ECRONICON OPEN ACCESS

EC PULMONOLOGY AND RESPIRATORY MEDICINE

Research Article

Clinical Features Effecting the Diagnostic Yield of Transthoracic Needle Aspiration Biopsy in Primary Malignant Lung Tumors

Halil Yanardag[1], Cuneyt Tetikkurt[2]*, Muammer Bilir[1], Seza Tetikkurt[3] and Emre Yanardag[4]

[1]Professor, Department of Internal Medicine Medicine, Cerrahpasa Medical Faculty, Istanbul Cerrahpasa University, Istanbul, Turkey

[2]Professor, Department of Pulmonary Medicine, Cerrahpasa Medical Faculty, Istanbul Cerrahpasa University, Istanbul, Turkey

[3]Professor, Department of Pathology, Demiroglu Bilim University Medical Faculty, Istanbul, Turkey

[4]Resident, Department of Internal Medicine, Haseki State Hospital, Istanbul, Turkey

***Corresponding Author:** Cuneyt Tetikkurt, Professor, Department of Pulmonary Medicine, Cerrahpasa Medical Faculty, Istanbul Cerrahpasa University, Istanbul, Turkey.

Received: October 01, 2020; **Published:** March 31, 2021

Abstract

The aim of this study was to determine the clinical and radiologic features that may predict the diagnostic yield of transthoracic needle aspiration biopsy in primary lung tumors. A retrospective evaluation for the final results of 284 patients was conducted to evaluate the clinical and the radiological manifestations associated with the diagnostic sensitivity and specificity of the transthoracic needle biopsy for primary pulmonary malignant tumors. Of these patients 246 had focal and 38 had diffuse lung diseases. All patients had chest x-ray and thorax CT. The patients underwent a transthoracic fine-needle aspiration biopsy under computed tomography guidance. The mean diameter of the pulmonary nodules was 24.2 ± 11.4 mm. Histopathological accuracy were obtained in 252 (88.7%) patients. Minor complications developed in %11.2 while pneumothorax occured in 6.4% of the individuals. Sensitivity and specificity of the TNA biopsy was noted to be 87.1% and 76.2%, respectively. The diagnostic accuracy of the TNA biopsy was 67.6% for primary lung tumors. Clinical and imaging manifestations were assessed to predict the diagnostic yield of the TNA biopsy for primary malignant lung tumors.

Certain radiologic features of the chest x-ray, thorax CT and PET/CT imaging were found to be extremely useful as the initial enterprises for predicting the sensitivity and specificity of the transthoracic needle aspiration biopsy for primary malignant lung tumors. Clinical manifestations revealed a low correlation relevant to the diagnostic yield of the TNAB. Imaging findings showed the highest correlation with the diagnostic accuracy of the TNA biopsy. Collaboration of the clinical and imaging results significantly increased the predictive diagnostic rendement of the TNA biopsy in regard to the sensitivity and specificity that is the hallmark to obtain adequate lung tissue compatible with the final diagnosis.

Keywords: *Lung Cancer; Pulmonary Nodule; Transthoracic Needle Aspiration Biopsy; TNAB; Malignant Pulmonary Nodule*

Introduction

Final diagnosis of malignant pulmonary nodules is vital for a successful treatment and a prolonged patient survival. Transthoracic needle aspiration biopsy (TNAB) has a high diagnostic accuracy and is a well-established procedure for obtaining a cytological sample in the evaluation of pulmonary nodules. As TTAB is a minimal invasive procedure with a high diagnostic rate, it has been used with great success especially for the identification of malignant lung lesions [1-18]. The efficiency of the procedure has gradually increased due to the developments in the radiological and cytological techniques during the recent years. There are many different factors consistent with the diagnostic yield of the TTNB. These features are lesion size, type of biopsy device, experience of the clinician, immediate on-site sample evaluation by a cytologist and the technique used.

Previous studies have reported results ranging from 77% to 97% for the preciseness of the TTNB for benign and malignant lesions of the lung [6-14]. As the sensitivity and specificity is the hallmark of the diagnostic adequacy for any laboratory investigation, it is crucial

to predict and determine the factors related to the rendement of any invasive procedure. It is a necessity for the clinician to maximize the accuracy according to the patient's clinical characteristics and to minimize potential side effects, especially for malignant pulmonary nodules. Selecting the appropriate diagnostic approach is the triangulation point of medical practice.

