). With the increase in the malignancy of lymph nodes, the degree of CT enhancement, the concentration of radioactive substances and SUV value increased, showing positive correlations.
Conclusion: Contrast-enhanced CT combined with PET/CT in the diagnosis of MLNM of NSCLC presents higher coincidence rate, sensitivity and accuracy. With the increase in tumor malignancy, the enhancement degree and radioactive substance concentration increase. The two methods are synergistic and complementary in diagnosing MLNM.

KEYWORDS: Contrast-enhanced CT; PET/CT; Non-small-cell lung cancer; Mediastinal lymph node metastasis; Differential diagnosis.

doi: https://doi.org/10.12669/pjms.38.5.5528

How to cite this:
Li X, Zheng X, Zhang T, Dong X, Su J. Clinical evaluation of contrast-enhanced CT combined with PET/CT in diagnosis of mediastinal lymph node metastasis of non-small-cell lung cancer. Pak J Med Sci. 2022;38(5):1343-1348.
doi: https://doi.org/10.12669/pjms.38.5.5528

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION
At present, lung cancer is one of the malignant tumors with the highest incidence and fatality in the world¹, which is a great threat to human life and health. Non-small-cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for...
about 85% of all pathological types of lung cancer. Surgery is the main treatment method for NSCLC. The evaluation of regional lymph node metastasis is vital for the selection of treatment method, and also an important factor affecting the prognosis of patients. For the preoperative evaluation of primary lesions and metastases, the most commonly used methods include CT and PET-CT. CT has a certain advantage in the diagnosis of primary lesions, but it is less sensitive for small metastases. PET-CT imaging can reflect not only the anatomical information of lesions, but also the biological activity of tumor lesions, so PET-CT is the gold standard to determine the tumor staging of lung cancer. In addition, PET-CT also has a superiority in the diagnosis of lymph node metastasis of lung cancer. Current studies are more inclined to CT and PET-CT in the evaluation of primary lesions, but rarely investigate mediastinal lymph nodes.

METHODS

A total of 120 patients with NSCLC combined with mediastinal lymphadenopathy hospitalized in our hospital were selected. All the patients received radical resection of lung cancer and mediastinal lymphadenectomy. After pathological diagnosis, they were divided into MLNM group (malignant group, n = 50) and non-MLNM group (benign group, n = 70). The malignant group included 33 males and 17 females, aging 58-75 years (average, 63.54 ± 7.28 years). In the benign group, there were 51 males and 19 females, with an age of 55-73 years (average, 62.31 ± 6.74 years). The general data (gender and age) showed no significant differences between the two groups (P > 0.05), suggesting comparability.

Ethical approval: The study was approved by the Institutional Ethics Committee of Affiliated Hospital of Hebei University, (Date May 27, 2021) and written informed consent was obtained from all participants.

Inclusion criteria:
• Patients diagnosed as NSCLC and mediastinal lymphadenopathy;
• Patients receiving radical resection of lung cancer and mediastinal lymphadenectomy;
• Patients undergoing chest CT or PET-CT within 1 month before surgery, with complete imaging data;
• Patients without chemoradiotherapy before admission;
• Patients with definite lesions detected by chest imaging examination (CT or MRI), and the size of lesions accurately evaluated;
• Patients with clear consciousness and no mental illness;
• Patients and their families with willingness and ability to cooperate to complete the study, and good treatment compliance.

Exclusion criteria:
• Patients with metastatic lung cancer or lung cancer of other pathological types;
• Patients without mediastinal lymphadenectomy or effectively evaluated nature of mediastinal lymph nodes;
• Patients with incomplete clinical data;
• Patients combined with severe cardiopulmonary diseases;
• Patients with mental illness or other cognitive impairment, and no ability to cooperate the study;
• Patients combined with malignant tumors in other parts.

Scanning method: In the supine position, fasting patients received scanning using Philips 128-slice spiral CT, with scanning parameters as follows: tube current, 50-300 mAs; tube voltage, 120 kV; spiral pitch, 0.984; rotation time, 0.4 s/revolution; noise figure, 10-11; slice thickness, 1.25 mm. All the subjects completed the scanning by holding their breath at the end of inspiration, ranging from the apex to the bottom of the lung. Ioversol (350 mg I/ml, 1.2 ml/kg) was injected through the peripheral vein at a flow rate of 3.0 ml/s. After the injection of contrast medium, scanning was performed 28 s and 45 s later, respectively.

