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RESEARCH

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Nonlinear association between lung needle path CT attenuation values and postprocedural immediate pneumothorax following computed tomography-guided lung biopsy: a retrospective cohort study

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Abstract

Background Pneumothorax is a potential complication following computed tomography-guided lung biopsy (CT-LB). However, the relationship between the lung needle path CT attenuation values and risk of post-procedural immediate pneumothorax remains unclear. The study aims to investigate this relationship.

Methods The present single-center retrospective cohort study analyzed the data obtained from 453 patients who underwent CT-LB from 2019 to 2022. The relationship between the lung needle path CT attenuation values and post-procedural immediate pneumothorax was assessed using restricted cubic splines, which were adjusted for potential confounders, and validated using linear and nonlinear binomial logistic models.

Results A total of 453 patients (mean age: 60.2 ± 12.0 years old, 217 male patients) were evaluated. The incidence of post-procedural immediate pneumothorax was 41.06% (186/453). The median needle path CT attenuation was −831 Hounsfield units (Hu). The linear models indicated an unstable association between lung needle path CT attenuation and post-procedural immediate pneumothorax (odds ratio: 0.99, 95% confidence interval: 0.99-1.00). The nonlinear analysis identified an inflection point at a CT attenuation value of -805 Hu. A stronger negative link was identified for needle path CT attenuation values below −805 Hu (odds ratio: 0.99, 95% confidence interval: 0.98–0.99) between the needle path CT attenuation value and pneumothorax, while no statistically significant association was identified between these when the CT attenuation value was above −805 Hu.

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Conclusion There is a nonlinear association between the lung needle path CT attenuation values and risk of post-procedural immediate pneumothorax. For CT attenuation values below −805 Hu, increasing the needle path CT attenuation values might reduce the risk of pneumothorax.

Keywords Computed tomography, Lung biopsy, Attenuation values, Pneumothorax, Inflection point, Interventional radiology

Background

Pulmonary nodules can be identified in approximately 50% of patients who received a computed tomography (CT) scan for lung cancer [1]. CT-guided lung biopsy (CT-LB) is one important diagnostic approach. Although this has been considered to be safe and effective [2, 3], CT-LB can cause serious complications, such as pneumothorax [4, 5], and these have occurred in 15–60% of patients who underwent CT-LB, which might be life-threatening [6]. Furthermore, approximately 3–15% of patients with pneumothorax eventually required chest tube placement or other urgent interventions [7–12]. In addition, CT-LB can cause pulmonary hemorrhage, with an incidence reaching up to 4.7% [13]. All these complications can lead to longer hospital stays [14], higher healthcare costs [15], and greater patient dissatisfaction. Therefore, it is important to minimize the risk factors associated to pneumothorax during CT-LB.

Various factors have been proposed as potential contributors to the occurrence of immediate pneumothorax in patients undergoing CT-LB. Previous studies have suggested that the CT attenuation values along the biopsy needle path are associated to the occurrence of pneumothorax. For example, the application of a sealant to the lung biopsy track [16–18], the pulmonary hemorrhage along the needle track [19], and the biopsy-side down position protocol, which are correlated to the elevated CT attenuation values of the lung biopsy track, can significantly minimize the risk of pneumothorax. Conversely, the pulmonary emphysema along the needle path, which presents with lower CT attenuation values, is a potential risk factor for the development of biopsy-associated pneumothorax [20, 21]. Therefore, the quantitative CT attenuation values along the needle path in pulmonary parenchyma can facilitate the risk estimation of immediate pneumothorax caused by CT-LB.

The potential association between the lung needle path CT attenuation values and incidence of post-procedural immediate pneumothorax remains unclear. The present observational cohort study aimed to investigate the hypothesis that higher needle path CT attenuation is correlated with reduced incidence of immediate pneumothorax following CT-LB.

