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Original Article

Pneumothorax and pulmonary hemorrhage frequency and risk factors of computed tomography-guided transthoracic pulmonary biopsy complications

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Abstract
Introduction: We aimed to analyze the frequency and risk factors of pneumothorax and pulmonary hemorrhage caused by Computed Tomography (CT) guided needle biopsy.
Methods: Demographical features, pneumothorax and pulmonary hemorrhage frequencies/risk factors, characteristics of lesions of patients who underwent a CT-guided lung biopsy in our institution between January 2013 and August 2013 were reviewed retrospectively. The lesions were classified to the groups as nodular lesions ≤ 3 cm in diameter, nodular lesions > 3 cm and consolidated lesions. Pneumothorax and pulmonary hemorrhage frequencies among groups were compared using a chi-square test. A $p < 0.05$ was accepted as statistically significant.
Results: A total number of 122 patients with a mean age of 61 ± 13 (19-88) years were included. 28 (23%) patients were female and 94 (77%) were male. 30 (24%) lesions were nodular lesions ≤ 3 cm in diameter, 57 (47%) were nodular lesions > 3 cm, and 35 (29%) were consolidated lesions. Pneumothorax developed in 15 (12%) patients while a chest tube insertion was required in 4 (3%) of them. Pulmonary hemorrhage occurred in 14 (11%) patients. Hemoptysis and hemothorax were not observed in this study. Pleura-based lesions was significantly less associated with pneumothorax when compared with ones far from pleura ($P < 0.001$). Usage of 17-gauge needle was significantly more associated with pneumothorax than 19-gauge (p:0.048). Pulmonary hemorrhage was significantly less observed during the biopsy of lesions > 3 cm than < 3 cm ($P < 0.001$).
Conclusion: Nodular lesions ≤ 3 cm, location far from pleura and usage of 17-gauge needle tend to be associated with more frequent lung biopsy complications.

Introduction

Lung cancer is the most common leading cause of cancer death. It may be associated with congenital conditions as well as environmental factors such as smoking and air pollution, which markedly increase the risk of neoplasm.[1] It is the most common cancer among males while the incidence is increasing among females due to the increased frequency of smoking.[2] The survival rates of patients with advanced-stage lung cancer are very poor. European Society of Radiology and European Society of Respiratory recommend annual CT scans with low dose radiation for the early detection of cancer in the individuals with risk factors. With the increased usage of CT, lung nodule detection and the number of nodule biopsies have been increased.[3,4] CT-guided transthoracic needle biopsy (CT-TTNB) is a minimally invasive procedure that prevents major surgical interventions and provides a safe and effective tissue sampling for the histopathological examination.[5,6] The indications of CT-TTNB include differentiation of malignant/benign lesions, grading the malignant diseases, the investigation of the primary source of a metastatic lesion, identification of parenchymal diseases, research infectious and non-infectious processes.[6] The coaxial technique in this method which provides multiple samplings after a single puncture following the placement of a guidewire, markedly reduces complication frequency.[7] However most of the complications are minor, but major and life-threatening complications are also observable among the patients. The patients must be followed closely and the major complications must be recognized and managed promptly.[6] For this reason, the severity and the frequency of the complications associated with lung biopsy and the risk factors for the complications must be well-known by the radiologists, interventional radiologists and clinicians.

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Methods

Patients

The medical records of a total of 122 patients who underwent a CT-TTNB were retrospectively screened on interventional radiology department reports and hospital database. All the patients were informed regarding the procedure and the symptoms-signs associated with possible complications of biopsy. Anticoagulant agents were stopped for at least 3 days before the procedure. The biopsy was not performed in the patients with an ınternational normalized ratio (INR) ≤ 1.5 and platelet count > 50 000 K/UL. Non-cooperative and disoriented patients, patients with contralateral pneumonectomy and severe chronic obstructive lung disease history were excluded from the study

Biopsy technique

The morphological characteristics, sizes, location and enhancement features of the lesions were evaluated on previous imagings of the patients. Biopsy routes were planned regarding the crossing interlobar fissures, presence of bullous lesions, neighboring major vascular-cardiac and mediastinal structures, and finally the most safest route was identified.