Result judgment: The original images were uploaded to the GE AW 4.7 post-processing station, and all the data were analyzed and processed using GSI Viewer. The homogeneous parts of the parenchymal lesions were selected as regions of interest (ROIs), and the energy spectrum curve was measured. The slope of the curve was calculated by two or more physicians above deputy director. According to the slope of the curve, the lymph nodes were preliminarily diagnosed: the slope difference between primary lesions and lymph nodes < 0.2, metastatic; > 0.2, non-metastatic.

PET-CT scanning was conducted using Philips Vereos PET/CT scanner. After fasting for more
than six hour, 0.12 mCi/kg 18F-FDG was injected intravenously. After resting for 60 minutes, whole-body PET-CT was performed in three-dimensional mode. PET-CT images were reconstructed by filtered back projection. After data acquisition, the data were transferred to the workstation of the system for image fusion, and the reconstructed images were collected and the SUV value of the lesions was obtained. Then, diagnosis was made through SUV measurement and visual inspection by two physicians above deputy director of nuclear medicine. SUV measurement results: normal: SUV value < 2.0; malignant: SUV value > 2.5; benign: SUV value = 2.0-2.5. Visual inspection results: lymph nodes without radioactive concentration were considered as benign lesions; lymph nodes with radioactive concentration were considered as malignant or metastatic lesions.

**Observation indicators:** The coincidence rate of different examination methods with pathological results was compared. The sensitivity, specificity and accuracy of contrast-enhanced CT alone and contrast-enhanced CT combined with PET/CT in the diagnosis of MLNM were compared. The correlations of mediastinal lymph nodes with different natures with CT enhancement and PET/CT radioactive concentration were compared.

**Statistical Analysis:** All data were statistically analyzed using SPSS 20.0. The measurement data were expressed as (X±S). Two independent samples t-test was used to analyze the data between groups, and χ² test was used to compare the rates. The correlation was expressed by Pearson correlation coefficient. P < 0.05 was considered as statistically significant.

**RESULTS**

The comparison of different examination methods with the pathological results (Table-II) showed that among the 50 patients with MLNM, contrast-enhanced CT diagnosed 31 cases, with a coincidence rate of 62%, and contrast-enhanced CT combined with PET-CT diagnosed 42 cases, with a coincidence rate of 84%. The coincidence rate had a statistically significant different between the two methods (P= 0.02).

Among the 120 patients with lung cancer, pathological examination confirmed MLNM in 50 patients and benign enlargement in 70 patients, contrast-enhanced CT alone detected metastasis in 40 patients and benign enlargement in 80 patients, and contrast-enhanced CT combined with PET-CT detected metastasis in 47 patients and benign enlargement in 73 patients. The sensitivity and

### Table-I: Comparison of general data between the two groups (X±S).

| Index                                      | Malignant group(50) | Benign group(70) | t/χ² | P     |
|--------------------------------------------|---------------------|------------------|------|-------|
| Age (years)Δ                              | 63.54±7.28          | 62.31±6.74       | 0.95 | 0.34  |
| Male (N %)Δ                               | 33(66%)             | 51(72.8%)        | 0.65 | 0.42  |
| Diameter of primary lesions (cm)*         | 3.40±0.85           | 2.76±0.32        | 5.76 | 0.00  |
| Pathological type                          |                     |                  |      |       |
| Adenocarcinoma                             | 15(30%)             | 22(31.4%)        | 0.13 | 0.91  |
| Squamous cell carcinoma                    | 28(56%)             | 35(50%)          | 0.24 | 0.62  |
| Others                                     | 7(14%)              | 13(18.6%)        | 0.44 | 0.51  |
| Diameter of mediastinal lymph nodes (cm)  | 1.24±0.12           | 1.21±0.15        | 0.78 | 0.44  |

Δp > 0.05, *p < 0.05.

