EFFICACY AND SAFETY OF IMAGING-GUIDED TRANSTHORACIC NEEDLE LUNG BIOPSY – A REAL-LIFE STUDY

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EFFICACY AND SAFETY OF IMAGING-GUIDED TRANSTHORACIC NEEDLE LUNG BIOPSY - A REAL-LIFE STUDY (Abstract): Despite global efforts, the challenge of early-stage diagnosis of lung cancer persists. To improve diagnose of peripheral lung tumors, a less invasive, cost-effective, and time-efficient sampling technique is essential. Percutaneous imaging-guided transthoracic lung biopsy meets these criteria. **Aims:** This study aims to determine the efficacy of imaging-guided transthoracic needle lung biopsy and to identify periprocedural complications and diagnostic success rate in a tertiary pulmonology center. **Materials and methods:** We conducted in "Marius Nasta" Institute of Pulmonology, from Bucharest, Romania, a retrospective, observational study on consecutive patients diagnosed with lung, pleural or chest wall tumors that underwent transthoracic Computed-Tomography (CT)-scan guided needle biopsy or ultrasound (US)-guided needle biopsy. The efficacy and safety of these procedures were assessed. **Results**: We enrolled 280 patients, with 261 undergoing CT-scan transthoracic guided percutaneous needle biopsy and 19 undergoing US-guided needle biopsy, between 2021 and 2023. Histopathological results were obtained in 267 cases (95.35%) of lung biopsies, with only 13 (4.64%) inconclusive specimens. The reports identified 225 (80.35%) malignant tumors and 42 (15%) other diseases. Out of 225 malignant tumors, 193 (85.77%) were NSCLC. Out of NSCLC 103 were lung adenocarcinomas (53.36%). Periprocedural complications rate was 23.22%, mainly pneumo-thorax, hemoptysis and alveolar hemorrhage. No fatal outcome was recorded. **Conclusions**: The study underscores the efficacy of percutaneous CT-guided or US-guided transthoracic needle lung biopsy in clinical practice, with an affordable risk of complications. The implication of a multidisciplinary team is essential for the best outcome. **Keywords**: LUNG CANCER, HISTOPATHOLOGICAL TYPE, CT-GUIDED TRANSTHORACIC LUNG BIOPSY, US-GUIDED TRANSTHORACIC LUNG BIOPSY.

INTRODUCTION

In 2022, according to the European Cancer Information System, the European Union (EU27) alone estimated a total number of 319,236 new cases of lung cancer (incidence rate 71.5 per 100,000). It is the

second most diagnosed cancer in men (incidence rate 93 per 100,000) after prostate cancer and the third after breast and colorectal cancers in women (incidence rate 50.9 per 100,000). It ranks as the second most frequent malignancy with an estimated total number in the EU27 of 803,644 cases (prevalence rate 170.4 per 100,000). In Romania 11,716 new cases were diagnosed (incidence rate 61.5 per 100,000), with a significant difference between men (incidence rate 92 per 100,000) and women (incidence rate 32.8 per 100,000). The prevalence rate in Romania was 143.6 per 100,000 (27,016 total cases). Additionally, lung cancer stands as the leading cause of cancer-related mortality, with a mortality rate of 18 per 100,000 people (1).

Despite these staggering statistics and world-wide efforts to improve survival rates, early-stage diagnosis remains challenging. Early diagnosis and treatment of small, localized lung tumors is highly recommended. To facilitate this, a tumoral lung biopsy and histopathology confirmation are mandatory. The sampling technique should be less invasive, cost-effective, with a lower complication rate, and more time-efficient for medical staff compared to classical surgical methods. While ultrasound (US)-guided transbronchial lung biopsy is efficient for contiguous lesions, it faces challenges for peripheral ones (limited availability of endobronchial-navigation equipment). Despite their high diagnostic success rate, open lung biopsy and video-assisted thoracoscopic surgery (VATS) come with restriction related to poor clinical status of some patients and greater morbidity and complications (2). A proposed alternative solution meeting the outlined criteria is imaging-guided transthoracic needle lung biopsy.

This study aims to determine the efficacy of imaging-guided transthoracic needle lung biopsy in "Marius Nasta" Institute of Pulmonology, Bucharest, Romania, a tertiary pulmonology center, and to identify periprocedural complications and diagnostic success rate.