Materials and methods

Study design and participants

A retrospective cohort study was conducted in consecutive adult patients who underwent CT-LB at Chongqing General Hospital, between January 1, 2019 and November 22, 2022. The study protocol was approved by the hospital institutional review board (Ethics 28 Committee of Chongqing General Hospital, ID: XJS S2022-052-01), and all methods were carried out in accordance to relevant guidelines and regulations. The requirement for informed consent was waived, and this was approved by the Ethics 28 Committee of Chongqing General Hospital due to the retrospective design of the study. The study was performed in accordance to the Declaration of Helsinki of 1964 and its subsequent amendments, and the STROCSS 2021 guidelines [22].

Main exposure

In the present study, all biopsy images were reviewed by a radiologist, who has 11 years of chest disease imaging diagnostic experience. The images were analyzed using the IntelliSpace Portal workstation (Philips Healthcare, Netherlands), with the lung window setting (window level of -600 Hounsfield units [Hu] and window width of 1,600 Hu), a slice thickness of 2 mm, and a spacing of 2 mm. Focus was given in measuring the lung needle path CT attenuation values for all patients.

In the pre-puncture images, the lung needle path CT attenuation was measured within an adjustable rectangle region of interest (ROI), and this was repeated three times (puncture needle plane, initial appearance plane, and initial disappearance plane). Then, the mean over these three measurements was calculated, retaining the integer results. The transverse diameter of the ROI was approximately 10 mm, and the length was determined by the depth of the CT-LB to avoid partial volume effects (Fig. S1).

Biopsy protocol

The patients were positioned in the lateral decubitus, prone, or supine position, based on the nodule location and patient comfort. They were instructed to remain relaxed, breathe normally, and remain motionless throughout the procedure. The optimal puncture route was selected to minimize the length of the biopsy tract, prevent puncturing through the emphysematous areas, blebs, bullae, pleural fissures and large blood vessels, and keep away from the scapula and ribs. Based on the selected route, a body surface marker and laser illumination were used to mark the skin puncture point. Local anesthesia was given with 2% lidocaine, from the skin puncture site to the pleura, under sterile technique.

At the end of inspiration during normal breathing, a guiding needle (17 gauge) was inserted into the pulmonary nodule, followed by an automated end cutting needle (18 gauge) for biopsy. In employing a technique similar to the coaxial needle, a Chiba needle (21 gauge) or Franssen needle (18 gauge) was used for the aspiration biopsy. All procedures were performed by three interventional radiologists, who have 3–17 years of biopsy experience.

After the procedure, a single thoracic CT scan was performed to detect for potential immediate complications, such as pneumothorax, pulmonary hemorrhage, or other possible complications, before the patient left the operating room. If a small and asymptomatic pneumothorax [21] was observed, the patient was closely observed in the post-anesthesia care unit. A chest X-ray was taken after 4–24 h, post-biopsy. However, when the pneumothorax worsened or the patient became unstable, the patient was directly admitted to the emergency intensive care unit where a thoracostomy was performed.

Outcomes

Pneumothorax was identified when there was free air within the thoracic cavity, but external to the lung parenchyma [23]. The primary outcome was post-operative immediate pneumothorax, which was defined as pneumothorax, as confirmed in the CT scan, which occurs after the puncture needle is withdrawn, but before the patient leaves the operating room. In addition, the intraprocedural pneumothorax was recorded, which occurred before puncture needle withdrawal, and the delayed pneumothorax was also recorded, which developed after the patient left the operating room, but within seven days, post-procedurally.

Another radiologist, who has five years of experience in diagnosing thoracic diseases, and was blinded to the CT attenuation values on the lung needle path, reviewed the puncture CT images in the Picture Archiving and Communication System (Kodak Carestream, NY, USA). This radiologist evaluated the existence of the pneumothorax, and recorded other biopsy-related measurements, except for the lung needle tract CT attenuation values, with detailed and accurate documentation.

Covariates

Covariates that might affect the relationship between the CT attenuation values and risk of pneumothorax were collected, which included the patient demographics, clinical characteristics, procedural-related factors, and pulmonary nodule features.

The demographics included gender, age, weight and height. The clinical characteristics included the following: blood pressure (BP), alcohol drinking (never, previously $\geq$1 year, currently or previously $<$1 year), smoking history (never, previously $\geq$1 year, current or previously $<$1 year), and chronic obstructive pulmonary disease (COPD).