### Table-II: Comparison in coincidence rate of different methods with malignancy (MLNM) (X±S) n = 50.

| Group                                      | Malignancy | Pathological diagnosis | Coincidence rate* |
|--------------------------------------------|------------|------------------------|-------------------|
| Contrast-enhanced CT                       | 31         | 50                     | 62%               |
| Contrast-enhanced CT combined with PET-CT  | 42         | 50                     | 84%               |
| χ²                                         |            |                        | 6.14              |
| p                                          |            |                        | 0.02              |

*P < 0.05.
accuracy of the latter were significantly higher than those of the former (sensitivity, $P = 0.01$; accuracy, $P = 0.01$), as seen in Table-III & IV.

The correlation analysis between nature of mediastinal lymphadenopathy and CT enhancement and PET/CT radioactive concentration demonstrated that with the increase in the malignancy of lymph nodes, the degree of CT enhancement, the concentration of radioactive substances and SUV value increased, showing positive correlations, indicating that contrast-enhanced CT and PET-CT have a synergistic effect in judging the nature of enlarged lymph nodes. Table-V

**DISCUSSION**

Lung cancer is the most common malignant tumor of the respiratory system, among which NSCLC is the most common. For patients with NSCLC, the main treatment method is surgery-based comprehensive treatment.$^{12}$ Its prognosis is closely related to the timing of treatment, early detection and timely treatment can present a satisfactory effect.$^{13}$ It is believed that$^{14}$ NSCLC with different genotypes have different tendencies of lymph node metastasis, which has a great influence on the selection of treatment methods. Yang et al.$^{15}$ believe that patients with lymph node metastasis and multiple-organ metastasis present poorer prognosis in terms of survival time, and a better understanding of lymph node metastasis can help clinicians better select treatment methods for NSCLC.

Mediastinal lymph node is a common metastatic site of NSCLC. The number and area of MLNM are closely related to the surgical method, resection range and postoperative recurrence.$^{16}$ At present, CT, bronchoscopy, mediastinoscopy and thoracoscopy are the methods for clinical diagnosis of MLNM. However, invasive surgery is not easily accepted by patients before definite diagnosis. With the rapid development of CT technology, it has gradually become an imaging method for noninvasive diagnosis of the pathological staging of NSCLC.$^{17}$ Nevertheless, the value of contrast-enhanced CT in the diagnosis of lymph

**Table-III: Correlations of contrast-enhanced CT alone and contrast-enhanced CT combined with PET/CT with pathological results.**

| Pathological results | Contrast-enhanced CT alone | Contrast-enhanced CT combined with PET/CT |
|----------------------|---------------------------|------------------------------------------|
|                      | Malignant | Benign | Total | Malignant | Benign | Total |
| Malignant            | 31        | 19     | 50    | 42        | 8      | 50    |
| Benign               | 9         | 61     | 70    | 5         | 65     | 70    |
| Total                | 40        | 80     | 120   | 47        | 73     | 120   |

**Table-IV: Analysis of diagnostic sensitivity, specificity and accuracy of contrast-enhanced CT alone and contrast-enhanced CT combined with PET/CT.**

| Group                              | Sensitivity* | Specificity | Accuracy* |
|------------------------------------|--------------|-------------|-----------|
| Contrast-enhanced CT               | 62% (31/50)  | 87% (61/70) | 76.6% (92/120) |
| Contrast-enhanced CT combined with PET-CT | 84%(42/50) | 92%(65/70) | 89.2% (107/120) |
| $\chi^2$                           | 6.14         | 1.27        | 6.62      |
| $P$                                | 0.01         | 0.26        | 0.01      |

*$P < 0.05$

**Table-V: Correlations between nature of mediastinal lymphadenopathy and CT enhancement and PET/CT radioactive concentration.**

| Nature of lymph nodes | CT enhancement | Radioactive concentration | SUV value |
|-----------------------|----------------|---------------------------|-----------|
| Malignant tumor       | 0.36           | 0.43                      | 0.37      |
| Benign enlargement    | 0.33           | 0.35                      | 0.31      |
| Normal lymph nodes    | 0.30           | 0.27                      | 0.24      |
node metastasis is limited. CT value reflects the attenuation ability of substances to X-ray, but conventional CT can not accurately reflect the attenuation characteristics of substances to X-ray, which is more obvious in small lesions.18

