Original Article

The risk of immediate pneumothorax after CT-guided lung needle biopsy: pleural tail sign as a novel factor

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Background: Pneumothorax is the most frequent complication in computed tomography-guided lung needle biopsy (CT-LNB) and generally appears immediately or within an hour after CT-LNB. Preventing pneumothorax after CT-LNB requires a preoperative evaluation of risk factors. This study investigated risk factors for the occurrence of immediate pneumothorax after CT-LNB.

Methods: A total of 311 CT-LNB procedures were conducted for 290 patients (217 males and 73 females) with persistent solid or part-solid pulmonary lesions in this case-control study. We retrospectively evaluated immediate postbiopsy pneumothorax complications and associated risk factors. The possible risk factors for immediate pneumothorax were analyzed, including 12 parameters in demographics, radiological features, and procedural factors. Univariate and multivariate logistic regression analyses were used to investigate independent risk factors for the occurrence of immediate pneumothorax after CT-LNB.

Results: All CT-LNB procedures (100%) were technically successful. Immediate pneumothorax after CT-LNB occurred in 115 out of the 311 procedures (36.9%). Chest tube placement was required for 12.2% (14/115) of the pneumothoraces (14/311, 4.5% of the total number of CT-LNB procedures). The other pneumothoraces were treated conservatively. Independent risk factors of immediate pneumothorax included a lesion with pleural tail sign [PTS; odds ratio (OR) =3.021, 95% confidence interval (CI): 1.703–5.359; P<0.001], smaller lesion size (OR =0.827, 95% CI: 0.705–0.969; P=0.019), a lesion in the middle or lower lobe (OR =2.237, 95% CI: 1.267–3.951; P=0.006), a higher number of pleural punctures (OR =2.710, 95% CI: 1.399–5.248; P=0.003), and a deep-seated lesion (OR =1.622, 95% CI: 1.261–2.088; P<0.001).

Conclusion: PTS is a novel risk factor for immediate pneumothorax and may increase the immediate pneumothorax rate after CT-LNB. Practitioners should be vigilant of the risk of immediate pneumothorax after CT-LNB in lung lesions with PTS.

Keywords: Lung biopsy; computed tomography-guided lung needle biopsy (CT-LNB); pneumothorax; risk factor

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Introduction

The minimally invasive procedure known as computed tomography-guided lung needle biopsy (CT-LNB) is used to obtain tissue samples to make a pathologic diagnosis of peripheral lung lesions (1,2). The sensitivity and specificity of CT-LNB for malignancy have reached 97% and 100%, respectively (3). Pneumothorax is the most frequent

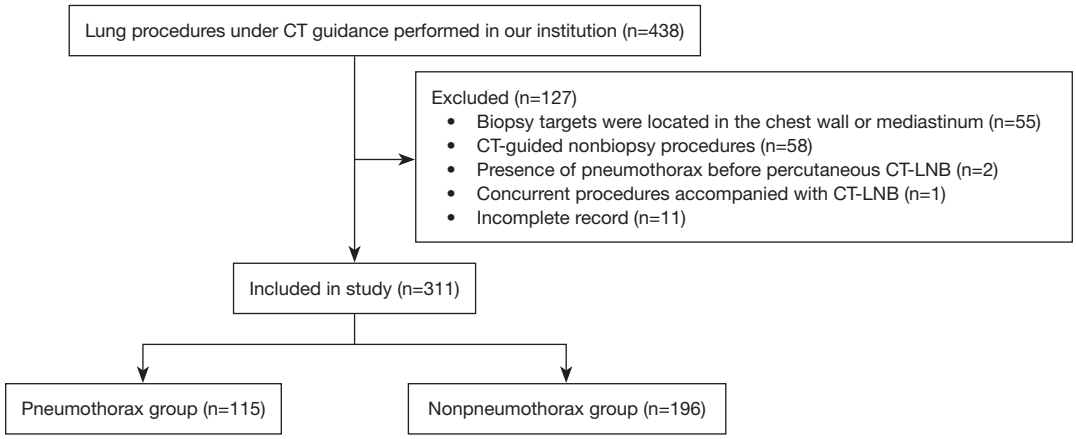

Figure 1 Patient selection flowchart. CT, computed tomography; CT-LNB, computed tomography-guided lung needle biopsy.

complication in patients with CT-LNB, and pneumothorax generally appears immediately or within an hour after CT-LNB (4). A recent meta-analysis found that the average rate of pneumothorax after CT-LNB was 25.9% (range, 4.3% to 52.4%) (5). Furthermore, the average rate of pneumothorax that required chest tube placement was 6.9% (range, 0% to 15.0%). The presence or severity of emphysema (6,7), smaller lesion size (6-8), greater lesion depth (6,9), and other risk factors are associated with a higher likelihood of pneumothorax. The management of pneumothorax includes observation, air aspiration, and tube drainage, and the prognosis is good in most patients with pneumothorax (3).