Biopsy procedures were performed by two radiologists (Y.D, Ü.Ç.) who have 7 and 10 years of experience in interventional chest radiology by a CT system (Pratico CT, Hitachi Medical System, Japan). All the patients were scanned from the level of lung apex to the level of the caudal endpoint of costophrenic angles by a routine thorax CT protocol (slice thickness 2,5 mm, 120 kV, 150-180 mAs). Samplings were performed by a 17-gauge or 19-gauge guide needle and an 18-gauge or 20-gauge co-axial semi-automatic biopsy device with 2 cm penetration depth (US Biopsy; A Division of Promex Technologies, Franklin, IN, USA) on the most eligible position (supine or prone or lateral decubitus).

The most suitable axial image regarding the biopsy plane was chosen on the first scans and the exam table of the CT device was placed at this level. The distance of the lesion from the midline was identified by a laser light originating from the device and the entry site was marked on the patients' skin. A local anesthesia with 1-2% lidocaine was performed after sterilization of this site. After a local anesthetization, a minor skin incision was followed by insertion of the guide needle to the chest wall. Before punching the pleura, the distance from the needle to the lesion and the correct angle of the needle were identified by the new scans. After the confirmation of the route and the angle, the needle was passed quickly and gently through the pleura when patients were breath-holding. The needle was advanced to the margin of the lesion and controlled on the scans. Only one puncture was performed an all patients. After the confirmation of the correct position of the needle in the margin of the lesion, a co-axial biopsy device was advanced to the lesion via the guide needle. Four samples were taken from various directions (perpendicular to each other) of each lesion. After the sampling, the stylet of the guide needle was replaced and the coaxial guide needle was removed gently. For the detection of the complications, a CT scan was performed 5 minutes after the procedure. After 4 hours, a control posteroanterior chest roentgenogram was obtained. Complications were recorded according to CT scans and chest roentgenograms. For patients with severe dyspnea and pneumothorax or hemothorax, a chest tube placement was performed.[8]

Groups and complications

CT features were reported regarding the lesion location (upper-lower-middle lobe), diameter (maximal axial diameter), and morphology(nodular ≤ 3 cm- nodular > 3 cm-consolidated). Patients were classified into two groups according to their age as < 65 and ≥ 65 years old. The size of the needle were selected regarding the guide needle diameter as 17- and 19-gauge. Also all the lesions were classified into two subgroups according their distance to pleura as pleura-based and intraparenchymal distinct from pleura (distance from pleura ≥1 mm) lesions. All these variables were compared with each other for complication types and frequency. Pneumothorax, hemothorax, parenchymal hemorrhage, and hemoptysis were identified as complications of the procedure.

The parenchymal hemorrhage was defined as the presence of parenchymal ground-glass opacity or consolidation around the lesion or along the biopsy route which was not observed before the procedure. Air in the pleural space was identified as pneumothorax and fluid as hemothorax which occurred during or after the procedure. Hemoptysis was accepted as fresh blood originating from the respiratory tract.[9-11]

Statistical analysis

Categorical variables were presented as frequency (n) and percentage (%), numerical variables were expressed as mean ± standard deviation, minimum and maximum. A chi-square test was used for the comparison of categorical variables. A $P < 0.05$ was considered statistically significant. All the statistical analyses were made by an SPSS 20 software program (IBM Corporation, Armonk, NY, USA).

Results

Among the studied 122 patients (mean age 61 ± 13 years (19-88)) included in this study, 28 (23%) were female and 94 (77%) were male. 65 (53%) lesions were observed in the right and 57 (47%) were in the left lung. Among 29 lesions in which complications occurred, 16 were in right (25%, 16/65) and 13 (23%, 13/57) in the left lung (Table 1). There was not statistically significant difference observed between two lungs regarding to the complication rate ($P = 0.815$).