MATERIALS AND METHODS

We conducted a retrospective, observational study on consecutive patients diagnosed with lung, pleural or parietal tumors that underwent transthoracic Computed-Tomography (CT)-scan guided needle biopsy or ultrasound (US)-guided needle biopsy, between 2021 and 2023. All patients were hospitalized. Coagulation tests (Prothrombin Activity, Activated Partial Thromboplastin Clotting Time, International Normalized Ratio), along with a total blood cell count and other routine analyses, were conducted before the procedure. Additionally, medications for bleeding control and platelet function were adjusted or ceased according to international guidelines.

For all subjects, bronchoscopy was performed previously and endobronchial or transbronchial biopsies were not possible or were inconclusive for histopathology diagnosis. All cases were selected by a team consisting of a pulmonologist, a radiologist and a thoracic surgeon. The procedure was made by a specialized radiologist, in the presence of a thoracic surgeon prepared for immediate intervention, if needed.

We made a rigorous patient selection, considering the following indications:

- New or growing solitary nodules (more than 8 mm in diameter) or masses on chest imaging that are not amenable to diagnosis by bronchoscopy or are unlikely to be accessible by bronchoscopy;
- Multiple nodules in a patient not known to have malignancy or who has experienced prolonged remission or has more than one primary malignancy;

- Persistent focal infiltrates or consolidations, either single or multiple, for which no diagnosis has been made by sputum or blood culture, serology, or bronchoscopy;

We used 16-slice computed tomography scanner Neusoft (CT-guided) and a 5 MHz curvilinear (ultrasound guided). Regarding the needles, Medax Medeasy semi-automatic spring-loaded biopsy system was used, with 16, or 18 gauge.

Informed consent was obtained from all patients after an extensive discussion. Relevant blood tests and radiological exams were reviewed prior to the procedure. In order to facilitate the safest and most effective needle pathway, the patient was positioned accordingly: supine, prone or lateral decubitus. A first CT-scan acquisition of the thorax was performed to locate the target lesion and to determine the entry level, where a dotted line of radio-opaque markers was applied on patient's skin. A second volumetric CT scan was done, centered on the markers and including the entire target lesion. A specific entry point from the line was chosen. Then, on the disinfected area (using povidone-iodine) local anesthesia with 1% lidocaine was performed. Using measurements and repeated CT scans of that range the introducer needle was positioned in the target lesion. Biopsies were performed using a 16G or 18G coaxial semiautomatic biopsy device with adjustable sample notch (10 mm/20 mm). Needle size, sample number and length depend on lesion dimensions, degree of necrosis, risk of complications and patient status. The number of specimens collected ranged between 1 and 8 fragments. Fragments were placed in a labelled recipient containing 4% formaldehyde solution and sent to the histopathology lab.

For ultrasound guided procedures, suitable patients were selected, and a 5 MHz curvilinear probe was used for biopsy guidance. A 16G or 18 G semiautomatic biopsy needle was used directly without the coaxial to remove the samples.

All patients were monitored: CT-scan immediately after procedure and a chest X-ray 2 hours after. If stable, elective patients without signs of complications were discharged in the same day. The others were monitored for 24 hours in the hospital.

All data were collected from the hospital's electronic medical record database and personal identification data of the patients were anonymized.

Patients consented for using the data for scientific purposes with the condition of anonymity. The approval of the study by the Ethics Committee of the Institute was obtained.

Statistical correlations were generated in *SPSS version 29.0.2.0* (IBM), while the database was collected and organized in Microsoft Office Excel. The results were expressed as mean values ± standard deviation or as an absolute number (percentages). The results were considered statistically significant for a value of $p<0.05$, and were represented using graphs, histograms and tables.

RESULTS

A number of 280 consecutive patients that underwent CT-guided or US-guided transthoracic needle biopsy for lung, pleural or chest wall tumors were included.

Regarding the types of guidance for transthoracic needle approach, we used two types of imaging guidance: computed tomography (261 cases) and ultrasound (19 cases). Ultrasound guidance was more frequently used for pleural histopathology, chest wall involvement and peripheral lung lesions (3).

From the total number of patients, 189 were males (67.5%) with a gender ratio was M: F = 2.07: 1. The mean age was

62.99 years ± 10.92 SD (fig. 1).

Regarding smoking status, 135 patients were smokers or former smokers (48.21%), 20 patients were non-smokers (7.1%), and for 125 patients (44.6%), we were not able to find data about smoking history in database. Occupational exposure was seen in 71 patients (25.35%).

Regarding comorbidities, 132 patients (47.14%) had respiratory diseases (fig. 2).