Pleural tail sign (PTS) is described as peripheral lung lesions shown on high-resolution CT that particularly occur in a subpleural perpendicular location (10,11), resulting in thin linear extensions to the visceral pleura surface and causing a dimpling in the visceral pleura (10,11). Pathologic correlation demonstrates that PTS arises from a thickening of the interlobular septa of the lung due to lymphatic obstruction, tumor infiltration, inflammation, or desmoplastic reaction (10,11). CT-LNB performed in lung lesions with PTS may cause local visceral pleural lacerations, which are considered the dominant factor contributing to pneumothorax caused by CT-LNB (12). To our knowledge, the potential relationship between PTS and immediate pneumothorax after CT-LNB remains unclear. Therefore, this study aimed to verify the potential independent risk factors, especially PTS, for CT-LNB-induced immediate pneumothorax. We present the following article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-22-474/rc).

Methods

Patient criteria

The study was authorized by the Chengdu Second People's Hospital Institutional Review Board. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Since the study was conducted retrospectively, informed consent was not obtained. This retrospective case-control study included all lung procedures under CT guidance performed from November 2015 to November 2021 in Chengdu Second People's Hospital. All patients were included for study inclusion (*Figure 1*). The included patients were then divided into a pneumothorax group and a nonpneumothorax group according to whether or not they presented with immediate pneumothorax after CT-LNB. Patients were included if (I) they were aged 18 or older; (II) their previous bronchoscopic biopsy revealed negative results or had no bronchoscopic indication before CT-LNB; (III) they had persistent solid or part-solid pulmonary lesions and underwent CT-LNB; (IV) they had an Eastern Cooperation Oncology Group score of 0–2, with predicted forced expiratory volume in the first second (FEV1) of more than 35%; and (V) their clinical and radiological data were complete. Patients were excluded if (I) the biopsy sites of the lesion were located in the chest wall or mediastinum; (II) they underwent CT-guided nonbiopsy procedures (such as drainage for abscess/pleural effusion, microwave ablation, etc.); (III) pneumothorax was present prior to CT-LNB procedures; (IV) they underwent concurrent procedures accompanied with CT-LNB, such as ablation and the implantation of radioactive seeds; or (V) they had an incomplete clinical record.

CT-LNB procedures

All CT-LNB procedures were performed by an experienced interventional radiologist (Y Ren, with 15 years of experience in CT-LNB). Before undergoing the CT-LNB, all patients either had a negative result from the bronchoscopic biopsy or had no bronchoscopic indication. All patients underwent a conventional chest CT scan (SOMATOM Drive, Siemens Healthineers, Erlangen, Germany) to evaluate the location and size of the target lesion before CT-LNB. CT-LNB was performed using a standard procedure. According to the location of the lesion, each patient was placed in the supine or prone position on the CT table. Before the CT scan began, all patients practiced breath-holding at deep expiration or inspiration. A lung biopsy with conventional CT scan guidance (SOMATOM Drive) and a coaxial image was performed in each patient to locate the target lesion. All biopsies were performed using a Biopsy Needle Set (Quick-Core, Cook Medical, Bloomington, IN, USA). This set includes one 19-gauge introducer needle and one 20-gauge automated cutting biopsy needle with 20 mm notches. The operator determined a skin puncture point through the body surface marker, and then measured the distance from the skin surface to the lesion and the direction of the puncture needle. The puncture needle path was planned to avoid relatively large vessels, interlobular fissures, and visible bronchi as much as possible. The skin puncture point was administered subcutaneously with 5 mL of 1% lidocaine as local anesthesia. Following this, 19-gauge introducer needles were introduced into the planned skin puncture point and advanced to the lesion. If the skin surface to lesion distance was long, repeat chest CT scans were performed to evaluate puncture access. The operator led the introducer needle along the access route until the introducer needle tip encountered the lesion. If the needle tip direction was incorrect, the operator would adjust the puncture orientation to an appropriate angle. When the 19-gauge introducer needle tip encountered the lesion under CT guidance, the internal stylet of the introducer needle was replaced by the 20-gauge automated cutting biopsy needle. The operator inserted the notch part of the biopsy needle into the lesion to obtain a specimen (*Figures 2,3*). Because there was no pathologist onsite, the operator repeatedly obtained specimens until specimen collection was considered adequate. Specimens obtained were immediately immersed in a 10% buffered formalin solution. Because the effects of certain techniques used to reduce the risk of pneumothorax, such as needle path plugs, have not been further verified, these techniques were not used in this study. Immediately after the acquisition of the specimens, chest CT scans were routinely performed to detect the presence of CT-LNB complications. After the CT-LNB, the patient was asked to stay in bed for 4 h. CT-LNB specimens were excised for standard pathological examination and immunohistochemical examination by an experienced pathologist.