Table 1. Features of the patients, lesions and the biopsy procedures

Variable	No. (%)
Gender	
Female	28 (23)
Male	94 (77)
Age (y)	
<65	69 (57)
≥65	53 (43)
Diameter of the lesion	
≤3 Nodular	30 (24)
>3 Nodular	57 (47)
Consolidation	35 (29)
Location of the lesion	
Upper lobes	64 (53)
Middle lobe	14 (11)
Lower lobes	44 (36)
Diameter of the needle	
19-Gauge	84 (69)
17-Gauge	38 (31)
Pleura-based	
Yes	70 (57)
No	52 (43)
Complication	
No complication	93 (76)
Pneumothorax	15 (12)
Hemorrhage	14 (11)
Hemoptisis	0 (0)
Hemothorax	0 (0)

The morphological appearance of 30 (24%) lesions were nodular ≤ 3 cm, 57 (47%) were nodular > 3 cm, and 35 (29%) were consolidated. The mean diameter of nodular lesions was 55 ± 49 mm (15 mm-100 mm). The complication frequency of nodular ≤ 3 cm lesions was 50%, nodular > 3 cm was 21%, and consolidation was 6%. The overall complication rate of nodular ≤ 3 cm lesions was statistically significantly higher than nodular > 3 cm and consolidated lesions ($P < 0.001$ and $P < 0.001$, respectively). Also the complication rate of nodular > 3 cm lesions was significantly higher than the consolidated lesions ($P = 0.047$).

Lesions were most commonly located in the upper lobes (n = 64, 53%)of the lungs. The complication rate was 22% in upper lobes, where 30% were in the lower lobes, and 14% in middle lobe. There was not statistically significant difference in the complication rates between upper-lower and middle lobes ($P = 0.366$, $P = 0.524$, and $P = 0.256$, respectively).

Pneumothorax occurred in 15 (12%) (Figure 1) patients while in 4 (3%) of them, a chest tube insertion was required. Pneumothorax was resolved spontaneously in 11 cases and in 4 cases no further intervention was required. Hemorrhage occurred in 14 patients (11%) (Figure 2), while none of them needed intervention (Table 2).

The occurrence of pneumothorax was not significantly different between females and males ($P = 0.970$) as well as between patients < 65 and ≥ 65 years old ($P = 0.788$). Pneumothorax occurred in 13% of the ≤ 3 cm nodular lesions, 16% of > 3 cm nodular lesions and 6% of consolidated lesions. The differences between the three groups were non-significant ($P = 0.761$, $P = 0.154$, and

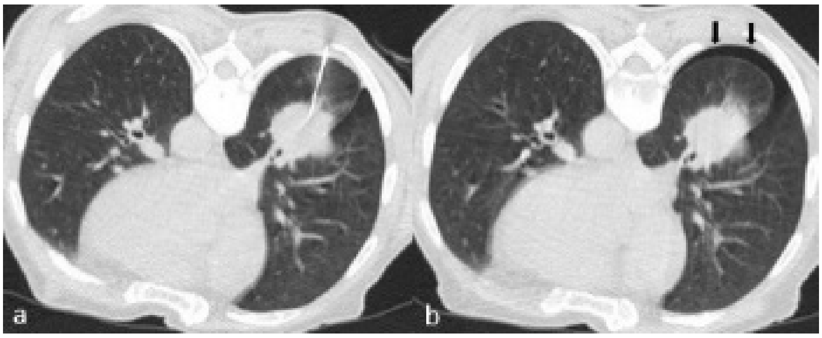

Figure 1. (a,b) Pneumothorax (black arrow) occurred after a CT-TTNB to the lesion in right upper lobe

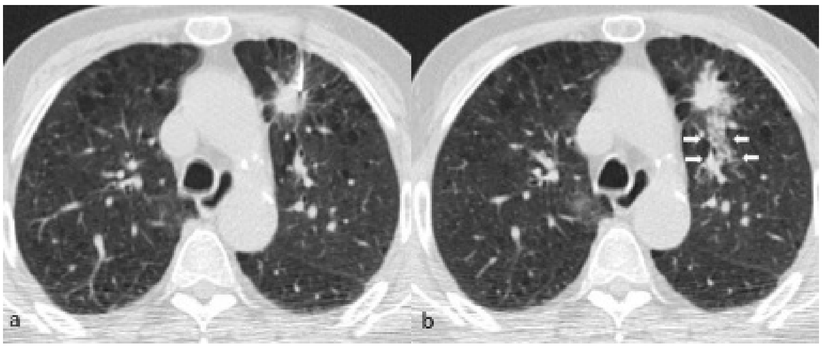

Figure 2. (a,b) Hemorrhage (white arrow) posterior to lesion the in left upper lobe after a CT-TTNB