Aim of the Study

The aim of this study was to appraise the clinical factors including patient, laboratory and imaging manifestations that play a role in the diagnostic accuracy of the TNAB in the dentification of primary malignant lung tumors.

Materials and Methods

A total of 284 patients admitted as out or inpatients to Cerrahpasa Medical Faculty between 1998 March and 2020 August were evaluated in the study. In forty-eight patients, the TNAB had been performed in various other university or state hospital centers. This retrospective study is an ongoing form of an antecendent preliminary research conducted by Yanardag., *et al* [15] previously. The diagnostic yield of the TNAB specimens was assessed for the sensitivity and specificity of the procedure in regard to the clinical manifestations and imaging findings. Of these patients, 198 (69.7%) were males and 86 (30.2%) were females. The mean age was 58.4±18.2, ranging from 28 to 76 years. Ninety eight subjects were non-smokers while forty six were passive smokers. All patients had serum biochemistry, complete blood count, coagulation tests, electrocardiogram, pulmonary functiont tests, chest x-ray and CT before TNAB was performed. Patients with a history of bleeding diathesis, coagulation defects, an abnormal coagulation test results and diffuse cystic lung disease or emphysema on the chest CT were excluded from the study due to the possible complications that may occur following biopsy. TNAB was performed under computed tomography guidance. For patients with a suspected malignant lesion on chest x-ray or thorax computed tomography, a PET/CT scan was performed. Since PET was not previously available during the study, it was only applicable in 102 (72/224, 35.9%) of the patients. Tumors metastatic to the lung and pleural, thoracic wall soft tissue or bone tumors were excluded to define the clinical factors associated with the diagnostic yield of TNAB for only primary malignant lung tumors.

BODE index and Karnofsky index were applied to assess the performance of the patients. Clinical features including age, gender, symptoms, laboratory findings, radiologic manifestations and histopathologic findings were evaluated retrospectively in regard to the diagnostic yield of procedure concerning sensitivity and specificity. Patients were placed on the computed tomography table in a prone, supine, or decubitus position in regard to the location of the pulmonary lesion. The shortest pathway perpendicular to the thoracic plane with the mininum parenchymal depth avoiding the ribs and vascular structures was chosen to insert the biopsy needle. Local anesthesia with 1% lidocaine was administered before the procedure and a biopsy needle between 20 or 22 gauge was used. The patients were asked to hold their breath while crossing the pleura. The biopsy sample was evaluated by a pathologist for the adequacy of the of the sample yield. Pathologic examination showed normal lung tissue, nonspecific inflammation, necrotic tissue or no pulmonary parenchymal tissue in the biopsy sample in which the TNAB result was accepted as incompatible with the final diagnosis.

Statistical analysis concerning gender, age, initial symptoms, smoking habitus, patient performance index, pulmonary function tests and histopathological features for the diagnostic rendement of the TNAB was performed. Radiologic features including lesion size, presence of necrosis, lineer spiculations, lesion location, solid, infiltrative or ground glass appearence and cavity wall thickness were used to define the predictive effect of the thorax CT imaging features for the TNAB. PET/CT manifestations like SUV, presence of metastatic lymph nodes and organs with metastatic foci were evaluated to estimate the diagnostic yield of the procedure. Accuracy of the procedure was calculated as the count of true positive and negative biopsy results divided by the total number of biopsies done while a final and a definitive pathologic diagnosis was obtained in all patients. Diagnostic rendement of the TNAB was assessed in the light of all the above aforementioned clinical and radiological manifestations.