Definition of final diagnosis

The CT-LNB results were categorized into diagnostic results and nondiagnostic results (3). Diagnostic results corresponded to malignant tumors or specific benign diseases. Nondiagnostic results were divided into 3 groups: nonspecific benign results, atypical cells with necrotic pneumonia, and atypical cells with mixed inflammatory cells. The final diagnosis was used as the criterion standard for the evaluation of the diagnostic performance of CT-LNB. According to the criteria defined by Priola *et al.* (13) and César *et al.* (14), final diagnoses were based on surgical results or at least 12 months of clinical-radiological follow-up. The final diagnose results were defined clearly depend on reaction to antitumor therapy or antibiotic treatment based on the CT-LNB results, or unchanged imaging findings in the absence of treatment. In order to calculate sensitivity and specificity for the diagnosis of malignancy, we considered malignant lesions as the main endpoint. True-positive results (malignant lesions) were defined as malignant proof with either the resected specimen or growth pattern evolution of malignancy. True-negative results (nonmalignant lesions) were defined as nonmalignant results obtained at pathological examination and no increase in the size of the lesion within 12 months of the chest CT scan, surgical resection with a confirmed benign diagnosis, or no evidence of distant metastases. False-negative results were defined as nonmalignant results with subsequent proof of malignancy or obvious malignant outcome. False-positive results of malignancy were defined as those that had been diagnosed as malignant according to pathological results that had subsequently been proven to be erroneous.

Complications management

CT-LNB complications were evaluated according to the criteria from the Society of Interventional Radiology and were divided into minor complications and major complications (15). Hemoptysis requiring specific therapy,

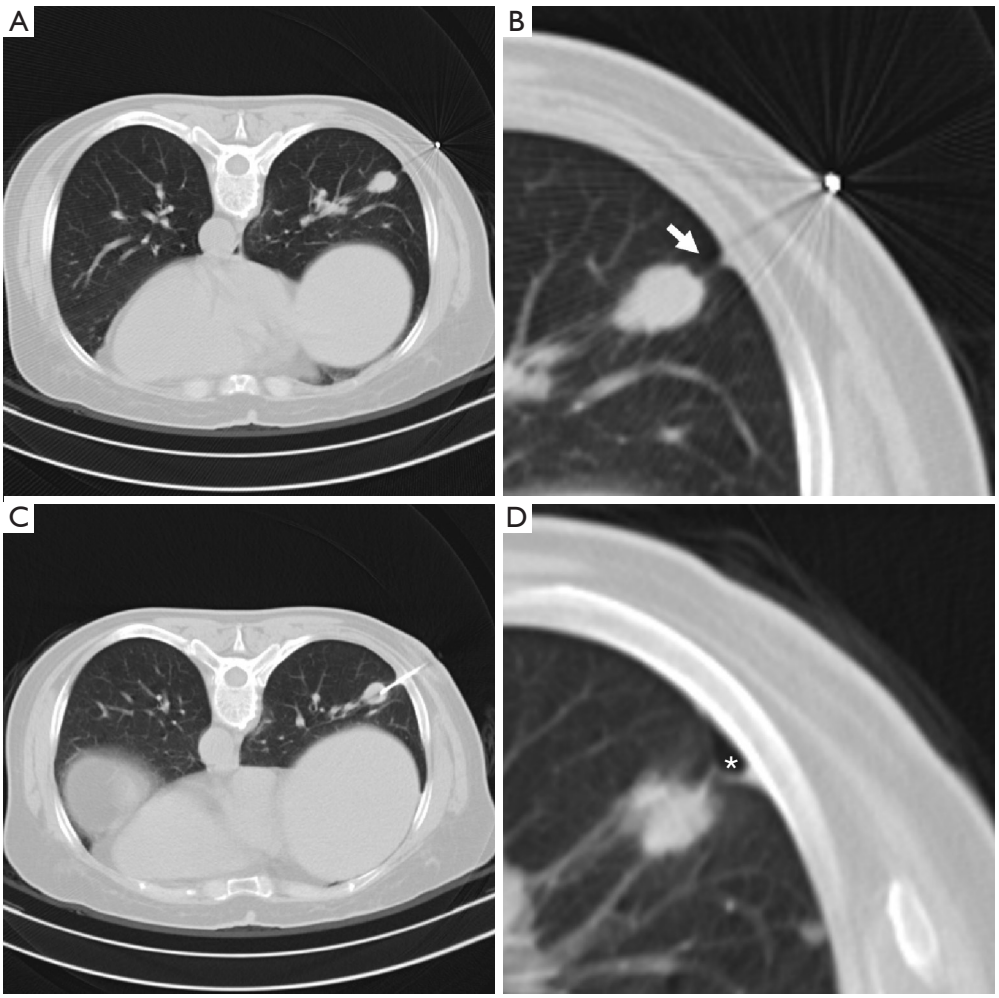

Figure 2 A typical case of a patient with squamous cell lung cancer with PTS lesion for whom CT-LNB was performed. (A) The pre-CT-LNB chest CT scan revealed the lesion location in right lower lobe. (B) The local CT image showed the presence of PTS (white arrow). (C) CT-LNB was performed with a needle tip within the PTS lesion. (D) Post-CT-LNB chest CT images obtained in the same patient showed a local small immediate pneumothorax (star). PTS, pleural tail sign; CT-LNB, computed tomography-guided lung needle biopsy; CT, computed tomography.