Table 2. Risk factors for pneumothorax and hemorrhage

Variable	Pneumothorax (n = 15)	Hemorrhage (n = 14)
	No. (%)	No. (%)
Gender		
Female	3 (20)	3 (21)
Male	12 (80)	11 (79)
Age		
< 65	8 (53)	6 (43)
≥ 65	7 (47)	8 (57)
Diameter of the lesion		
≤ 3 cm nodular	4 (27)	11 (79)
> 3 cm nodular	9 (60)	3 (21)
Consolidation	2 (13)	0 (0)
Location of lesion		
Upper lobes	7 (47)	7 (50)
Middle lobes	2 (13)	0 (0)
Lower lobes	6 (40)	7 (50)
Diameter of the needle		
19-Gauge	7 (47)	8 (57)
17-Gauge	8 (53)	6 (43)
Pleural-based		
Yes	2 (13)	6 (43)
No	13 (87)	8 (57)

$P = 0.293$, respectively).

Pneumothorax was detected in 25% of the intraparenchymal lesions and 3% of pleura-based lesions. The difference in pneumothorax frequency between intraparenchymal and pleura-based lesions was statistically significant ($P < 0.001$). Moreover, pneumothorax occurred in 21% of the procedures in which a 17-gauge and 8% in a 19-gauge guide needle was used. The difference in the pneumothorax frequency rate between 17- and 19-gauge groups was statistically significant ($P = 0.048$).

No statistically significant difference was observed for the hemorrhage frequency between females and males, between pleura-based and intraparenchymal lesions, and between 19-gauge and 17-gauge needle patients ($P = 0.886$, $P = 0.417$, $P = 0.243$, $P = 0.315$, respectively).

A Statistically significant difference was observed for hemorrhage frequency between ≤ 3 cm nodular lesions (36.7%) and > 3 cm nodular lesions (5.2%) ($P < 0.001$). In none of the consolidated lesions, hemorrhage was detected. On the other hand, hemorrhage frequency was significantly higher in ≤ 3 cm nodular lesions than the consolidated lesions ($P < 0.001$). But the difference between > 3 cm nodular lesions and consolidated lesions was not statistically significant ($P = 0.168$).

Discussion

Despite all the precautions and appropriate managements, complications may occur after the biopsy procedures. But early recognization and prompt management of the complications of CT-TTNB markedly reduce morbidity and mortality rates and also prevents major invasive interventions. Pneumothorax and parenchymal hemorrhage are the most common complications of CT-TTNB followed by hemoptysis, hemothorax, infection, and air embolism.[4,12,13]

In a meta analysis by Heerink et al, the total frequency of pneumothorax was 25.3% for the coaxial needle biopsy while the frequency of pneumothorax with intervention requirement was 5.6%.[4]

Previous studies suggested small lesion diameters as an important risk factor for pneumothorax with a negative correlation between lesion diameter and pneumothorax frequency.[14,15] Compatible with these studies, we also detected higher overall complication frequency in smaller lesions in this study. But contrary to previous studies, we did not find a statistically significant correlation between lesion diameter and pneumothorax frequency. In a study of Laurent et al, they found mildly higher pneumothorax frequency for lesions > 2 cm (16%) when compared with lesions < 2 cm (15%).[16]

In the literature, many studies reported higher pneumothorax frequency in intraparenchymal when compared with pleura-based lesions and also suggested a positive correlation between distance of the lesion from pleura and pneumothorax frequency.[11,17-19] Lim et al found a statistically significant higher pneumotorax frequency in intraparenchymal when compared with pleura-based lesions ($P < 0.001$).[10] Compatible with previous studies, we also found a similar statistically significant difference ($P < 0.001$).