Analysis for dermographics and clinical manifestations were done by using categorial statistics. Pearson correlation test, binary logistic regression analysis and chi-square were carried out for statistical analysis. Pearson test was utilized to determine the correlation

between different variables. Correlation coefficient was designated as weak ($r < 0.3$), intermediate ($0.3 \leq r \leq 0.7$) or strong ($r > 0.7$). A p value less than 0.5 determined statistical significance. Clinical, laboratory and radiological manifestations were evaluated individually in terms of their contribution to the diagnostic TNAB yield. A positive TNAB was denominated as true positive in regard to the final definite pathologic diagnosis for all cases. A negative TNAB was considered as true negative with final pathologic confirmation or with the dissapearence or the stability of the lesion during the follow-up a period for at least two years. Negative TNAB result was considered as false-negative if the final diagnosis revealed a malignant primary lung tumor. All the patient findings including the clinical, laboratory, pathologic and the imaging manifestations were first evaluated by themselves for the diagnostic efficiency of the TNAB. The collaboration of the clinical, laboratory, pathologic and the imaging findings were then analyzed to determine the predictive diagnostic yield of the TNAB collectively. Correlation of the clinical and the radiologic manifestations for the predictive accuracy of the TNAB yield including the sensitivity, specificity and the complication rate of the TNAB was assessed in regard to the final definitive diagnosis.

Results

Dermographic features of the patients including age, gender, smoking history, basic laboratory findings and pulmonary function test results are depicted in table 1. The initial clinical symptoms, laboratory findings, PFT results, performance status including BODE and Karnofsky index, radiologic and PET/CT manifestations of the patients are shown in table 2. The mean lesion size ranged between 10 mm and 68 mm, with an average of 28.4 ± 16.8 mm diameter. Diagnostic sensitivity and specificity of the TNAB were 91.9% and 82.1%, respectively. The PPV of the method was 96.4%, while the NPV was found to be 73.2%. There was not any significant correlation between the age or the gender of the patients for the positive diagnostic biopsy results. Patient symptoms including cough, hemoptysis, chest pain, dyspnea, lassitude and weight loss (more than 6 kg in the last three months) did not show a significant correlation with the diagnostic efficiency of the TNAB for primary malignant lung tumors. Complete blood count and serum biochemistry results were not relevant for the TNAB rendement. A significant intermediate correlation ($r: 0.4$; $p \leq 0.05$) was found between the amount of cigarettes and the diagnostic yield of the TNAB (Table 3).

Dermographics	Total # of patients	Male	Female
	284	198	86
Age, years	58.4 ± 18.6	68.6 ± 14.8	62.8 ± 12.4
Non-smoker < 15 p-y ≥15 p-y	98 62 124	68 42 96	30 20 28
Laboratory			
ERS (mm)	42.4 ± 12.6	34.8 ± 10.4	26.8 ± 14.2
CRP (mg/L)	14.6 ± 8.2	12.4 ± 9.6	10.6 ± 6.8
SGOT (U/L)	38.4 ± 20.6	40.6 ± 18.2	38.6 ± 16.4
SGPT (U/L)	36.8 ± 14.2	42.6 ± 12.4	38.8 ± 11.8
LDH (U/L)	296.8 ± 46.8	292.4 ± 42.6	284.2 ± 38.4
Spirometry and DLCO			
FEV_1, % predicted	78.2 ± 20.2	74.8 ± 16.8	79.4 ± 18.6
FVC, % predicted	86.4 ± 16.2	78.6 ± 14.2	80.4 ± 12.2
TLC, % predicted	81.4 ± 12.8	76.6 ± 18.4	76.8 ± 16.4
DLCO/VA, % predicted	84.8 ± 14.6	82.6 ± 12.8	80.2 ± 18.2

Table 1: *Dermographics, basic laboratory findings and pulmonary function test results of the patients. Data are presented as mean ± SD or %. FEV_1: Forced Expiratory Volume in One Second; FVC: Forced Vital Capacity; TLC: Total Lung Capacity; DLCO/VA: Diffusing Capacity Divided by the Alveolar Volume (DLCO/VA).*

Patient features	Total (%)	Male (%)	Female (%)
Weight loss	23 (8.1)	15 (5.3)	8 (2.8)
Cough	46 (16.2)	32 (11.3)	14 (4.9)
Hemoptysis	26 (9.2)	19 (6.7)	7 (2.5)
Chest pain	34 (11.9)	24 (8.4)	12 (4.2)
Lassitude	26 (9.2)	15 (5.3)	11 (3.9)
BODE index	42 (14.8)	30 (10.6)	12 (4.2)
Karnofsky index	52 (18.3)	38 (13.4)	14 (4.9)
Serum biochemistry	68 (23.9)	42 (14.8)	26 (9.1)
PFTs	92 (32.4)	62 (21.8)	30 (10.6)
Chest x-ray findings*	98 (34.5)	67 (23.6)	32 (11.3)
Thorax CT findings*	134 (47.2)	96 (33.8)	38 (13.4)
PET/CT findings*	100 (35.2)	76 (26.8)	24 (8.4)
SBPFXCP**	146 (51.4)	106 (37.3)	40 (14.1)

Table 2: *Clinical and imaging manifestations of the patients including collaboration of the patient findings.*

**Manifestations associated with lung carcinoma.*

PFTs: Pulmonary Function Tests, CT: Computed Tomography, PET/CT: Positron Emission Tomography/Computed Tomography.