The pulmonary nodule-related covariates included the lesion location within the lungs and lobes, and the size of the lesion that was recorded as the maximum long-axis diameter in puncture plane.

The procedure-related covariates included the length of the lung biopsy track (the distance from the pleural puncture point to the edge of the lung nodule), the needle-pleura angle (calculated as the angle between the line perpendicular to the tangent, where the needle enters the pleura, and the needle longitudinal axis [24]), the operation duration (the time period from needle insertion to the completion of the final CT scan after biopsy), the operator experience, the number of pleural punctures and needle redirections, the interlobar fissure puncture, the patient puncture position (supine, prone, or others), the pulmonary hemorrhage along the needle pathway (maximum transverse diameter in the lung window CT images), and the needle gauge.

Statistical analysis

The participants were categorized into quartiles, based on the lung needle path CT attenuation values. Continuous variables were expressed in mean $\pm$ standard deviation (SD) or median with interquartile range (IQR), depending on the normality of the test results. Categorical variables were presented in numbers with percentages. In comparing the potential significant differences among groups with different needle path CT attenuation values, one-way ANOVA was applied for normally distributed continuous data, Kruskal-Wallis H test was applied for non-normally distributed continuous variables, and Pearson Chi-square test or Fisher exact test was applied for categorical variables.

In order to elucidate the potential relationship between the lung needle path CT attenuation values and post-operative immediate pneumothorax, three different logistic regression models were constructed, which were linear and nonlinear, and unadjusted and adjusted for specific covariates. These models included a non-adjusted model (without covariate adjustment), a minimally adjusted model (adjusted for gender, age, weight, height, alcohol consumption, smoking status, systolic BP, diastolic BP, and COPD), and a fully adjusted model (adjusted for the aforementioned variables plus the operator experience, patient position, lesion location and size, biopsy track length, needle-pleura angle, number of pleural punctures and needle redirections, interlobar fissure puncture, puncture needle gauge, operation duration, and needle path pulmonary hemorrhage). The association coefficient (odds ratio, OR) with 95% confidence interval (95% CI) was calculated.

A continuous scale with a restricted cubic spline curve from a fully adjusted logistic regression model was used to assess the association between the needle path CT attenuation values and immediate pneumothorax. Considering the overfitting and best fit in the main splines for immediate pneumothorax incidence, the modeling was conducted with four knots (at the 5th, 35th, 65th and 95th percentiles) for the lung CT attenuation values (the reference was the 5th percentile), following the recommendation of Harrell [6]. The Wald test was employed to evaluate nonlinearity by testing the null hypothesis, that is, the regression coefficient of the spline transformation equaled to zero [25]. When a nonlinear relationship was identified, the penalty function method (smoothing curve fitting) with a generalized additive model was used to validate the nonlinear relationship, and a recursive algorithm and bootstrapping were used to calculate the inflection point. Then, a segmented linear model on either side of the inflection point was created using a two-piece binary logistic regression model. The OR and 95% CI were reported.

In order to further investigate the association between the needle path CT attenuation values and immediate pneumothorax, and evaluate the robustness of the primary analysis results, a limited modeling approach was applied to enhance the specificity of the present study cohort. Specifically, merely patients who underwent biopsy procedures, in the supine or prone position, were included, ensuring methodological uniformity. Furthermore, to establish a homogeneous cohort and prevent any influences from potential confounders, patients with intraprocedural pneumothorax were excluded from the present analysis.

All statistical analyses were performed using the R software (version 4.2.3, https://www.r-project.org/), utilizing various packages for the data analysis. The significance was set at $p<0.05$ for two-tailed tests.