hemothorax requiring thoracostomy tube placement, air embolism, and pneumothorax with thoracostomy tube placement were considered major complications. Meanwhile, pneumothorax without thoracostomy tube placement, asymptomatic intrapulmonary hemorrhage, and self-limiting hemoptysis were considered minor complications. Based on the validated criterion in the previous literature, quantification of the pneumothorax size was calculated by using interpleural distance (16). Patients with small, asymptomatic pneumothoraces were treated conservatively (oxygen inhalation or manual evacuation in procedure), and follow-up CT scanning was conducted after 4 h to evaluate the stability of the pneumothorax. If the pneumothorax remained stable within 4 h, the pneumothorax volume was less than 30%, and the patient still had no symptoms, follow-up monitoring was carried out. Chest tube placement was performed if a patient had symptomatic pneumothorax or if the pneumothorax accounted for about 30–40% or more of the hemithorax. The chest tube remained in place until the pneumothorax was completely drained. If patients developed dyspnea or hypoxemia during the CT-LNB postprocedure bed rest, an erect chest CT scan was taken immediately to detect delayed pneumothorax. Slight hemoptysis and asymptomatic intrapulmonary hemorrhage were usually self-limiting. Most cases were managed by appropriate

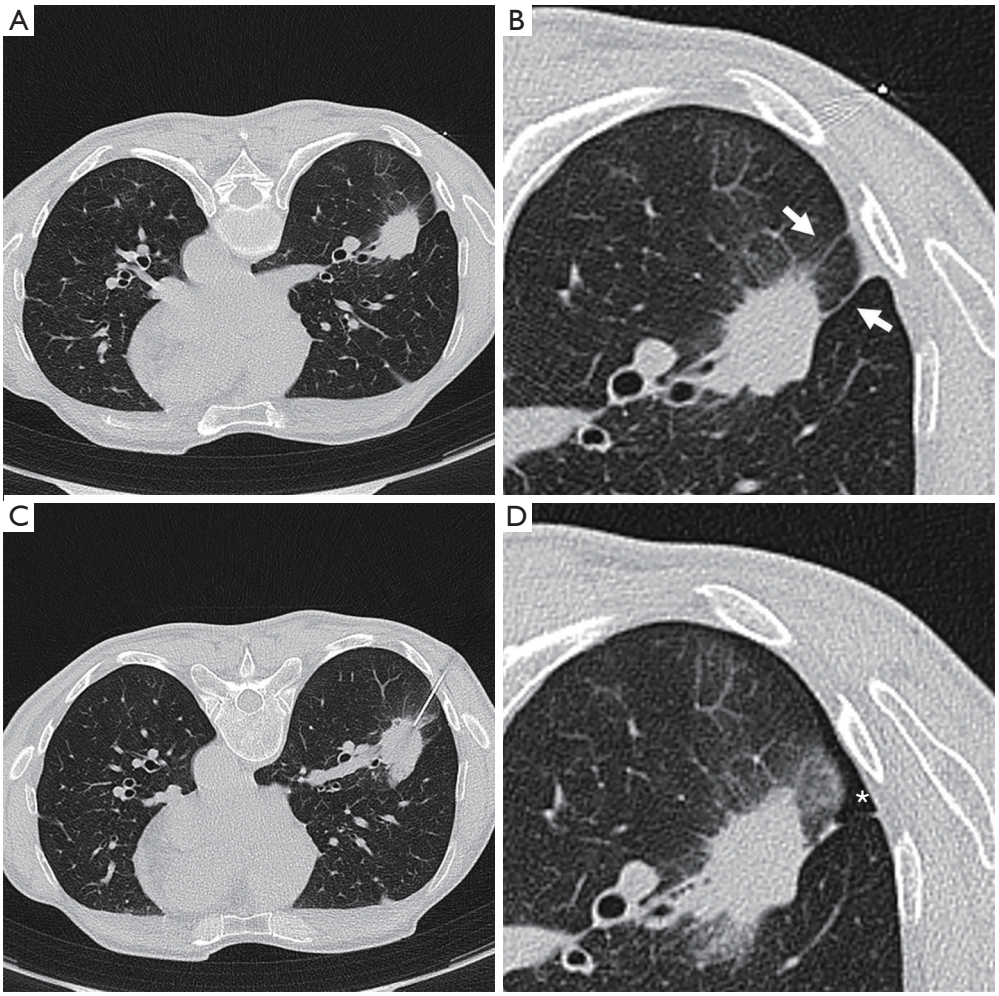

Figure 3 Another patient with adenocarcinoma squamous cell lung cancer with a PTS lesion for whom CT-LNB was performed. (A) The pre-CT-LNB chest CT scan revealed the location in right lower lobe. (B) The local CT image showed the presence of 2 PTS signs (white arrows). (C) CT-LNB was performed with a needle tip within the PTS lesion. (D) Post-CT-LNB chest CT images obtained in the same patient showed persistent immediate pneumothorax (star) and asymptomatic intrapulmonary hemorrhage. The retraction of the lung surface and dimpling in the visceral pleura could be observed. This patient was treated conservatively during hospital admission. PTS, pleural tail sign; CT-LNB, computed tomography-guided lung needle biopsy; CT, computed tomography.

conservative treatment. If hemothorax developed after CT-LNB, necessary management was required in time, and a chest CT scan monitored the amount of hemothorax. If the hemothorax was continuously growing, transcatheter artery angiography was performed to identify the location of arterial bleeding, and embolization of the injured arteries could be performed to treat arterial bleeding (3).

