Accuracy of Metabolic Imaging-guided Transthoracic Biopsy in Lung Cancer

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ABSTRACT

Objective: To compare the detection of transthoracic tru-cut biopsy performed on metabolically active areas in positron emission tomography (PET) for the diagnosis of lung cancer, compared to only CT scan-guided biopsy.

Study Design: Descriptive study.

Place and Duration of Study: Department of Thoracic Surgery, Kayseri City Training and Research Hospital, Turkey, between December 2020 to June 2021.

Methodology: Patients of suspected lung cancer with pre-transthoracic biopsy chest computerised tomography and without positron emission tomography were included in Group A; while, patients with both and positron emission tomography chest computerised tomography were included in Group B. Based on the CT findings of the patients in Group A, a biopsy was obtained from the most appropriate place. The patients in Group B were evaluated by a nuclear medicine specialist and the place with the highest maximum standardised uptake value before the biopsy was marked and the area to be biopsied was determined.

Results: The malignancy detection rate was significantly higher in Group B (48/50 patients, 96%) than in Group A (36/50 patients, 72%, $p=0.001$). Two lesions in the Group B (4 %) and 14 lesions in the Group A (28 %) were found to give benign results ($p=0.001$). Biopsy was repeated in one patient of Group B, and in five patients of Group A due to an initial negative diagnosis. The sensitivity of PET/CT in predicting malignant tumor was 96%, with the positive predictive value (PPV) of 98.0%; while the sensitivity of CT was 74.5%, with PPV of 82%.

Conclusion: Transthoracic biopsies taken by considering metabolically active areas of the mass in positron emission tomography-guided can both increase diagnosis rate and reduce the complication rate by preventing repeated biopsies.

Key Words: Transthoracic biopsy, PET/CT, Metabolic active lesion, Malignant tumor.

How to cite this article: Tezcan MA, Ozsoy IE, Karacavus S, Karaman H. Accuracy of Metabolic Imaging-guided Transthoracic Biopsy in Lung Cancer. *J Coll Physicians Surg Pak* 2022; **32(02)**:152-156.

INTRODUCTION

Tissue diagnosis is required for treatment planning in suspicious lung lesions. With the emergence of new imaging and biopsy techniques in peripheral, mediastinal and intraparenchymal lesions where fiberoptic bronchoscopy (FOB) was the most commonly used method for the diagnosis of lung lesions, transthoracic biopsies (TTB) are now preferred.¹ PET/CT is a functional imaging system based on defining differences in glucose metabolism of tissues.^{2,3}

The specificity is 70%-89% with fine needle biopsy; it is 93%-100% in tru-cut biopsy with an appropriate sample.⁴ Depending on the anatomical region, a higher rate has been reported in tru-cut biopsy. Few recently published studies concluded that the accuracy rate of tru-cut biopsy is higher.⁵ Positron emission tomography/computed tomography (PET/CT) is a hybrid imaging method combining positron emission tomography (PET) and computerised tomography (CT). Fluorine, which has the longest half-life, is the most used radionuclide. Lung cancer has been one of the areas where imaging has been accepted as a clinical priority. Owing to its high diagnostic accuracy, today fluorodeoxyglucose (FDG) PET/CT imaging is included as a routine diagnostic method.⁶⁻⁸ Fluorodeoxyglucose accumulates in cancer cells more than in normal cells; therefore, its localisation and intense metabolic activity in tumor tissue can be monitored. By using this feature, the sensitivity in biopsy can be increased.⁹

Lung cancers can be very heterogeneous, especially in large tumors, and cancer cells may not be present throughout the lesion. The lesion may be seen as normal lung tissue such as

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Received: July 13, 2021; Revised: November 28, 2021;

Accepted: December 24, 2021

DOI: <https://doi.org/10.29271/jcpsp.2022.02.152>

inflammatory tissue, necrosis and atelectasis in CT. In such patients, metabolism can be evaluated with FDG PET/CT to obtain the appropriate biopsy specimen from the neoplastic area, and repeated biopsy can be prevented.¹⁰

The present study was intended to determine the significance of transthoracic tru-cut biopsy performed on metabolically active areas in positron emission tomography for diagnosis.