Results

Characteristics of the participants

In the present study, 674 candidates were initially assessed. The following subjects were excluded: subjects with a history of lung or pleural surgery on the same side as the biopsy, subjects with significant pleural thickening with calcification, or subjects with pneumothorax that resulted from local anesthesia. In order to minimize the potential sources of bias, patients who used a sealant for the biopsy track or those who underwent a repeat biopsy within one week prior to the procedure were excluded. Finally, the present study cohort consisted of 453 patients. The flowchart for the participant selection is presented in Fig. 1. Among these participants (Table 1), 52.10% were female, and the median age was 61 years old (IQR: 53–70 years old). The median needle path CT attenuation value was −831 Hu (IQR: -861 Hu, -802 Hu). The incidence of intraprocedural pneumothorax, immediate post-procedural pneumothorax, and delayed post-procedural pneumothorax was 9.27% (42/453), 41.06% (186/453), and 2.20% (10/453), respectively.

The participants were divided into quartiles, based on the lung needle path CT attenuation values: Q1 -881 Hu (IQR: -894 Hu, -870 Hu), Q2 -847 Hu (IQR: -854 Hu, -836 Hu), Q3 -815 Hu (IQR: -823 Hu, -809 Hu), and Q4 -776 Hu (IQR: -790 Hu, -743 Hu). There was no significant difference in the different lung needle path CT attenuation value groups, in terms of the covariates of COPD, alcohol consumption, BP, height, gender, lesion location, biopsy tract length, puncture through the interlobar fissure, needle-pleura angle, number of pleural punctures, intraprocedural pneumothorax, and delay pneumothorax (all, $p>0.05$). Compared to patients with the lowest CT attenuation values (-894 Hu, -870 Hu), patients with the highest needle path CT attenuation values (-790 Hu, -743 Hu) presented with significant differences, in terms of smoking status, weight, age, operator experience, needle gauge, patient puncture position, immediate pneumothorax, lesion diameter, operation duration, and pulmonary hemorrhage along the needle path ($p<0.05$. Table 1).

There were 10 (2.20%), 7 (1.50%), 5 (1.10%), 5 (1.10%), 4 (0.90%), and 3 (0.70%) patients with missing results for height, weight, systolic BP, diastolic BP, alcohol consumption, and smoking status, respectively. These missing data, which was <8% for all variables, was omitted from the regression analysis.

Binary logistic regression model with unadjusted covariates

The binary logistic regression analysis revealed that the lung needle path CT attenuation values, weight, age, needle gauge, patient puncture position, lesion diameter, number of pleural punctures, and pulmonary hemorrhage along the needle path were significantly associated to post-procedural immediate pneumothorax (Table S1).

Multivariable analysis with the linear and nonlinear binomial logistic models

In order to determine the relationship between the lung needle path CT attenuation values and post-procedural immediate pneumothorax, three models were created using the linear and nonlinear binary logistic regression analysis. The linear binary logistic regression models revealed a significant association between the lung needle