***SBPFXCP: Collaboration of the clinical, laboratory and imaging findings relevant to pulmonary malignancy.*

(S: Symptoms, B: Biochemistry, P: Performance Status [BODE and Karnofsky], F: Pulmonary Function Tests, X: Chest X-Ray, C: Computed Tomography, P: Positron Emission Tomography/Computed Tomography).

Patient features, laboratory and imaging findings	Correlation of the clinical manifestations with the TNAB diagnostic yield	p value
Age (years)	r: 0.11	< 0.16
Gender	r: 0.14	< 0.24
Smoking history		
Non-smoker	r: 0.24	< 0.18
< 15 packages-year	r: 0.12	< 0.20
≥15 packages-year	r: 0.42	< 0.28
Initial symptoms*	r: 0.16	< 0.18
Patient performance**	r: 0.14	< 0.26
Serum biochemistry*	r: 0.24	< 0.21
PFT***	r: 0.18	< 0.32
Chest x-ray findings*	r: 0.56	< 0.05
Thorax CT manifestations*	r: 0.61	< 0.01
PET/CT findings*	r: 0.72	< 0.01
Imaging findings***	r: 0.58	< 0.05
SBPFXCP ****	r: 0.89	< 0.01

Table 3: *Correlation of the clinical manifestations with the diagnostic yield of the TTNA biopsy.*

**: Manifestations associated with lung carcinoma.*

***: BODE and Karnofsky index.*

****: Collaboration of the imaging manifestations*

*****: Collaboration of the clinical, laboratory and imaging findings.*

Clinical manifestations including performance status (BODE dyspnea and Karnofsky index) and pulmonary function test results did not show a noteworthy correlation with the TNAB (Table 3) diagnostic yield. There was no significant correlation between the tumor site and the diagnostic TNAB rendement. The radiologic features of the tumor appearence on the chest x-ray and thorax CT exhibited an intermediate correlation in regard to the diagnostic yield of the TNAB. PET/CT tumor manifestations displayed a moderate relevance with the diagnostic TNAB trenchancy. TNAB yield was lowest in lesions with a radiologically infiltrative or a ground glass appearance. The diagnostic rendement of the TNAB was significantly lower for pulmonary malign nodules less than two centimeters ($r: 0.68$, $p < 0.05$). The collaboration of the chest-x ray, CT and PET/CT imaging findings that indicated malignant tumor features revealed a significant intermediate correlation with an accurate TNAB yield. The overall diagnostic accuracy of TNAB revealed the highest correlation in regard to final definitive diagnosis when the clinical manifestations and the imaging findings including chest x-ray, CT and PET/CT findings were collaborated (Table 3).

Among the primary lung tumors, TNAB provided the highest diagnostic rendement for adenocarcinoma (72.4%, $p < 0.05$) followed by small cell carcinoma (62.8%, $p < 0.05$). Efficiency of the TNAB was not influenced by the parenchymal location of the malignant nodules. Although not statistically significant, the diagnostic yield of the TNAB was lower in tumors adjacent to the diaphragm and deeper than 6 cm in the lung parenchyma. The most frequent complication associated with the TNAB procedure was pneumothorax that was observed in 6.2% which necessitated drainage only in 2.8% of the patients. Incidence of the TNAB complications was significantly higher (4%) in lesions located at the inner one third of the lung. All patients who developed pneumothorax had bullous or cytic lung lesions on thorax computed tomography. Pulmonary hemorrhage appeared as the second most common (2.4%) complication while none of the patients that developed a complication required any treatment. A final definitive pathological or clinical diagnosis was obtained in all of the patients who participated in the study.