Factor assessments

Patient demographics (age, sex), and procedural information (patient position, number of pleural punctures) were recorded after CT-LNB. Two radiologists (L Liu and Y Hu, all with >5 years of experience in diagnostic radiology) assessed in consensus all preprocedure CT images and evaluated radiological features and procedural factors. They were not involved in the CT-LNB procedures and blinded from the occurrence of CT-LNB complications. The relevant risk factors were as follows: PTS, lesion size, distance to pleura, lesion-involved lobe location, emphysema along the needle path, adjacent lobe invasion, lesion contact to pleura, and pleural puncture angle. PTS was detected

in preprocedure CT images and defined as a radiodense line extending without interruption from the surface of the lesion to the pleura. Lesions associated with remote Kerley B lines and lesions associated with linear densities not reaching the pleura were excluded (10,11). Lesion size (short-axis size of the lesion) and distance to pleura (lesion depth from the pleura) were measured in centimeters on the CT lung window [window width 1,500 Hounsfield units (HU); window level −400 HU]. The lesion was divided into the upper lobe and middle or lower lobe according to lobar anatomy. The diagnosis of emphysema was made according to the Goddard visual score (17). Adjacent lobe invasion was defined as a lesion that crossed fissures and invaded the adjacent lobe. Lesion contact to pleura was defined as pleural contact. The pleural puncture angle was described according to the literature (18,19). The pleural puncture angle was defined as the angle of deviation between the longitudinal axis of the needle and the normal line of puncture point (the normal line being a line that is perpendicular to a given object in geometry) on 2-mm CT transverse section. Pleural puncture angle was divided into 5 subsets as categorical variables in statistical analysis.

Statistical analysis

Before data processing, normality tests were performed on continuous variables. Normally distributed continuous variables are described as mean and standard deviation (SD), and nonnormally distributed continuous variables are described as the median with interquartile range. Categorical variables are described as frequencies and percentages. SPSS 25.0 (IBM Corp, Armonk, NY, USA) for Windows was used for statistical analysis. For continuous variables, the Student *t*-test, Mann-Whitney test, and Wilcoxon test were used, and for categorical variables, the chi-square test was used. P values less than 0.05 were considered to indicate statistical significance. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were obtained by correlating the CT-LNB pathological results with the final diagnostic results and conducting a diagnostic accuracy analysis. The possible risk factors for immediate pneumothorax after CT-LNB were included in univariate regression analyses. Factors with P values less than 0.1 in the univariate analyses were entered as candidate variables into the multivariate logistic regression analyses.

Results

Patient characteristics

A total of 311 CT-LNB procedures for 290 patients were included in this study, which comprised 217 males (74.8%) and 73 females (25.2%), with a median of 62.0 years (range, 25.0 to 93.0 years). Of these patients, 21 underwent multiple lung biopsy procedures. There were 133 lesions (42.8%) located in the upper lobe, and 178 lesions (57.2%) located in the middle or lower lobe. The median lesion size (short-axis size of the lesion) was 3.2 cm (range, 0.5 to 11.1 cm). The distance to the pleura ranged from 0 to 5.1 cm. PTS was detected in 99 lesions (31.8%) of the 311 lesions. The median angle of the pleural puncture angle was 72.0° (range, 14.0° to 90.0°). The demographics between the pneumothorax and nonpneumothorax groups are shown in *Table 1*.

Results of final diagnosis and diagnostic performance

All 311 procedures (100%) were technically successful, and specimens were successfully obtained from all 311 lesions. All CT-LNB procedures had histopathological diagnosis results. Biopsy pathological results and final diagnoses are shown in *Table 2*. A total of 257 lesions were finally considered malignant, including 237 malignant CT-LNB lesions and 20 nonmalignant CT-LNB lesions with a malignant surgical outcome or malignant progression in follow-up. Among these, 54 nonmalignant CT-LNB lesions were finally considered benign according to surgical findings or clinical-radiological follow-up criteria. Finally, there were 237 true-positive and 54 true-negative results, and 0 false-positive and 20 false-negative results (*Table 3*). The overall accuracy was 93.5% [(237+54)/311], with a sensitivity of 92.2% (237/257), a specificity of 100.0% (54/54), a PPV of 100.0% (237/237), and a NPV of 73.0% (54/74).

Clinical outcomes

The details of patients with complications of CT-LNB are presented in *Table 4*. The overall incidence of immediate pneumothorax was 36.9% (115/311). Chest tube placement was required for 12.2% (14/115) of the pneumothoraces (14/311, 4.5% of the total number of procedures). Only 2 (0.6%) patients had severe hemothorax requiring thoracostomy tube placement with prolonged admission.