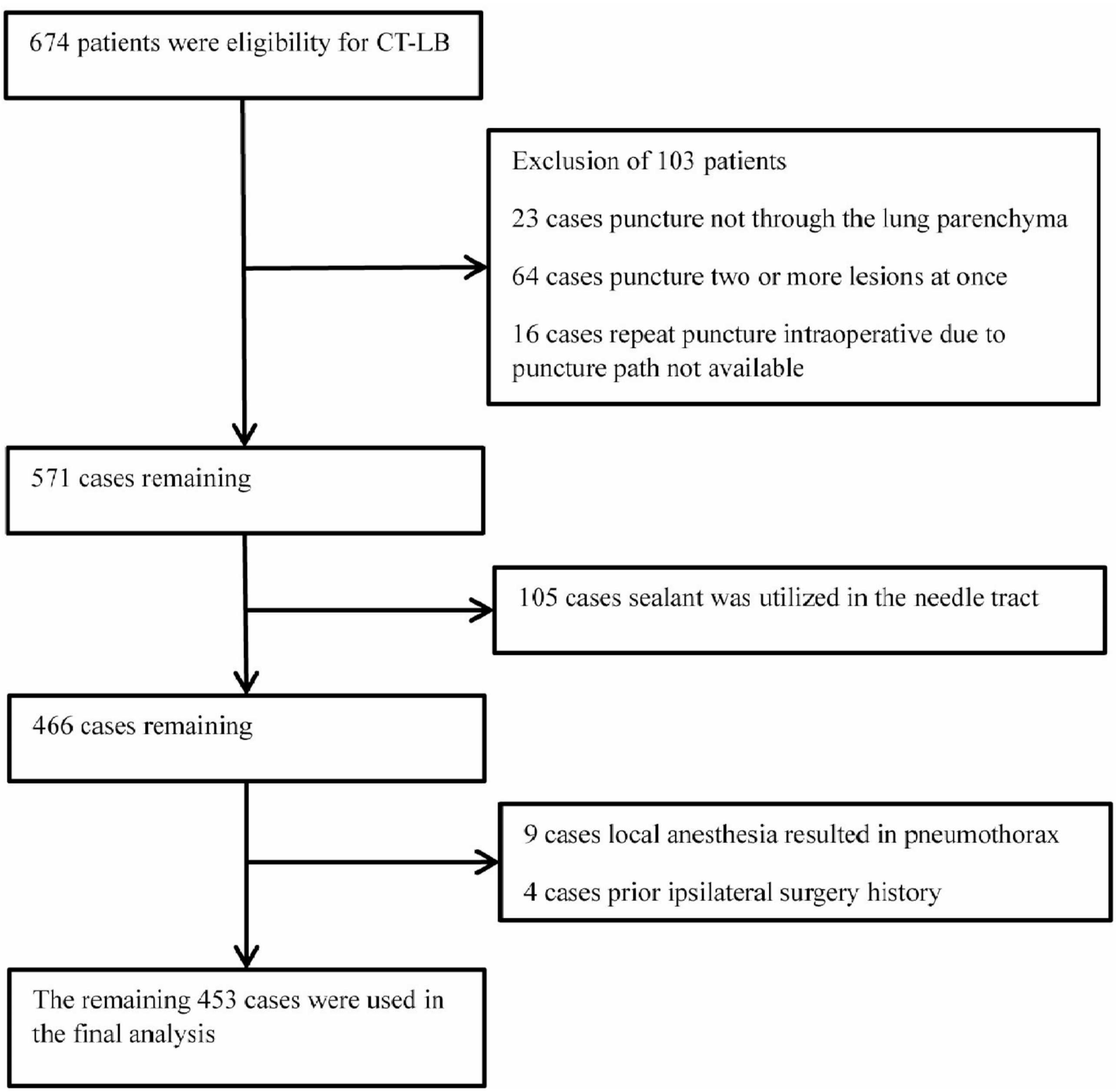

Fig. 1 Participant selection flowchart

path CT attenuation values and post-procedural immediate pneumothorax in Model 1 (OR: 0.99, 95% CI: 0.98–0.99) and Model 2 (OR: 0.99, 95% CI: 0.98–0.99), but not in Model 3 (OR: 0.99, 95% CI: 0.99-1.00) (Table 2).

In the adjusted logistic regression with a restricted cubic spline curve, the association between the needle path CT attenuation values and immediate pneumothorax was identified to be nonlinear with an inflection point, as confirmed by the Wald test ($p<0.05$), suggesting that this nonlinear model provides a better fit, when compared to the linear model (Fig. 2a). Furthermore, the nonlinear relationship was confirmed using the smooth curve fitting, with the adjusted same covariables as restricted cubic spline curves (Fig. 2b). Subsequently, a two-piece linear logistic model was applied to assess the independent association between the lung needle path CT attenuation values and post-procedural immediate pneumothorax incidence. The inflection point was identified at -805 Hu. The log-likelihood ratio test revealed a statistically significant difference ($p<0.05$, Table 2). After adjusting for all confounding factors, a strong negative association was identified between the lung needle path CT attenuation values and immediate pneumothorax rate. When the lung needle path CT attenuation