Discussion

Transthoracic needle aspiration biopsy is a minimally invazive clinical tool for the identification of pulmonary parenchymal lesions that has become more accurate and efficient in regard to its diagnostic yield due to the advances in clinical medicine. It is a crucial diagnostic modality for lung diseases and has provided a high accuracy, especially for the assessment of primary malignant lung tumors [5-11,16-28]. Our main aim was to determine the predictive diagnostic preciseness of this procedure in advance to provide an accurate or an approximately indubitable approach for the final definitive diagnosis. Determining and predicting the efficiency of the TNAB will be a useful acces for clinicians to designate the best paradigm for the identification of malignant lung tumors. Such an implementation will also ensure that an effective treatment can be administered without diagnostic delay. The results of our study revealed that imaging manifestations were the most noteworthy constituent that predicted the diagnostic accuracy of the TNAB. Patient characteristics, symptoms, laboratory and pulmonary function test results showed a weak and a negligible correlation with the TNAB acquisition. Imaging manifestations including chest x-ray, thorax CT and PET/CT findings revealed significant correlation with the rendement of the TNAB results. On the other hand, the best predictive assessment for the diagnostic TNAB yield was obtained when all the clinical and imaging manifestations were collaborated and thereby evaluated mutually.

The overall pooled diagnostic accuracy of the TNAB is 92.1% while the sensitivity may reach to 96% for detecting malignant lesions. Specificity for malignancy identification approaches to 100% with rare false positives. Within each individual study, one cardinal factor influencing the diagnostic accuracy of the TNAB the is the lesion size or diameter. However, validating the lesion dimension as a foreseen diagnostic futileness was not identified as a failure factor in these studies. The diagnostic accuracy was almost perfect in nodules less than 2 cm with a 92.8% specificty and a 92.3% sensitivity. No significant difference in terms of diagnostic accuracy was observed even for nodules below one centimeter in regard to sensitivity and specificity [18-22]. The common feature in all of these studies is that the diagnostic accuracy was evaluated only on the size of the lesion and no other factors relevant to other clinical or imaging features were evaluated. In addition, these studies were not able to provide a definitive predictive assessment for the clinician in terms of diagnostic

accuracy for any patient, as they only evaluated the diagnostic yield relevant only to lesion size [22-30]. It is clear that such an approach would not naturally be able to detect the diagnostic sensitivity and specificity for the TNAB with a predicted significant accuracy. On the other hand, our study concluded its findings by evaluating all the clinical data consistent with the patient characteristics collectively in order to determine the diagnostic accuracy of the TNBA more precisely.

Our study put forward that such an approach for the TNAB revealed a noteworthy sensitivity and specificity for the identification of the primary malignant lung tumors. The main limitations that decreased the diagnostic yield were small lesion size and increased tumor depth in the lung parenchyma. The low diagnostic yield in tumors located in the 1/3 inner region of the lung parenchyma may be associated with the more timid approach and drawback of the clinicians for such deeply sited tumors due to occurence of adverse effects such as pneumothorax and hemorrhage. Individual patient manifestations including patient symptoms or performance status, laboratory and PFT data of the subjects did not establish a significant correlative predictive determinant in terms of the TNAB rendement. The weak correlation between the amount of cigarettes smoked and the diagnostic accuracy of the biopsy is probably related to the fact that primary lung cancers are most frequently seen in smokers. The most prominent clinical data that predicted and determined the diagnostic yield of the TNAB were the malignancy specific or relevant imaging findings of the chest x-ray, thoracic CT and PET/CT alone. The collaborative evaluation of the imaging manifestations of the aforementioned imaging modalities further carried the predictive value of diagnostic biopsy yield to a more statistically significant level. Consequently, a collective assessment of the clinical findings and the radiologic manifestations before the application of the procedure established a reliable diagnostic accuracy for the TNAB yield. As the results of our study reveal, such an approach will prevent time delay that may arise in terms of accurate diagnosis and will facilitate the implementation of oncological treatment options as soon as possible by ensuring that the clinician proceeds in the right diagnostic pathway which is the hallmark of a successful outcome in these patients.