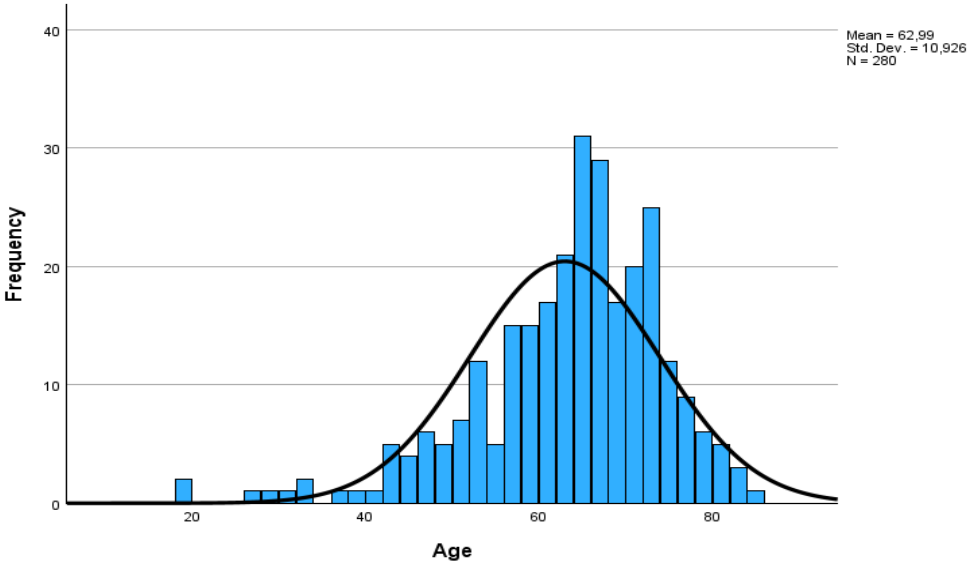

Fig. 1. Age distribution of the patients

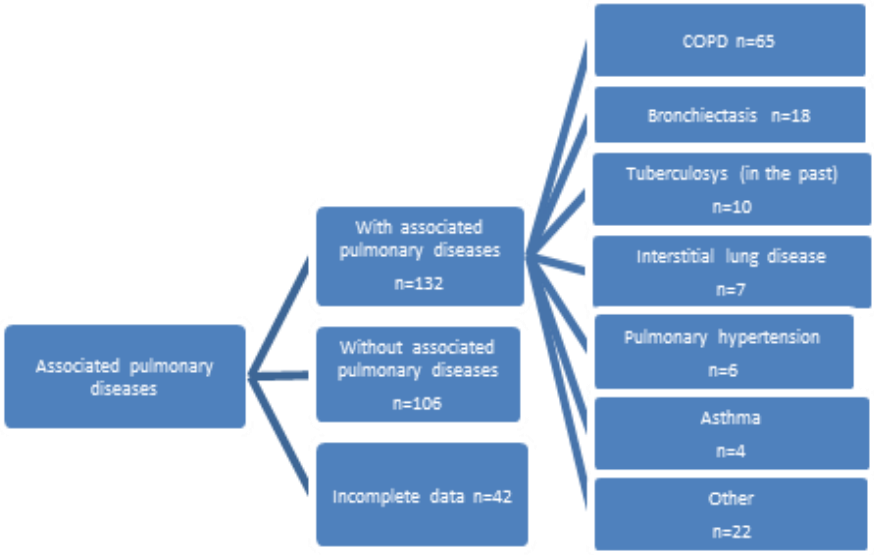

Fig. 2. Distribution of pulmonary comorbidities

The main pulmonary disease was chronic obstructive pulmonary disease (65 patients). A number of 191 subjects had other comorbidities, mainly cardio-vascular and metabolic disorders (fig. 3).

Anemia is only present in 12 patients, while 50 subjects had no other diagnosis.

Out of 280 imaging-guided transthoracic needle biopsies, 267 were diagnostic (95.35%). Only 13 biopsies were inconclusive. Positive results for malignant tumors were obtained in 225 cases (84.26%). Lung cancer was the most frequent (194 cases) with only one case of Small-Cell Lung Cancer (SCLC) and 193 cases of Non-Small-Cell Lung Cancer (NSCLC), with the following subtypes: adenocarcinomas (103 cases, 53.36%), NSCLC-no other specified (NOS) (47 cases, 24.35%), Squamous Cell Carcinoma (32 cases, 16,58%) and undifferentiated carcinoma (11 cases, 5.69%).