Table 1 Baseline characteristic comparisons

Characteristics	CT attenuation values quartile, median (IQR, Hu)				
	Q1 **-881 (-894, -870)**	**Q2** **-847 (-854, -836)**	**Q3** **-815 (-823, -809)**	**Q4** **-776 (-790, -743)**	***p*-value**
Patient number	114	113	113	113	
COPD, *n* (%)	5 (4.39%)	4 (3.54%)	4 (3.54%)	4 (3.54%)	1.000
Smoking status, *n* (%)					0.029
Never	69 (61.10%)	74 (66.70%)	80 (70.80%)	72 (63.70%)	
Former	26 (23.00%)	23 (20.70%)	12 (10.60%)	13 (11.50%)	
Current	18 (15.90%)	14 (12.60%)	21 (18.60%)	28 (24.80%)	
Alcohol consumption, *n* (%)					0.923
Never	75 (68.20%)	78 (69.00%)	82 (72.60%)	77 (68.10%)	
Former	21 (19.10%)	20 (17.70%)	15 (13.30%)	18 (15.90%)	
Current	14 (12.70%)	15 (13.30%)	16 (14.20%)	18 (15.90%)	
Systolic BP, median (IQR, mmHg)	126 (115, 138)	125 (116, 139)	133 (117, 147)	128 (114, 141)	0.089
Diastolic BP, Mean (SD, mmHg)	78.60 (8.63)	80.10 (10.40)	82.20 (10.40)	80.90 (11.00)	0.072
Height, median (IQR, cm)	161 (155, 168)	162 (155, 168)	162 (158, 167)	162 (158, 168)	0.760
Weight, median (IQR, Kg)	59.00 (51.20, 65.00)	60.00 (54.00, 69.00)	60.00 (53.80, 70.00)	63.00 (57.00, 70.50)	0.005
Age, median (IQR, years)	65.00 (55.00, 71.00)	62.00 (53.00, 70.00)	60.00 (49.00, 67.00)	59.00 (52.00, 67.00)	0.011
Gender, *n* (%)					0.699
Female	57 (50.00%)	56 (49.60%)	64 (56.60%)	59 (52.20%)	
Male	57 (50.00%)	57 (50.40%)	49 (43.40%)	54 (47.80%)	
Lesions located in the lungs, *n* (%)					0.503
Left	53 (46.50%)	44 (38.90%)	45 (39.80%)	42 (37.20%)	
Right	61 (53.50%)	69 (61.10%)	68 (60.20%)	71 (62.80%)	
Lesions located in lobes, *n* (%)					0.194
Upper	73 (64.00%)	66 (58.40%)	82 (72.60%)	65 (57.50%)	
Lingual/Middle	5 (4.39%)	3 (2.65%)	3 (2.65%)	3 (2.65%)	
Lower	36 (31.60%)	44 (38.90%)	28 (24.80%)	45 (39.80%)	
Immediate pneumothorax, *n* (%)					< 0.001
No	47 (41.20%)	49 (43.40%)	87 (77.00%)	84 (74.30%)	
Yes	67 (58.80%)	64 (56.60%)	26 (23.00%)	29 (25.70%)	
Lesion diameter, median (IQR, cm)	1.30 (0.90, 2.50)	1.10 (0.90, 2.00)	1.20 (0.90, 2.00)	1.70 (0.90, 2.80)	0.025
Puncture needle gauge, *n* (%, gauge)					0.003
> 17 G	67 (58.80%)	74 (65.50%)	65 (57.50%)	47 (41.60%)	
≤ 17 G	47 (41.20%)	39 (34.50%)	48 (42.50%)	66 (58.40%)	
Operator experience, *n* (%, years)					0.019
> 10	65 (57.00%)	72 (63.70%)	64 (56.60%)	87 (77.00%)	
5–10	44 (38.60%)	37 (32.70%)	44 (38.90%)	25 (22.10%)	
≤ 5	5 (4.39%)	4 (3.54%)	5 (4.42%)	1 (0.88%)	
Patient puncture position, *n* (%)					< 0.001
Supine or prone	67 (58.80%)	91 (80.50%)	109 (96.50%)	112 (99.10%)	
Other	47 (41.20%)	22 (19.50%)	4 (3.54%)	1 (0.88%)	
Tract length in the lungs, median (IQR, cm)	1.90 (1.30, 2.68)	1.70 (1.20, 2.70)	2.00 (1.30, 2.70)	1.70 (1.10, 2.60)	0.238
Needle-pleura angle, median (IQR, degree)	73.00 (56.20, 81.80)	74.00 (58.00, 82.00)	70.00 (54.00, 83.00)	65.00 (50.00, 80.00)	0.138
Puncture though the interlobar fissure, *n* (%)					0.940
No	113 (99.10%)	112 (99.10%)	111 (98.20%)	112 (99.10%)	
Yes	1 (0.88%)	1 (0.88%)	2 (1.77%)	1 (0.88%)	
Number of pleural punctures, *n* (%)					0.745
1	110 (96.50%)	108 (95.60%)	110 (97.30%)	110 (97.30%)	
2	3 (2.63%)	5 (4.42%)	3 (2.65%)	2 (1.77%)	
3	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.88%)	
4	1 (0.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Number of needle redirections, median (IQR)	4.00 (3.00, 5.75)	4.00 (3.00, 5.00)	4.00 (3.00, 6.00)	4.00 (3.00, 6.00)	0.258
Operation duration, median (IQR. minutes)	10.00 (5.00, 15.00)	9.00 (6.00, 14.00)	10.00 (6.00, 17.00)	11.00 (7.00, 17.00)	0.014