Figure 1: A PET/CT-guided biopsy was planned for a male patient with a history of CT-guided biopsy. There was a part suggesting necrosis in the remainder of the mass, showing intense FDG uptake. PET/CT guidance was very important in guiding the biopsy needle to the metabolically active part of the disease.

METHODOLOGY

Ethical approval was obtained for this study from the Ethical Committee (Date: 24/12/2020, Decision No. 249). The study was planned prospectively.

In this study, patients with suspected lung cancer, who could not be diagnosed by other diagnostic methods and required transthoracic biopsy were divided into 2 groups. Patients with pre-TTB chest CT and without PET/CT were included in Group A; while, other patients with PET/CT and chest CT were included in Group B. There were 50 patients respectively selected in each group. Hemogram and international normalised ratio (INR) controls of all patients were performed before a biopsy. The anti-aggregant drugs used by patients were discontinued 3-5 days before the procedure.

Based on the CT findings of the patients in Group A, a biopsy was obtained from the most appropriate place. The patients in Group B were evaluated by a nuclear medicine specialist and the place with the highest maximum standardized uptake value (SUVmax) before the biopsy was marked and the area to be biopsied was determined. The area was considered hypermetabolic, if the SUVmax value was ≥ 2.5 . The biopsy was taken by matching the CT images with the sections determined as hypermetabolic in PET/CT (Figure 1). All patients were asked to attain the most appropriate position (supine, prone, and lateral) according to the lesion localization. After field disinfection with povidone-iodine, 2-5 cc local anaesthetic (2% prilocaine) was applied. After the lesion site was marked, a semi-automatic biopsy needle (18Gx10cm) was placed in the appropriate place. It was re-evaluated with control chest radiography 3-4 hours after TTB. While patients who did not develop complications were discharged on the same day, patients who developed complications were followed up. Positron emission tomog-

raphy and computerised tomography scans of all patients were performed using a Siemens Biograph Horizon brand device in Nuclear Medicine Department. The biopsy samples taken were evaluated in the Pathology Department.

Patients older than 18 years of age with lung, pleura and mediastinal tumors were included in the study. Patients younger than 18 years of age with thrombocytopenia, one lung, chronic cough, diffuse bullous emphysema and uncooperative were excluded from the study. The indications and contraindications of TBB are shown in Table I.

Table I: Indications and contra-indications of transthoracic biopsy.

Indications	Contraindications
Lung tumors	Vascular lesions (Aneurysm, AVM)
Mediasten tumors	Trombositopenia (<50.000/mm ³), INR value of >1.5
Pleura tumors	Respiratory failure (FEV1<%35)
Chest Wall tumors	Pulmonary hypertension
Immunohistochemical and Molecular Examination of Lung Cancers and Metastases	Single lung
Pathological diagnosis in inflammation	MI story (<6 weeks)
	Non-cooperative patient
	Chronic cough
	Bullous emphysema
	Hydatid cyst

AVM: Arteriovenous malformation; INR: International normalised ratio; FEV1: Force expiratory volume in 1 s; MI: Myocardial infarct.

Table II: Data of the patients and localisation of lesion and histopathological diagnose.