PET-CT is a newly developed scanning method in recent years. In clinic,19F-FDG, as a deoxyglucose analogue, is often used as a PEF-labeled nuclide. After entering the human body, it can be rapidly transported across the cell membrane by glucose transporters and enter the cell fluid, and then is transformed into F-FDG-6-PO4 by the phosphorylation of hexokinases in the cell fluid. The latter can not be recognized by fructokinase-1 and is catalysed for further metabolic process, so it can be retained in histocytes for a long time for developing.19 Compared with normal tissues, F-FDG is highly absorbed by human tumor tissues, presenting obviously local development, which can be used for early detection and diagnosis of malignant tumors. It has been pointed out that PET-CT scanning has higher detection rate and more significant application value in the diagnosis of lung cancer and lymph node metastasis.20

However, Wang et al.21 believe that the sensitivity and specificity of PET-CT for MLNM need further prospective evaluation. Moreover, invasive surgery and pathological confirmation are needed.22,23 A meta-analysis24 has found that PET/CT has moderate sensitivity and specificity in predicting MLNM in patients with NSCLC, and it may not be used to predict or exclude lymph node metastasis in patients with NSCLC.

Additionally, the study of Bustos25 suggested that18F-FDG PET-CT had a sensitivity of 53.8%, a specificity of 76.6%, a positive predictive value of 38.9%, a negative predictive value of 85.7%, and an accuracy of 71.7% in diagnosing MLNM. Multivariate analysis showed that the factors related to false negative results were moderate differentiation ($P = 0.005$) and SUVmax > 4 of primary tumors ($P = 0.027$). Considering the high false positive rate, it is suggested that the positive cases should be confirmed by histology.

Contrast-enhanced CT combined with PET/CT has a complementary effect in determining the malignancy of lesions,26 and can improve the diagnostic accuracy. Our study confirmed that with the increase in the malignancy of lymph nodes, the degree of CT enhancement, the concentration of radioactive substances and SUV value all increased, showing positive correlations. Compared with the postoperative pathological results, the coincidence rate of CT alone and CT combined with PET-CT was 62% and 84%, respectively, with a statistically significant difference ($P = 0.02$). The positive rate of MLNM was 75.5% in patients with primary lesions > 3 cm, and 41.2% in patients with primary lesions < 3 cm. Patients with primary lesions > 3 cm were more prone to MLNM ($P = 0.00$), but there was no significant correlation between MLNM and lymph node size ($P = 0.44$). The sensitivity and accuracy were 62% and 76.6% in contrast-enhanced CT alone, and 84% and 89.2% in contrast-enhanced CT combined with PET-CT, respectively, showing statistically significant differences (sensitivity, $P = 0.01$; accuracy, $P = 0.01$). Furthermore, the diagnostic sensitivity and accuracy of contrast-enhanced CT combined with PET-CT were significantly higher than those of PET-CT alone reported in literature.

Limitation of this study: It includes small sample size. Retrospective study of patients with mediastinal lymphadenopathy was carried out, without stricter N staging and more rigorous analysis according to N staging. We are further collecting cases and clinical data, and carried out a prospective analysis of some patients, in the expectation to early and accurate assessment of patients, so that more patients benefit.

CONCLUSION

Contrast-enhanced CT combined with PET/CT in the diagnosis of MLNM of NSCLC presents higher coincidence rate, sensitivity and accuracy. With the increase in tumor malignancy, the enhancement degree and radioactive substance concentration increase. The two methods are synergistic and complementary in diagnosing MLNM.

Declaration of conflicting interest: None.

Funding: This study was sponsored by Science and Technology Projects in Baoding (17ZF193).

REFERENCES

1. Chassagnon G, Bennani S, Revel MP. Nouvelle classification TNM des cancers du poumon non a petites cellules [New TNM classification of non-small cell lung cancer]. Rev Pneumol Clin. 2017;73(1):34-39. doi: 10.1016/j.pneumo.2016.12.006
2. Shi YM, Niu R, Shao XL, Zhang FF, Shao XN, Wang JF, 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(5):459-468. doi: 10.1097/MNM.0000000000001173
3. Lardinois D, De Leyn P, Van Schil P, Porta RR, Waller D, Passlick B, et al. ESTS guidelines for intraoperative lymph node staging in non-small cell lung cancer. Eur J Cardiothorac Surg. 2006;30(5):787-792. doi: 10.1016/j.ejcts.2006.08.008
4. Moulla Y, Gradistanac T, Wittenkind C, Eichfeld U, Gockel I, Dietrich A. Predictive risk factors for lymph node metastasis in patients with resected non-small cell lung cancer: a case control study [published correction appears in J Cardiothorac Surg. 2019 Feb 5;14(1):31]. J Cardiothorac Surg. 2019;14(1):11. doi: 10.1186/s13019-019-0851-0