Table 1 (continued)

Characteristics	CT attenuation values quartile, median (IQR, Hu)				
	Q1 -881 (-894, -870)	Q2 -847 (-854, -836)	Q3 -815 (-823, -809)	Q4 -776 (-790, -743)	*p*-value
Intraprocedural pneumothorax, *n* (%)					0.107
No	99 (86.80%)	100 (88.50%)	104 (92.00%)	108 (95.60%)	
Yes	15 (13.20%)	13 (11.50%)	9 (7.96%)	5 (4.42%)	
Pulmonary hemorrhage along the needle path, median (IQR, mm)	2.00 (1.00, 5.75)	3.00 (1.00, 7.00)	5.00 (3.00, 11.00)	6.00 (3.00, 13.00)	< 0.001
Delayed pneumothorax *n* (%)					0.316
No	108 (94.70%)	112 (99.10%)	111 (98.20%)	112 (99.10%)	
Yes	6 (5.30%)	1 (0.90%)	2 (1.80%)	1 (0.90%)	
No chest-tube insertion	3 (2.63%)	1 (0.88%)	1 (0.88%)	1 (0.88%)	
With chest-tube insertion	3 (2.63%)	0 (0.00%)	1 (0.88%)	0 (0.00%)	

BP, blood pressure; COPD, chronic obstructive pulmonary disease; IQR, interquartile range

Table 2 Linear and two piecewise linear regression model

Models	Immediate pneumothorax ratio (OR, 95% CI, *p*-value)
Model 1	
Model fitted by linear regression	0.98 (0.98, 0.99) < 0.001
Model fitted by two-piecewise linear regression on the infection point of the lung needle path CT attenuation, (Hu)	
≤ -805	0.98 (0.97, 0.99) < 0.001
> -805	1.00 (0.99, 1.01) 0.879
p-value for the log-likelihood ratio test	0.003
Model 2	
Model fitted by linear regression	0.99 (0.98, 0.99) < 0.001
Model fitted by two-piecewise linear regression on the infection point of the lung needle path CT attenuation, (Hu)	
≤ -805	0.98 (0.97, 0.99) < 0.001
> -805	1.00 (0.99, 1.01) 0.748
p-value for the log-likelihood ratio test	0.001
Model 3	
Model fitted by linear regression	0.99 (0.99, 1.00) 0.013
Model fitted by two-piecewise linear regression on the infection point of the lung needle path CT attenuation, (Hu)	
≤ -805	0.99 (0.98, 0.99) 0.001
> -805	1.00 (0.99, 1.01) 0.566
p-value for the log-likelihood ratio test	0.028