	Group A Mean $\pm$ S.D/ Median (IQR)/ n (%)	Group B Mean $\pm$ S.D/ Median (IQR)/ n (%)	p
Age	68.1 $\pm$ 9.5	65.9 $\pm$ 10.5	0.282 ^t
Gender			
Women	9 (18.0%)	6 (12.0%)	0.401 ^{x²}
Man	41 (82.0%)	44 (88.0%)	
Tumor size (mm)	57.2 $\pm$ 27.9	52.9 $\pm$ 32.1	0.220 ^m
Distance of lesion the chest Wall (cm)			
0-2	26 (52%)	26 (52%)	0.976 ^{x²}
2-5	16 (32%)	13 (26%)	
>5	8 (16%)	11 (22%)	
Biopsy position			
Supine	23 (46%)	23 (46%)	0.687 ^{x²}
Prone	23 (46%)	25 (50%)	
Lateral	4 (8%)	2 (4%)	
Biopsy time(minute)	18.7 $\pm$ 3.7	19 $\pm$ 3.5	0.648 ^m
Benign	14 (28%)	2 (4%)	0.001 ^{x²}
Malign	36 (72%)	48 (96%)	
Cavitary lesion	12 (24%)	9 (18%)	0.461 ^{x²}
Complication			
Pneumothorax	3 (6%)	2 (4%)	0.646 ^{x²}
Intraparanchymal hemorrhage	-	1 (2%)	

t: Independent sample t test, x²: Chi-square test, m: Mann-Whitney U-test, IQR: 25th percentile-75th percentile.

Statistical analysis of the data was performed using SPSS software (IBM SPSS version 27.0, IBM, Armonk, NY, USA). Descrip-

tive statistics were used to express the measures of central tendency. The distribution of variables was assessed with the Kolmogorov-Smirnov test. The Independent sample t-test was used to compare parametric continuous variables. The Mann-Whitney U-test was used to compare non-parametric continuous variables, in the statistical analysis. The Chi-square test was used in the analysis of qualitative independent data. A p -value < 0.05 was considered statistically significant.

RESULTS

Group A had 50 patients (41 men and 9 women), and Group B had 50 patients (44 men and 6 women). The mean age was 68.1 ± 9.5 (ranging from 47-84) years in Group A, and 65.9 ± 10.5 (ranging from 45-83) years in Group B. Patients in both groups did not differ significantly in terms of age, gender distribution and tumor size ($p > 0.05$). Data of these patients and characteristics of the lesions and the lobes in which they are located based on the patients' CT reports along with post-biopsy histopathological diagnoses are shown in Table II.

The malignancy rate was significantly in 48/50 patients in Group B (96%) higher than that in 36/50 patients in Group A (72%, $p=0.001$). Benign results were found in the two lesions in the Group B (4%) and in the remaining 14 lesions in the Group A (28%, $p=0.001$). The biopsy results were decided due to suspicious imaging features and/or clinical expertise in case 6/100 (6%) in all patients. Though the biopsy was repeated in 1/50 patients (2%) in Group B and in 5/50 patients (10%) in Group A were diagnosed by performing a biopsy again due to an initial negative diagnosis. In the Group A, 5/5 rebiopsies turned positive results for malignancy, while the same was true for 1/1 rebiopsies in the PET/CT Group B. The sensitivity of PET/CT in predicting malign tumors was 96%, the positive predictive value was 98.0%, while the sensitivity of CT was 74.5%, the positive prediction was 82%.

Complications were observed in five (5%) of the 100 patients, who underwent TTB. Although pneumothorax developed in three patients in Group A (two patients were treated with nasal oxygen, one patient each underwent tube thoracostomy, and had intraparenchymal haemorrhage. In Group B, pneumothorax treated with tube thoracostomy, developed in one patient only. There was no significant difference between the two groups in terms of biopsy duration, the distance of the lesion from the thoracic wall, biopsy position, cavitation and complication rates ($p=0.976$, $p=0.687$, $p=0.461$ and $p=0.646$, respectively).

DISCUSSION

Percutaneous lung biopsy is the most preferred method for the definitive diagnosis of peripheral lung lesions with lung cancer risk.¹¹ Transthoracic biopsy is an effective diagnostic modality for solitary pulmonary nodules and masses that cannot be reached bronchoscopically, newly detected or growing solitary pulmonary nodules and masses, patients with persistent lung infiltration undiagnosed by examinations such as sputum culture or bronchial lavage, hilar lesions that could not be diag-

nosed by bronchoscopy and chest wall masses.¹² TTB should be performed by professionals and should not be performed in high-risk patients.¹³ This department has experience in performing TTB on more than 500 patients.