Table 1 Demographics and univariate analysis of immediate pneumothorax risk factors after CT-LNB

Risk factor	Overall (n=311)	Pneumothorax group (n=115)	Nonpneumothorax group (n=196)	Statistic value	P value
Age (year)	62.0 (56.0, 72.0)	64.0 (57.0, 72.0)	65.0 (55.2, 71.0)	3.659	0.272
Gender, n (%)				9.141	0.003*
Male	233 (74.9)	75 (65.2)	158 (80.6)		
Female	78 (25.1)	40 (34.8)	38 (19.4)		
Procedures factors, n (%)					
Position				2.285	0.131
Prone	172 (55.3)	70 (60.9)	102 (52.0)		
Supine	139 (44.7)	45 (39.1)	94 (48.0)		
Number of pleural punctures				23.662	<0.001*
1	250 (80.4)	76 (66.1)	174 (88.8)		
≥2	61 (19.6)	39 (33.9)	22 (11.2)		
Radiological features					
Lesion size (cm, short-axis size of the lesion)	3.2 (2.4, 4.8)	2.7 (2.1, 3.5)	3.7 (2.6, 5.4)	22.628	<0.001*
Distance to pleura (cm)	0 (0, 1.4)	1.0 (0, 2.0)	0 (0, 0.8)	14.308	<0.001*
Lesion location, n (%)				5.842	0.016*
Upper lobe	133 (42.8)	39 (33.9)	94 (48.0)		
Middle or lower lobe	178 (57.2)	76 (66.1)	102 (52.0)		
Emphysema along the needle path, n (%)	107 (34.4)	37 (32.3)	70 (35.7)	0.403	0.526
Adjacent lobe invasion, n (%)	116 (37.3)	31 (27.0)	85 (43.4)	8.346	0.004*
Pleural contact, n (%)	226 (72.7)	66 (57.4)	160 (81.6)	21.444	<0.001*
PTS, n (%)	99 (31.8)	62 (53.9)	37 (18.9)	40.998	<0.001*
Pleural puncture angle (°)	72.0 (56.0, 82.0)	72.0 (58.0, 82.0)	73.0 (55.0, 82.0)	0.328	0.809
Subsets, n (%)	311	115	196	0.978	0.783
<50	58 (18.6)	22 (19.1)	36 (18.4)		
50–60	37 (11.9)	14 (12.2)	23 (11.7)		
60–70	50 (16.1)	19 (16.5)	31 (15.8)		
70–80	75 (24.1)	27 (23.5)	48 (24.5)		
80–90	91 (29.3)	33 (28.7)	58 (29.6)		

For categorical variables, frequencies and percentages are reported, whereas median (interquartile range) is reported for nonnormality continuous variables. *, the variables with a significant difference in statistical analyses. CT-LNB, computed tomography-guided lung needle biopsy; PTS, pleural tail sign.

The overall incidence of asymptomatic intrapulmonary hemorrhage in postprocedure chest CT images was 17.6% (55/311). All intrapulmonary hemorrhages were self-limiting and did not require further treatment. The incidence of self-limiting hemoptysis was 4.1% (13/311) in this study. No patient had severe hemoptysis or air embolism.

Table 2 Detailed biopsy pathological results and final diagnoses of CT-LNB lesions

Biopsy pathological results	n (%)	Final diagnoses
Diagnostic results		
Adenocarcinoma	105 (33.8)	Adenocarcinoma: 105
Squamous cell carcinoma	52 (16.7)	Squamous cell carcinoma: 52
Small cell lung cancer	26 (8.4)	Small cell lung cancer: 26
Other carcinomas	33 (10.6)	Other carcinomas: 33
Metastatic carcinoma	21 (6.8)	Metastatic carcinoma: 21
Tuberculosis	27 (8.7)	Tuberculosis: 27
Nonspecific inflammation	24 (7.7)	Nonspecific inflammation: 23
		Squamous cell carcinoma:1
Nondiagnostic results		
Nonspecific benign results	6 (1.9)	Nonspecific inflammation: 3
		Adenocarcinoma: 2
		Squamous cell carcinoma: 1
Atypical cells with necrotic pneumonia	11 (3.5)	Adenocarcinoma: 6
		Squamous cell carcinoma: 4
		Small cell lung cancer: 1
Atypical cells with mixed inflammatory cells	6 (1.9)	Adenocarcinoma: 3
		Squamous cell carcinoma: 1
		Small cell lung cancer: 1
		Tuberculosis: 1

CT-LNB, computed tomography-guided lung needle biopsy.

Table 3 Diagnostic accuracy of the CT-LNB malignant lesions

CT-LNB pathological results	Final diagnosis		Total
	Malignant	Nonmalignant	
Malignant	237 (true positive)	0 (false positive)	237
Nonmalignant	20 (false negative)	54 (true negative)	74
Total	257	54	311

CT-LNB, computed tomography-guided lung needle biopsy.