5. Takahashi Y, Suzuki S, Matsutani N, Kawamura M. 18F-fluorodeoxyglucose positron emission tomography/computed tomography in the evaluation of clinically node-negative non-small cell lung cancer. Thorac Cancer. 2019;10(3):413-420. doi: 10.1111/1759-7714.12978

6. Ju FL, Még PQ, Hu HL, Liu J. Association between BMP4 expression and pathology, CT characteristics and prognosis of non-small cell lung cancer. Eur Rev Med Pharmacol Sci. 2019;23(13):5787-5794. doi: 10.26355/eurrev_201907_18317

7. Smith DE, Fernandez Aramburu J, Da Lozzo A, Montagne JA, Beveraggi E, Dietrich A. Accuracy of positron emission tomography and computed tomography (PET/CT) in detecting nodal metastasis according to histology of non-small cell lung cancer. Updates Surg. 2019;71(4):741-746. doi: 10.1007/s13304-019-00680-x

8. Darling GE. Lymph node assessment in early stage non-small cell lung cancer lymph node dissection or sampling?. Gen Thorac Cardiovasc Surg. 2020;68(7):716-724. doi: 10.1007/s11748-020-01345-y

9. da Cunha Santos G, Shepherd FA, Tsao MS. EGFR mutations of non-small cell lung cancer lymph node dissection or sampling?. Gen Thorac Cardiovasc Surg. 2019;71(4):741-746. doi: 10.1007/s13304-019-00680-x

10. Balata H, Fong KM, Hendriks LE, Lam S, Ostroff JS, Peled N, et al. Prevention and Early Detection for NSCLC: Advances in Thoracic Oncology. 2018. J Thorac Oncol. 2019;14(9):1513-1527. doi: 10.1016/j.jtho.2019.06.011

11. Okazaki E, Seura H, Hasegawa Y, Okamura T, Fukuda H. Prognostic Value of the Volumetric Parameters of Dual-Time-Point 18F-FDG PET/CT in Non-Small Cell Lung Cancer Treated with Definitive Radiation Therapy. AJR Am J Roentgenol. 2019;213(6):1366-1373. doi: 10.2214/AJR.19.21376

12. Chen B, Wang X, Xu Y, Xia WJ, Zhao H, Li XF, et al. Lymph node metastasis in Chinese patients with clinical T1 non-small cell lung cancer: A multicenter real-world observational study [published correction appears in Thorac Cancer. 2019 Sep;10(9):1852]. Thorac Cancer. 2019;10(10):533-542. doi: 10.1111/1759-7714.12978

13. Zhang J, Liu L, Wang G, Huang C, Chen Y, Zhang Y, et al. New perspective to evaluate N1 staging: The peripheral lymph node metastasis status of non-small cell lung cancer. Thorac Cancer. 2019;10(12):2253-2258. doi: 10.1111/1759-7714.13213

14. Liu Z, Liang H, Lin J, Cai X, Fan Z, Liu J, et al. The incidence of lymph node metastasis in patients with different oncogenic driver mutations among T1 non-small-cell lung cancer. Lung Cancer. 2019;134:218-224. doi: 10.1016/j.lungcan.2019.06.026

15. Yang J, Peng A, Wang B, Gusdon AM, Sun X, Jiang G, et al. The prognostic impact of lymph node metastasis in patients with non-small cell lung cancer and distant organ metastasis. Clin Exp Metastasis. 2019;36(5):457-466. doi: 10.1007/s10188-019-09985-y

16. Kuzucuoglu M, Gokyer A, Kula O, Yekdes AC, Sunal BS, Karakustalpoglu YA, et al. Relationship between the Size and Location of the Mass and Hilary and Mediastinal Lymph Node Metastasis in Early and Locally Advanced Non-Small Cell Lung Cancer. J Coll Physicians Surg Pak. 2020;30(2):172-176. doi: 10.29271/jcpsp.2020.02.172