The higher the SUVmax value, the higher is the likelihood of malignancy. Twelve studies have shown that the SUVmax value is very effective in distinguishing malignant and benign nodules > 1 cm.^{14,15} 18F-FDG-PET is not specific for malignancies. Inflammatory lung diseases may cause false-positive results even though they are not malignant because of their high metabolic activity. In addition, it may cause false-negative results in tumors with low glucose retention.^{14,16} In Group B, the mean SUVmax values of 3 patients with biopsy histopathology results indicated for infection was 11.58.

Nodule localisation and types of a malignant tumor do not affect PET/CT accuracy. Factors such as gender, tumor size, and age affect accuracy.¹⁷ The accuracy rate is 51.1% in benign tumors, 88.3% in malignant tumors and 77.6% in general. In addition, it has been shown that the higher the size, the higher is the accuracy rate.¹¹ In this study, the sensitivity of PET/CT in predicting malignancy was 57.4%, positive prediction 96.0%.

In a few studies, the rate of a positive diagnosis of TTB is in the range of 85%-95%.¹⁸ The rate of diagnosis increases up to 69% with tru-cut biopsy, especially in benign lesions.¹⁹ In this study, the rate of diagnosis in malignant lesions was found to be 96%.

In another study, biopsy results did not differ significantly in terms of lesion diameter, lesion's distance from the thoracic wall and age distribution. SUVmax value was determined as a more significant criterion than mass size.²⁰ In this study, the two groups did not differ significantly in terms of biopsy results and duration, thoracic wall distance from the tumor, biopsy position and age distribution ($p=0.976$, $p=0.687$ and $p=0.282$, respectively).

PET/CT shows tumor atelectasis better than chest CT. Images appear larger and more realistic in PET/CT.²¹ In this study, the cavitation feature of the lesion was not significantly different ($p = 0.461$).

The accuracy rate of a biopsy performed with PET/CT was found to be 90.9%; whereas, it was found to be 73.3% in a biopsy performed with CT.¹⁷ In this study, while the rate of diagnosis was 96% in Group B, it was found to be 72% in Group A.

The experience level of the person who is performing the biopsy also affects the results.¹⁴ In another study, biopsy repetition was found to be higher in biopsies performed only with chest CT compared to those performed with FDG-PET/CT.¹⁹ In this study, a repeat biopsy was performed in one patient (2%) in Group B and 5 patients (10%) in Group A.

Mortality rates have been reported between 0.15% and 47% in the literature. Mortality usually occurs in the early period and its causes include air embolism, acute massive haemoptysis, and massive haemothorax.²² There was no mortality in our study.

One study reported the rate of pneumothorax occurrence in TTB as ranging from 8%-61%. The rate of performing tube thoracotomy when pneumothorax develops was reported to be 21%. In this study, pneumothorax occurred in four patients (4%).

Parenchymal bleeding is the second most common complication of TTB. It has been reported that the risk of bleeding around the lesion or needle tract during the biopsy is between 5%-17%.^{14,23} In this study, parenchymal bleeding was observed in one patient (1%) only.

This study has several limitations. First, the study was based on a single institution and the population of cases were relatively small. Thus, the results of this study should be interpreted only in the present context and not as conclusion. Second, this study did not include very small lung nodules (<10 mm). Thus, these results cannot be generalised to very small lung nodules.

CONCLUSION

Transthoracic biopsies, taken by considering metabolically active areas of a lung mass in positron emission tomography-guided, can both increase diagnosis rate and reduce the complication rate by preventing repeated biopsy.

ETHICAL APPROVAL:

Ethical approval was obtained for this study from the Ethical Committee (Date: 24/12/2020, Decision No. 249).

PATIENTS' CONSENT:

Informed consents by patients or their first-degree relatives were obtained before the study started.

CONFLICT OF INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

MAT: Conception, analysis or interpretation of data, discussion and literature review.

IEO: Data analysis, results, and discussion.

SK: Literature search, analysis and interpretation of data.

HK: Analysis, conception, design, and acquisition of data.

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