Univariate analysis and multivariate analysis

In order to further clarify the relationship between clinical-radiological features and immediate pneumothorax after CT-LNB, the possible risk factors were analyzed by logistic regression analyses. The results of univariate and multivariate logistic regression analyses are presented in *Tables 1*,*5*. Univariate and multivariate analysis showed that lesions with PTS [odds ratio (OR) =3.021, 95% confidence interval (CI): 1.703–5.359; P<0.001], smaller lesion sizes (OR =0.827, 95% CI: 0.705–0.969; P=0.019), lesions in middle or lower lobe (OR =2.237, 95% CI: 1.267–3.951; P=0.006), a higher number of pleural punctures (OR =2.710, 95% CI: 1.399–5.248; P=0.003), and deep-seated lesions (OR =1.622, 95%

Table 4 Detailed complications of PTS and non-PTS lesions treated with CT-LNB

Complication	Overall (n=311)	PTS lesions group (n=99)	Non-PTS lesions group (n=212)
Major			
Hemoptysis requiring specific therapy or prolonged hospitalization	0	0	0
Hemothorax requiring thoracostomy tube placement requiring prolonged admission, catheter exchange, or pleurodesis	2 (0.6%)	0	2 (0.9%)
Air embolism	0	0	0
Pneumothorax with thoracostomy tube placement	14 (4.5%)	4 (4.0%)	10 (4.7%)
Minor			
Pneumothorax without thoracostomy tube placement	115 (36.9%)	62 (62.6%)	53 (25.0%)
Asymptomatic intrapulmonary hemorrhage	55 (17.6%)	20 (20.2%)	35 (16.5%)
Self-limiting hemoptysis	13 (4.1%)	3 (3.0%)	10 (4.7%)

PTS, pleural tail sign; CT-LNB, computed tomography-guided lung needle biopsy.

Table 5 Multivariate analysis of immediate pneumothorax risk factors after CT-LNB

Risk factor	Regression coefficient	Standard error	Wald χ^2 value	P value	OR	95% CI of OR
PTS	1.106	0.292	14.287	<0.001*	3.021	1.703–5.359
Lesion size	–0.190	0.081	5.488	0.019*	0.827	0.705–0.969
Lesion location	0.805	0.290	7.699	0.006*	2.237	1.267–3.951
Number of pleural punctures	0.997	0.337	8.742	0.003*	2.710	1.399–5.248
Distance to pleura	0.484	0.129	14.142	<0.001*	1.622	1.261–2.088
Gender	0.271	0.322	0.709	0.400	1.311	0.698–2.465
Adjacent lobe invasion	–0.448	0.302	2.201	0.138	0.639	0.353–1.155
Pleural contact	0.087	0.370	0.055	0.815	1.090	0.528–2.252
Constant	–1.344	0.434	9.582	0.002	0.261	–

*, the variables have statistically significant differences. CT-LNB, computed tomography-guided lung needle biopsy; PTS, pleural tail sign.

CI: 1.261–2.088; P<0.001) were significant independent risk factors of immediate pneumothorax.

Discussion

CT-LNB is a minimally invasive diagnostic procedure for histopathological diagnosis of lung tumor lesions and tumor mimics. Usually, these peripheral lung lesions cannot be diagnosed through bronchoscopic biopsy. Because CT-LNB can distinguish benign from malignant diseases and facilitate molecular and genomic profiling to guide the use of targeted therapy drugs, the demand for CT-LNB is growing in the clinic. A recent meta-analysis published in 2019 reported a pooled sensitivity for CT-LNB of 97% and a pooled specificity of 100% (20). Pneumothorax is the most frequent complication of CT-LNB and generally appears immediately or within an hour after CT-LNB. National multicenter cross-sectional surveys reported that pneumothorax rates after CT-LNB range from 15.0% to 35.0% and that pneumothorax chest tube drainage rates range from 3.1% to 6.6% (3). Meanwhile, a very recent meta-analysis in 23,104 patients from 36 articles (5) reported pooled rates for pneumothorax after CT-LNB of 25.9% (range, 4.3% to 52.4%) and pooled rates of pneumothorax

requiring chest tube placement of 6.9% (range, 0% to 15%). The above results are generally consistent with the guidelines of the Society of Interventional Radiology (15). In our study, the pneumothorax rate after CT-LNB was 36.9% (115/311), which was higher than the rate previously reported. We considered these were mainly caused by various baseline characteristics and operator experience. However, the pneumothorax rate in our study is still within a reasonable range. Pneumothorax rates are relatively higher than those of other complications and can lead to dyspnea, chest pain, and other symptoms (3,15). However, the symptoms of most patients can be relieved through observation, manual evacuation, and conservative chest tube placement. In our study, of the 115 patients with immediate pneumothorax, only 14 patients (12.2% of pneumothoraces and 4.5% of CT-LNB procedures) required chest tube drainage. The remaining patients with pneumothorax recovered with oxygen inhalation or manual evacuation in the procedure.

The purpose of this study was to the evaluate demographics, radiological features, and procedural factors that could potentially influence the immediate CT-LNB-caused pneumothorax rate in order to further minimize the pneumothorax rate by factor management in the clinic. Risk factors for pneumothorax after CT-LNB have been researched extensively. Various studies indicate higher CT-LNB pneumothorax rates to be associated with factors of older age (6,8), male sex (6,21), cigarette smoking (6,8), emphysema (6,7), emphysema along the puncture access (18,21), deep lesions (6,9), small lesion size (6-8), pleural contact (8,9), multiple pleural punctures (6,21), biopsy needle traversing the interlobal fissure (18), lower lobe lesions (21,22), and acute pleural puncture angle (18,19).