17. Cong M, Feng H, Ren J, Xu Q, Cong L, Hou Z, et al. Development of a predictive radiomics model for lymph node metastases in pre-surgical CT-based stage IA non-small cell lung cancer. Lung Cancer. 2020;139:73-79. doi: 10.1016/j.lungcan.2019.11.003

18. Sha X, Gong G, Qiu Q, Duan J, Li D, Yin Y. Discrimination of mediastinal metastatic lymph nodes in NSCLC based on radiomic features in different phases of CT imaging. BMC Med Imaging. 2020;20(1):12. doi:10.1186/s12880-020-04146-3

19. Ohno Y, Fujisawa Y, Sugihara N, Kishida Y, Seki S, Koyama H, et al. Dynamic Contrast-Enhanced Perfusion Area-Detector CT: Preliminary Comparison of Diagnostic Performance for N Stage Assessment with FDG PET/CT in Non-Small Cell Lung Cancer. AJR. Am J Roentgenol. 2017;209(5):W253-W262. doi: 10.2214/AJR.17.17959

20. Yang DD, Mirvis E, Coldring J, Patel ARC, Wagner T. Improving diagnostic performance of 18F-FDG-PET/CT for assessment of regional nodal involvement in non-small cell lung cancer. Clin Radiol. 2019;74(10):818.e17-818.e23. doi: 10.1016/j.crad.2019.07.009

21. Wang Y, Zhu Y, Yip R, Lee DS, Flores RM, Kaufman A, et al. Pre-surgical assessment of mediastinal lymph node metastases in Stage IA non-small-cell lung cancers. Clin Imaging. 2020;68:61-67. doi: 10.1016/j.clinimag.2020.06.016

22. Dingemans AC, Hendriks LEL, Berghmans T, Levy A, Hasan B, Fairen-Finn C, et al. Definition of Synchronous Oligometastatic Non-Small Cell Lung Cancer-A Consensus Report. J Thorac Oncol. 2019;14(12):2109-2119. doi: 10.1111/jtho.2019.07.025

23. Hegde P, Molina JC, Thivierge-Southidara M, Jain RV, Gowda A, Ferraro P, et al. Combined Endosonographic Mediastinal Lymph Node Staging in Positron Emission Tomography and Computed Tomography Node-Negative Non-Small-Cell Lung Cancer in High-Risk Patients. Semin Thorac Cardiovasc Surg. 2020;32(1):162-168. doi: 10.1053/j.semtcvs.2019.07.007

24. Seol HY, Kim YS, Kim SJ. Predictive Value of 18F-Fluorodeoxyglucose Positron Emission Tomography or Positron Emission Tomography/Computed Tomography for Assesment of Occult Lymph Node Metastasis in Non-Small Cell Lung Cancer. Oncology. 2021;99(2):96-104. doi: 10.1597/00509988

25. Bustos Garcia de Castro A, Ferreiros Dominguez J, Delgado Bolton R, Fernandez Perez C, Cabeza Martinez B, Garcia Garcia-Esquinaz M, et al. PET-CT in presurgical lymph node staging in non-small cell lung cancer: the importance of false-negative and false-positive findings. La PAT-TC en la estadificacion ganglionar prequirurgica del carcinoma de pulmon de celulas no pequenas: implicacion de los falsos negativos y falsos positivos. Radiologia. 2017;59(2):147-158. doi: 10.1016/j.rx.2016.12.001

26. Suh YJ, Park CM, Han K, Jeon SK, Kim H, Hwang EJ, et al. Utility of FDG PET/CT for Preoperative Staging of Non-Small-Cell Lung Cancers Manifesting as Subsolid Nodules With a Solid Portion of 3 cm or Smaller. AJR Am J Roentgenol. 2020;214(3):514-523. doi: 10.1159/000509988

Authors’ Contributions:

XL & XZ: Designed this study and prepared this manuscript, are responsible and accountable for the accuracy and integrity of the work.

TZ & XD: Collected and analyzed clinical data.

JS: Significantly revised this manuscript.

Authors:

1. Xiaodong Li, Department of Nuclear Medicine, Xiaoming Zheng, Clinical Laboratory,
2. Tianle Zhang, Department of Radiology,
3. Xi Dong, Department of Nuclear Medicine,
4. Jian Su, Department of Nuclear Medicine,
5. Affiliated Hospital of Hebei University, Baoding 071000, Hebei, China.