The frequency of pneumothorax decreases with the decrease in the diameter of the needle. Kuban et al reported pneumothorax frequency as 35% in the procedures performed with 18-gauge and as 23% with 19-gauge guide needle.[7] Also Geraghty et al, suggested statistically significantly ($p < 0.001$) lower pneumothorax frequency with 19-gauge when compared with 18-gauge needle in their series with 846 procedures.[20] We also found a statistically significant difference between 17- and 19-gauge procedures ($P = 0{,}048$) for the pneumothorax frequency.

Hemorrhage may occur after CT-TTNB anywhere along the biopsy tract. Rarely, due to the injury of the vessels located on the way of the needle, hemothorax and chest wall hematoma can be observed. Most of the hemorrhage cases after CT-TTNB, do not require intervention and usually resolve spontaneously.[6] Hypertrophic bronchial arteries, hypervascular tumor, central location, pulmonary hypertension, and bleeding diathesis increase the risk of hemorrhage.[21] The most severe complication of lung biopsy is massive pulmonary hemorrhage. Massive pulmonary hemorrhage must be promptly recognized and treated because it leads to a mortal rapid decrease in O2 saturation in patients with especially limited cardiac reserves.[22]

In a retrospective study of Wiener et al, they found hemorrhage frequency of transthoracic lung biopsy as 12% in their large series.[23] Consistent with this study, we found a similar frequency (n = 14, 11%) in our patients.

Smaller lesion diameters and the longer distance from the pleura to the lesion increased the hemorrhage frequency. In the smaller lesions, the needle exceeds the lesion margin and takes tissue from the intact neighboring lung tissue which leads to a higher hemorrhage frequency.[24-26] Consistent with our study, Tai et al reported a statistically significant higher hemorrhage frequency in the lesions < 3 cm ($P < 0.001$).[27] In addition, it is relatively harder to reach deeper located small nodules and longer procedure time-malposition of the needle due to the movements are more commonly observed in such cases. Also because a longer distance must be traversed by the needle, a vascular injury risk increases.[27] Previous studies suggested that diameter of the needle, location of the lesions and the age of the patients were not associated with hemorrhage risk.[27-29]

Conclusion

Radiologists and the clinicians must be aware of the risk factors, radiological clinical findings of complications and also take precautions to prevent complications such as choosing a suitable needle with optimal sizes and short penetration depth.

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Authors' Contribution

Conceptualization: Yeliz Dadalı, Sercan Özkaçmaz, Ümit Çalıkoğlu.
Data curation: Yeliz Dadalı, Sercan Özkaçmaz, Ümit Çalıkoğlu.
Formal analysis: Yeliz Dadalı.
Investigation: Yeliz Dadalı, Sercan Özkaçmaz.

Study Highlights

What is current knowledge?

- The Computed Tomography-Guided Transthoracic Pulmonary Biopsy is a relatively safe diagnostic method which have various complicaton frequencies regarding the location, sizes, morphological structure of the lesion and the diameter of the needle.

What is new here?

- Intraparenchymal lesions (ones far from pleura) were significantly more commonly associated with pneumothorax when compared with pleura-based lesions.
- Pneumothorax was more frequently observed in the lung biopsy procedures with 17-gauge than with 19-gauge needles
- Pulmonary hemorrhage was significantly less seen during the biopsy of lesions>3 cm than≤3 cm.

Methodology: Yeliz Dadalı, Sercan Özkaçmaz.
Project administration: Yeliz Dadalı.
Resources: Yeliz Dadalı, Ümit Çalıkoğlu.
Supervision: Yeliz Dadalı.
Validation: Yeliz Dadalı.
Visualization: Yeliz Dadalı, Sercan Özkaçmaz, Ümit Çalıkoğlu.
Writing–original draft: Yeliz Dadalı, Sercan Özkaçmaz, Ümit Çalıkoğlu.
Writing–review & editing: Yeliz Dadalı, Sercan Özkaçmaz, Ümit Çalıkoğlu.

Competing Interests

Authors declare no conflict of interest in this study.

Ethical Approval

Authors declared that procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. This retrospective study was approved by a university ethics committee on the date of 22.08.2013 with a number of 005077. Because of the retrospective nature of the study the signed consent form was could not be obtained from the patients.

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