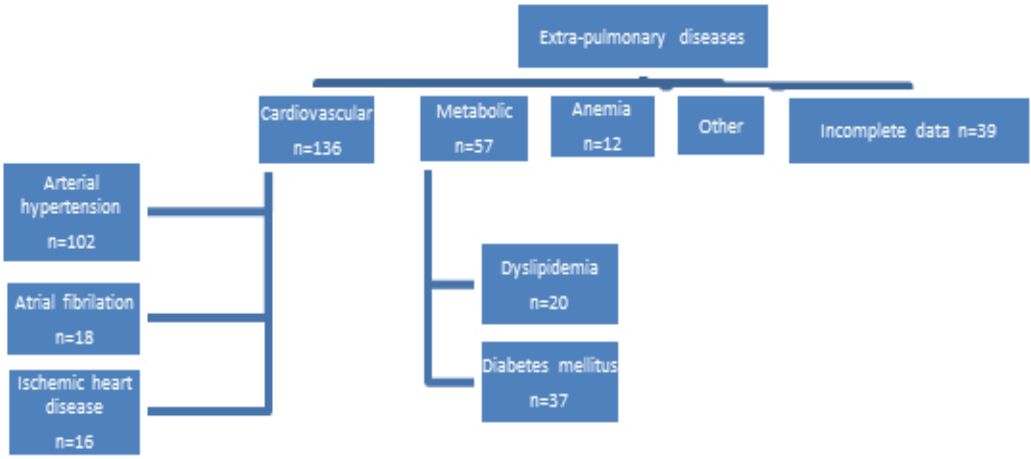

Fig. 3. Extra pulmonary comorbidities distribution

In other 31 cases, malignancy was confirmed, as following: 12 metastases from other distant malignant tumors, 4 neuroendocrine origin tumors other than SCLC, 5 Non-Hodgkin lymphomas, 3 lymphoproliferative malignant disorders, 1 sarcoma, 1 plasmacytoma and 5 only malignant tumoral aspect without definite histopathological pattern.

Among the remaining results, from the 267 conclusive results, 28 cases (10.48%) had “no tumoral aspect”. Additionally, 14 cases (4.86%) were benign lesions: 8 chronic inflammation, 2 pulmonary tuberculosis, 2 fibrinoid pleural mass, 1 organizing pneumonia, and 1 case of thymoma (fig. 4).

Post-procedural complications were seen in 23.22% of procedures (65 cases): 51 cases of small to mild pneumothorax (18.21%), 10 alveolar hemorrhage (3.57%), 7 hemoptysis (2.5%), and 2 subcutaneous emphysema (0.71%) (fig. 5). No severe nor fatal outcome occurred.