To our knowledge, this is the first study in literature to evaluate the predictive diagnostic TNAB yield. The first limitation of our study appears to be the small sample size. In cases with a benign inflammatory TNAB sample result a second attempt with a larger gauge needle was not performed that may have effected the diagnostic accuracy of the procedure in our study. Since this is a single center study with a limited number of patients, the outcome should be evaluated accordingly. The second restriction for our study is the lack of a prospective assessment. Further large-multi center trials comprising numerous patients with different clinical features are required for more accurate results concerning the diagnostic yield of the procedure. The method, the biopsy needle type and the quality of the imaging modalities used may have effected the rendement of the TNAB because these auxiliary factors constitute the most crucial elements in achieving for obtaining accurate pathological samples. The experience of the clinicans may be considered as a limiting factor for the definitive TNAB results. As our study population consisted of only Caucassian people, inclusion of patients with different racial and genetic characteristics may appear as another requisite to attain more definite and unequivocal data. Despite all the limitations mentioned above, we believe that our study puts forward the criteria to be considered before biopsy in terms of reaching definitive and accurate pathological results with the TNAB procedure.

Lung cancer is the leading cause of cancer deaths worldwide. Determining the pathological diagnosis probability of TNA biopsy before the procedure by evaluating the clinical and imaging characteristics of the patients will establish beneficial results for the clinicians. A predicted diagnostic yield of TNAB for lung cancer is required for accurate assessment, proper treatment including surgical resection, chemotherapy or radiotherapy of the primary malignant pulmonary tumors. Such an approach will increase the prospect of an accurate pathological diagnosis thereby significantly reducing the potential delays of diagnosis and treatment for the lung cancer patients. Appropriate use of the TNAB procedure carries a crucial importance in terms of instant diagnosis and early treatment for patients that will be highly beneficial for patient survival. Forecasting the features or factors for a definitive diagnostic yield of TNAB is the cardinal hallmark that leads the clinician in the correct diagnostic pathway. The results of our study clearly demonstrate that the application of a predictive approach for TNAB will be extremely useful clinically. The other benefit of such an approach is avoidance of useless attempts that will not

provide a definitive diagnosis thereby precluding a financial burden. Another useful aspect of this algorithmic application is the use of other different interventions for the idenification of benign inflammatory lesions which have a very low probability of definitive diagnosis with the TNAB procedure.

The aim of our study was to improve the diagnotic accuracy of the TNAB for the diagnosis of malignant pulmonary tumors. Before performing the TNAB, determining the clinical, laboratory and imaging characteristics of the patient or the malignancy probability of the pulmonary nodules have significantly increased the diagnostic accuracy of the TNAB. Application of such an algorithmic pattern has clearly improved the diagnostic sensitivity and specificty of the TNAB yield. Such an approach not only increases the diagnostic efficiency of the procedure, but also minimizes the potential adverse effects, precludes the probable time and financial loss during the diagnostic intervention. CT-guided TTNA biopsy of the lung is an accurate and at the same time a relatively safe procedure for the diagnosis of pulmonary malignant nodules. Many studies have analyzed the diagnostic accuracy, effectiveness and complication rate of TNAB up to now [2,4,6,11,16,19,20,30-38]. As far as we know, this is the first study in literature to evaluate and thereby to predict the diagnostic accuracy of the TNAB that included clinical, laboratory and radiologic manifestations by themselves also incorporating a collaborative approach for all patient data. If the probability of the predicted diagnosis from biopsy is low according to the criteria we have set out, the clinicians may use other procedures to prevent delay and financial burden relevant to the diagnostic pathway. Implementation of such an algorithmic approach prior to the TNAB may at the same time prevent the serious potential complications related to the procedure such as pneumothorax or bleeding that may lead to significant morbidity and mortality in cancer patients.

Conclusion

Since lung cancer is the most common and fatal cancer of our age, diagnosis emerges as the paramount step to prolong the life expectancy of such patients. Although many laboratory and imaging methods are being investigated or developed currently that may speed up the diagnosis, the TNAB plays a pivotal role as the cornerstone for diagnostic evaluation of the malignant pulmonary nodules. The aim of TNAB is to provide the definite pathological diagnosis of lung lesions, especially the primary malignant nodules. Rational use of conventional procedures may provide a significant and an efficient contribution that may facilitate the final diagnosis. As many different factors may have been consistently associated with a lower diagnostic yield, selecting an appropriate approach according to the clinical features of the patients may improve the diagnostic accuracy and preclude the potential adverse effects. Since the malignant potential of a pulmonary nodule is predicted by patient risk factors, laboratory and imaging manifestations, such an algorithmic application for the conventional TNAB procedure not only increases the diagnostic accuracy of the intervention but may also reduce the diagnostic delay and preclude the potential complications encountered during this conventional intervention. The algorithmic pathway put forward in this study provides an important support for the clinicians in regard to the definitive diagnosis of primary malignant pulmonary nodules.