Among these known risk factors, some risk factors affecting pneumothorax remain controversial. In published studies, some factors are consistent, while others are inconsistent or even contradictory, which may be due to the different baseline characteristics, procedure techniques, and statistical methods employed across different studies. We found a higher pneumothorax rate in smaller lesions (OR 0.827; P=0.019), which is consistent with a number of studies supporting the relationship between higher pneumothorax rate and smaller lesion size (6-8). Since a puncture is difficult when the lung lesion is small, further pleural puncture may be required, increasing the risk of pneumothorax. However, the results of Hiraki *et al.* (22) and Zhao *et al.* (23) are inconsistent with our findings, as the lesion size did not correlate with the pneumothorax rates. These authors deduced that the smaller the lesion is, the more needle adjustment may be required, which may lead to greater pleural tearing and longer procedure time. In other words, pleural injury and operation time, rather than lesion size, are the potential underlying reasons for this association. The correlation between pneumothorax rate and the distance from the lesion to pleura is also considerably controversial. Previous studies show that a longer length from lesion to pleura is associated with a higher pneumothorax rate (24-26). Kinoshita *et al.* (27) suggested that a deeper lesion depth implies a longer puncture path, which may lead to a greater chance of tearing the visceral pleura during the procedure. On the contrary, Yeow *et al.* (8,9) reported that pleural contact lesions, rather than lesions farther from the pleura, were correlated with a higher pneumothorax rate. This may be because the subpleural lesions can easily cause the needle tip to move into the pleural cavity as the patient breathes, further causing air leakage through the needle flowing to the pleural cavity. By definition, subpleural lesions are essentially 0 cm deep to the pleura, and prior studies have included lesions with a depth of 0 cm into the pleura in the regression analysis (9,22,25,28). In our study, multivariate logistic regression analysis noted that pleural contact (OR 1.090; P=0.815) was not significantly associated with the occurrence of pneumothorax. According to this result, the depth of the lesion from the pleura was included in our regression analysis. A deep-seated lesion was found to be a risk factor for pneumothorax in this study if it did not contact the pleura.

In our study, PTS was found in up to 31.8% of the target CT-LNB lesions on CT. The relationship between PTS and immediate pneumothorax after CT-LNB was explored using multiple logistic regression analysis. Univariate and multivariate logistic regression analyses showed that PTS (OR 3.021; P<0.001) had statistical significance. This result demonstrated that lesions with PTS involve a higher risk for immediate pneumothorax when compared to lesions without PTS. To our knowledge, our study is the first to report that patients with PTS lesions undergoing CT-LNB have a significantly higher pneumothorax rate.

The reasons why patients with PTS lesions who are subjected to CT-LNB have a greater chance of developing an immediate pneumothorax are still unclear. Pathologic correlation demonstrates that PTS results from the thickening of the interlobular septa of the lung due to either lymphatic obstruction, tumor infiltration, inflammation, or desmoplastic reaction (10,11). Hence, PTS produces a series

of morphological changes in the local visceral pleura near the lesion. There are 2 potential mechanisms involved in this phenomenon. (I) PTS causes local pleural deformation and local tensile stress, which reduces the elastic properties of the lung parenchyma. Throughout the above condition, if the biopsy needle is inserted, there is a potential possibility that the pleura will tear, increasing the risk of an immediate pneumothorax. This is comparable to the relationship between the occurrence of pneumothorax and the biopsy needle penetrating through the lung's emphysematous changes (28,29). (II) The needle penetrating PTS may cause an elongated and bigger pleural hole during the CT-LNB procedure and further tear the visceral pleura. Visceral pleural laceration is usually considered the main reason for pneumothorax after CT-LNB (30). Moore *et al.* (31,32) thought that the shape of the pleural hole influences how much air leaks into the pleural cavity. A smaller puncture pinhole can sustain more atmospheric pressure than can a relatively large pleural laceration fissure. Although we speculated that PTS in lesions has an effect on the visceral pleura, the mechanism remains unclear. Since PTS, as a persistent radiological feature, is related to the high immediate pneumothorax rate after CT-LNB, the next step is to explore whether the incidence of pneumothorax can be reduced through enacting certain procedural measures, such as using a long-path puncture to avoid PTS, in CT-LNB.

Some limitations of this study should be noted. First, selection bias and subjective assumptions might have arisen due to the retrospective nature of the study. Second, this study did not take into account some risk factors, such as the pulmonary function index. Finally, we are unable to interpret why some risk factors, such as emphysema and pleural puncture angle, did not significantly affect the incidence of pneumothorax. Previous literature suggests that emphysema and pleural puncture angle are pneumothorax risk factors after CT-LNB (18,19).

Conclusions

Independent risk factors of pneumothorax after CT-LNB include PTS, smaller lesion size, a lesion in the middle or lower lobe, a higher number of pleural punctures, and a deep-seated lesion. PTS is a novel independent risk factor for immediate pneumothorax after CT-LNB and may increase the immediate pneumothorax rate after CT-LNB. Therefore, practitioners should be vigilant of the risk of immediate pneumothorax after CT-LNB for patients with lung lesions with PTS.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-22-474/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-474/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Chengdu Second People's Hospital Institutional Review Board, and individual consent for this retrospective analysis was waived.

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