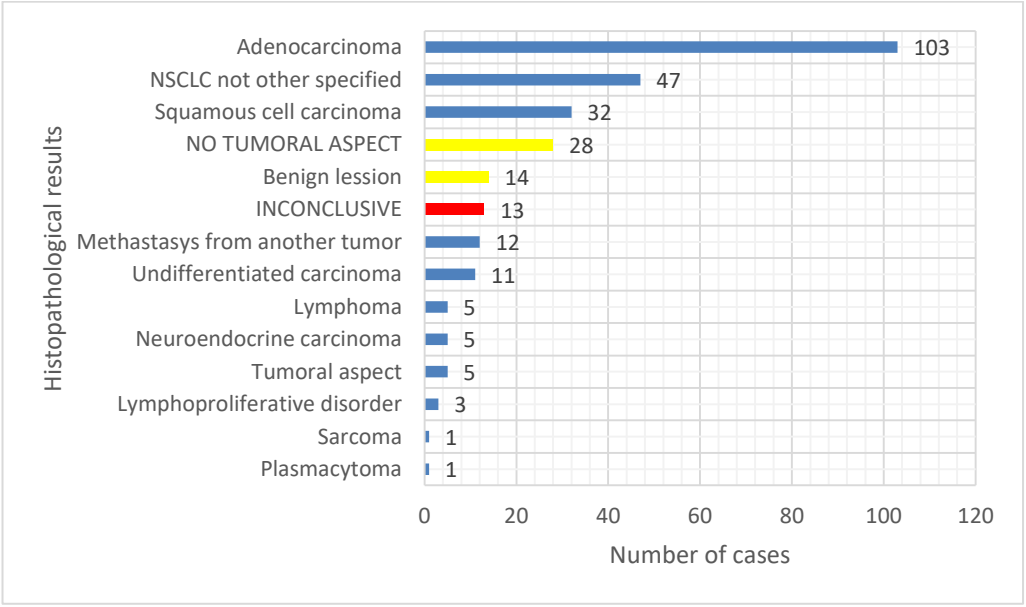

Fig. 4. Distribution of histopathological results

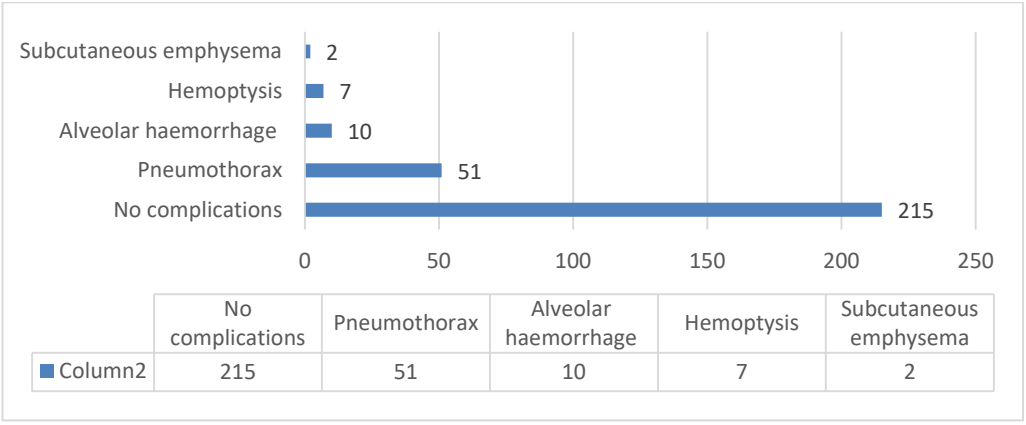

Fig. 5. Post-procedural complications

DISCUSSION

Lung cancer remains a major contributor to cancer-related morbidity and mortality worldwide. Achieving an accurate diagnosis is essential for guiding effective treatment strategies, with histopathological examination serving as a cornerstone in the diagnostic process for pulmonary tumors. Two minimally invasive techniques, bronchoscopy and CT-guided transthoracic biopsy, have proven instrumental in obtaining tissue samples for histological analysis. For centrally located tumors, bronchoscopy is the preferred method, offering direct access to the lesion. However, peripheral tumors pose a greater challenge for tissue sampling. While surgical approaches, such as classical thoracotomy or video-assisted

thoracoscopy (VATS), are highly effective for obtaining biopsies, they are invasive. A less invasive alternative is imaging-guided transthoracic needle biopsy, which uses CT or ultrasound guidance to target and sample peripheral lesions. Histopathological analysis of tissue samples obtained via these methods enables precise tumor characterization, including subtyping of non-small cell lung cancer (NSCLC) versus small cell lung cancer (SCLC), and assessing molecular biomarkers crucial for personalized therapy. This multimodal diagnostic approach plays a vital role in early detection, staging, and treatment planning of lung cancer, improving patient outcomes in this challenging disease.

The aim of this study was to determine the efficacy of imaging-guided transthoracic needle lung biopsy in a tertiary pulmonology center in Romania, and to identify periprocedural complications.

Out of 280 consecutive patients that underwent CT-guided or US-guided transthoracic needle biopsy for thoracic tumors, 267 yielded a definitive diagnosis, resulting in a diagnostic accuracy of 95.35%. This aligns with data reported in the literature, which highlights a high diagnostic success rate ranging from 78%-85% (4-6) to 92.9%-96.8% (7, 8). However, for nodules smaller than 1.5cm, the diagnostic rate is lower (9). These favorable outcomes were achieved through a multidisciplinary team approach involving pulmonologists, radiologists, and thoracic surgeons. This collaborative team carefully selected candidates for the procedure, maintaining a balance between benefits and potential risks. An important issue is to exclude extensive necrosis of the tumor, honeycombing, and large emphysema areas. High risks patients, for which the benefits would have been limited, were not accepted to undergo the procedure. For example, the case of a patient with a history of pneumonectomy due to lung cancer (10 years before the actual evaluation) and extensive emphysema with a lung nodule was rejected due to high risk of respiratory failure.

Out of 267 confirmed cases, 225 were malignant tumors, lung cancer being the most prominent (194 cases). This distribution is according to our expectations, given the hospital's focus on pulmonary diseases.