Financial disclosure and Conflicts of Interest

All authors state explicitly that potential conflicts of interest relevant to this study do not exist.

Authorship and Contributorship

Halil Yanardag prepared the patient data.

Cuneyt Tetikkurt designed and wrote the manuscript.

Muammer Bilir performed the statistical analysis.

Seza Tetikkurt wrote the pathological data of the study.

Emre Yanardag prepared the references.

Bibliography

1. Harrison BD., *et al.* "Percutaneous Trucut lung biopsy in the diagnosis of localised pulmonary lesions". *Thorax* 39.7 (1984): 493-499.

2. Lourenco R., *et al.* "CT-guided percutaneous transthoracic biopsy in the evaluation of undetermined pulmonary lesions". *Revista Portuguesa de Pneumologia* 12.5 (2006): 503-524.

3. Swischuk JL., *et al.* "Percutaneous transthoracic needle biopsy of the lung: review of 612 lesions". *Journal of Vascular and Interventional Radiology* 9.2 (1998): 347-352.

4. Montaudon M., *et al.* "Factors influencing accuracy of CT-guided percutaneous biopsies of pulmonary lesions". *European Radiology* 14.7 (2004): 1234-1240.

5. Ohno Y., *et al.* "CT-guided transthoracic needle aspiration biopsy of small (< or = 20 mm) solitary pulmonary nodules". *American Journal of Roentgenology* 180.6 (2003): 1665-1669.

6. Yoshimura N., *et al.* "The factors determining diagnostic accuracy in CT-guided percutaneous needle biopsy of small pulmonary nodules". *Nihon Kokyuki Gakkai Zasshi* 40.2 (2002): 101-105.

7. Laurent F., *et al.* "CT-guided transthoracic needle biopsy of pulmonary nodules smaller than 20 mm: results with an automated 20-gauge coaxial cutting needle". *Clinical Radiology* 55.4 (2000): 281-287.

8. Santambrogio L., *et al.* "CT-guided fine-needle aspiration cytology of solitary pulmonary nodules: a prospective, randomized study of immediate cytologic evaluation". *Chest* 112.2 (1997): 423-425.

9. Mazza E., *et al.* "On-site evaluation of percutaneous CT-guided fine needle aspiration of pulmonary lesions. A study of 321 cases". *La Radiologia Medica* 110.3 (2005): 141-148.

10. Moulton JS and Moore PT. "Coaxial percutaneous biopsy technique with automated biopsy devices: value in improving accuracy and negative predictive value". *Radiology* 186.2 (1993): 515-522.

11. Anderson JM., *et al.* "CT-guided lung biopsy: factors influencing diagnostic yield and complication rate". *Clinical Radiology* 58.10 (2003): 791-797.

12. Haramati LB. "CT-guided automated needle biopsy of the chest". *American Journal of Roentgenology* 165.1 (1995): 53-55.

13. Birchard KR. "Transthoracic needle biopsy". *Seminars in Interventional Radiology* 28.1 (2011): 87-97.

14. Klein JS and Zarka MA. "Transthoracic needle biopsy". *Radiologic Clinics of North America* 38.2 (2000): 235-266.

15. Yanardag H., *et al.* "Diagnostic value of transthoracic needle biopsy in 121 cases with peripheral pulmonary mass". *The Internet Journal of Internal Medicine* 4:2 (2004): 67-70.

16. Hiraki T., *et al.* "CT fluoroscopy-guided biopsy of 1,000 pulmonary lesions performed with 20-gauge coaxial cutting needles: diagnostic yield and risk factors for diagnostic failure". *Chest* 136 (2009): 1612-1617.

17. Inoue D., *et al.* "CT fluoroscopy-guided cutting needle biopsy of focal pure ground-glass opacity lung lesions: diagnostic yield in 83 lesions". *European Journal of Radiology* 81 (2012): 354-359.

18. Hur J., *et al.* "Diagnostic accuracy of CT fluoroscopy-guided needle aspiration biopsy of ground-glass opacity pulmonary lesions". *American Journal of Roentgenology* 192 (2009): 629-634.

19. Zhuang YP., *et al.* "Diagnostic accuracy and safety of CT-guided fine needle aspiration biopsy in cavitary pulmonary lesions". *European Journal of Radiology* 82 (2013): 182-186.

20. Lee SM., *et al.* "C-arm cone-beam CT-guided percutaneous transthoracic needle biopsy of lung nodules: clinical experience in 1108 patients". *Radiology* 271 (2014): 291-300.

21. Choo JY., *et al.* "Percutaneous transthoracic needle biopsy of small (≤ 1 cm) lung nodules under C-arm cone-beam CT virtual navigation guidance". *European Radiology* 23 (2013): 712-719.

22. De Filippo M., *et al.* "Predictive factors of diagnostic accuracy of CT-guided transthoracic fine-needle aspiration for solid noncalcified, subsolid and mixed pulmonary nodules". *La Radiologia Medica* 118 (2013): 1071-1081.

23. Inoue D., *et al.* "CT fluoroscopy-guided cutting needle biopsy of focal pure ground-glass opacity lung lesions: diagnostic yield in 83 lesions". *European Journal of Radiology* 81 (2012): 354-359.

24. Yamagami T., *et al.* "Percutaneous needle biopsy for small lung nodules beneath the rib under CT scan fluoroscopic guidance with gantry tilt". *Chest* 126 (2004): 744-747.

25. Ng YL., *et al.* "CT-guided percutaneous fine-needle aspiration biopsy of pulmonary nodules measuring 10 mm or less". *Clinical Radiology* 63 (2008): 272-277.

26. Zhuang YP., *et al.* "Diagnostic accuracy and safety of CT-guided fine needle aspiration biopsy in cavitary pulmonary lesions". *European Journal of Radiology* 82 (2013): 182-186.

27. Lee SM., *et al.* "C-arm cone-beam CT-guided percutaneous transthoracic needle biopsy of lung nodules: clinical experience in 1108 patients". *Radiology* 271 (2014): 291-300.

28. Zhan P., *et al.* "Management strategy of solitary pulmonary nodules". *The Journal of Thoracic Disease* 5 (2013): 824-829.

29. Ost D., *et al.* "Clinical practice. The solitary pulmonary nodule". *The New England Journal of Medicine* 348 (2003): 2535-2542.

30. Li H., *et al.* "Diagnostic accuracy and safety of CT-guided percutaneous needle aspiration biopsy of the lung: comparison of small and large pulmonary nodules". *AJR* 167 (1996): 105-109.

31. Haaga JR and Alfidi RJ. "Precise biopsy localization by computer tomography". *Radiology* 118 (1976): 603 -607.

32. Cohan RH., *et al.* "CT assistance for fluoroscopically guided transthoracic needle aspiration biopsy". *Journal of Computer Assisted Tomography* 8 (1984): 1093-1098.

33. Moore EH. "Technical aspects of needle aspiration lung biopsy: a personal perspective". *Radiology* 208 (1998): 303-318.

34. Westcott JL. "Direct percutaneous needle aspiration of localized pulmonary lesions: result in 422 patients". *Radiology* 137 (1980): 31-35.

35. Kazerooni EA., *et al.* "Risk of pneumothorax in CT-guided transthoracic needle aspiration biopsy of the lung". *Radiology* 198 (1996): 371-375.

36. Garcia-Rio F., *et al.* "Use of spirometry to predict risk of pneumothorax in CT-guided needle biopsy of the lung". *Journal of Computer Assisted Tomography* 20 (1996): 20-23.

37. Laurent F., *et al.* "Pneumothoraces and chest tube placement after CT-guided transthoracic lung biopsy using a coaxial technique: incidence and risk factors". *AJR* 172 (1999): 1049 -1053.

38. Ko JP., *et al.* "Factors influencing pneumothorax rate at lung biopsy: are dwell time and angle of pleural puncture contributing factors?" *Radiology* 218 (2001): 491-496.

Volume 10 Issue 4 April 2021