Positive results for malignant tumors were obtained in 225 cases (84.26%). Lung cancer was the most frequent (194 cases), 193 cases being Non-Small-Cell Lung Cancer (NSCLC). Pulmonary adenocarcinoma was the most prevalent (103 cases, 53.36%), which is similar to other study where 60% were adenocarcinomas (10), reinforcing the well-established trend of adenocarcinoma predominance in the last decade. This is probably due to peripheral location of the adenocarcinomas (11), that means that imaging-guided transthoracic needle biopsy is the appropriate tool to manage this situation. Other histopathological types were: NSCLC-no other specified (NOS) (47 cases, 24.35%), Squamous Cell Carcinoma (32 cases, 16,58%) and undifferentiated carcinoma (11 cases, 5,69%). For NSCLC-NOS specimens were sent to immunohistochemistry analysis to better characterize the tumor.

Statistical analysis revealed a significant correlation between COPD and malignant results (p=0.019; CI=95%), as both diseases are smoke-related diseases.

Among the non-malignant results, 28 cases (10.48%) had “no tumoral aspect”, and 14 cases (4.86%) were benign lesions: 8 chronic inflammation, 2 pulmonary tuberculosis, 2 fibrinoid pleural mass, 1 organizing pneumonia, and 1 case of thymoma. We noticed only 2 cases of pulmo-

nary tuberculosis aligned with the decreasing incidence of tuberculosis in Romania in the last decade.

In order to identify possible complications associated with the technique, a thoracic CT scan was performed immediately after the procedure, and an additional chest X-ray was done 2 hours later. These were performed to assess the presence of pneumothorax, hemothorax, or alveolar hemorrhage. Complications, such as pneumothorax, hemoptysis, alveolar hemorrhage and air embolism may occur in 25.8%, as described in one meta-analysis (12). Pneumothorax was the main complication, between 23.3 and 25.9% as in one large meta-analysis on 23,104 patients (13). Higher frequency was observed in elderly individuals with underlying diseases such as emphysema or honeycombing (14).

Our study shows a post-procedural complications rate of 23.22% with 65 cases of complications, but none of them being severe or lethal. We reported small to mild pneumothorax in 18.21% of cases, alveolar hemorrhage 3.57%, hemoptysis 2,5%, and subcutaneous emphysema in 0,71% of cases. Notably, lesions located in the lower lobes were associated with a significantly higher risk of complications (p=0.043; 95% CI).

Periprocedural complication rates appeared higher with age (p=0.046; CI=95%). Underlying COPD, diabetes mellitus, anemia, chronic heart failure, atrial fibrillation, arterial hypertension did not significantly correlate with complications (p>0,05). The lack of correlation might suggest the high safety profile of the procedure.

Additionally, the number of samples was not correlated with complications (p=0.069; CI=95%). The number of specimens collected ranged between 1 and 8 fragments, with a mean value of 3.03+/-1.15. As mentioned before, we did not determine the quantity and/or the quality of the specimens. Although this study's purpose was not to evaluate a standardized quality and quantity of the samples, we observed that a higher number of samples was not significantly correlated with a suitable, conclusive biopsy (p=0.069; CI 95%), which might suggest that the quality of specimens may be more important. Moreover, advanced lung cancer (presence of metastasis) does not correlate with higher diagnostic rate (p=0.35; CI 95%), though, regarding the technique, CT-guided technique tended to offer a higher number of fragments (p=0.01; CI 95%).

Limitations of the study: Data regarding smoking or exposure status was limited due to the patient's refusal to provide the information or the information not being tracked in the available documents. Another constraint encountered is the availability of internal immunohistochemistry infrastructure. In this situation, immunohistochemistry tests were done by external laboratories for multiple samples.

CONCLUSIONS

This study underscores the significance of a less invasive, cost-effective technique with a lower complication rate for lung biopsy. The success diagnostic rate is 95.35% and is not correlated with higher number of fragments, highlighting the importance of a quality specimen. Further studies might include a standardized qualitative and quantitative analysis of the samples in order to validate the hypothesis. Complication rate of the procedure significantly correlates with older age, and lower lobes localization.

Lung adenocarcinoma diagnosis was the main histopathological subtype of lung cancer diagnosed by this procedure.

In our center, imaging-guided lung biopsy has significantly reduced the time between detecting suspicious lung lesions and initiating appropriate oncological treatment (once confirmed). The implication of a pneumologist-radiologist-thoracic surgeon team is essential, as they proceed to select the patients in order to minimize inconclusive samples and to evaluate risk benefits ratio.

CONFLICT OF INTEREST AND FUNDING

The authors declare no conflicts of interests. The research did not receive external funding.

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