Model 1: no adjustment; Model 2: adjusted for age, gender, height, weight, chronic obstructive pulmonary disease, alcohol consumption, smoking status, systolic blood pressure, and diastolic blood pressure; Model 3: adjusted for model 2, plus lesions located in the lungs and lobes, lesion diameter, tract length in the lungs, needle-pleura angle, puncture through the interlobar fissure, number of needle redirections, number of pleural punctures, puncture needle gauges, operation duration, pulmonary hemorrhage along the needle path, operator experience, and patient puncture position. CI, confidence Interval; Hu, Hounsfield units; OR, odds ratio

value was less than −805 Hu, the OR was 0.99 (95% CI: 0.98–0.99). However, when the CT attenuation value was greater than −805 Hu, the needle path CT attenuation values and immediate pneumothorax rate had no statistical significance (OR: 1.00, 95% CI: 0.99–1.01) (Table 2).

Sensitivity analysis

In order to determine whether the inverse association between the needle path CT attenuation values and increased risk of immediate pneumothorax can be confounded by puncture position or the presence of intraprocedural pneumothorax, the present cohort was refined by excluding subjects with intraprocedural pneumothorax. The present findings remained consistent with the primary analysis results (Table S2 and Fig. S2). Similarly, when the analysis was restricted to patients in the supine or prone puncture position, similar results were obtained (Table S2 and Fig. S3). The refined cohort analysis reaffirmed the nonlinear relationship, and demonstrated the divergent effect values on both sides of the inflection point. This further substantiates the robustness of the present primary findings.

Discussion

Previous studies have identified the presence of emphysema and obstructive pulmonary function abnormalities as potential risk factors for pneumothorax following a percutaneous transpulmonary puncture [26, 27]. Furthermore, a correlation was observed, in which the biopsy-associated pneumothorax ratio was associated to emphysema on the chest CT images [28, 29]. The present study revealed that needle path CT attenuation values are associated to the occurrence of post-procedural immediate pneumothorax following CT-LB. This result is consistent with the results reported by a previous study conducted by Saade et al. [21], which included 179 patients. In that study, a mean parenchymal lung density along the needle trajectory path, and a mean lobar

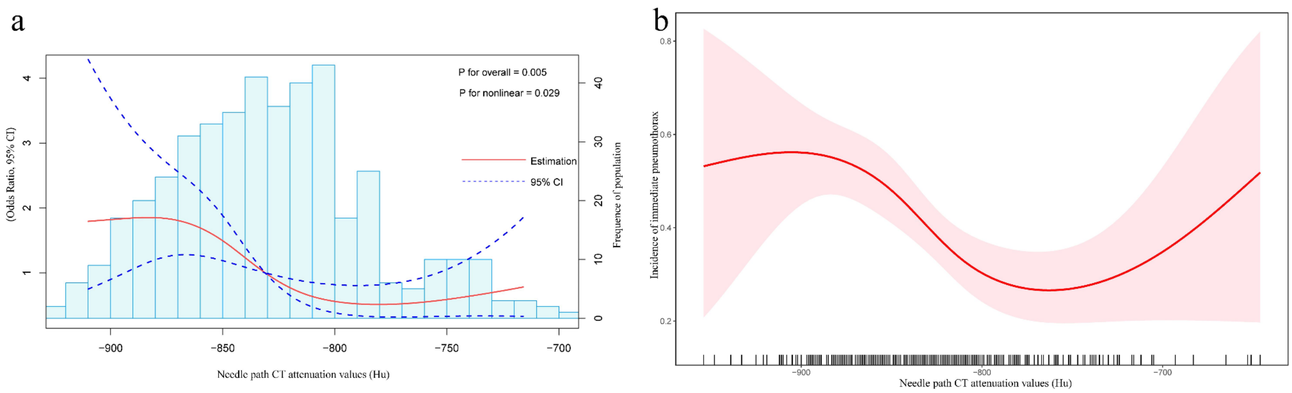

Fig. 2 The nonlinear association between the needle path CT attenuation values and immediate post-procedural pneumothorax was demonstrated using a restricted cubic spline curve (**a**), and a smooth curve fitting (**b**). Both a and b were adjusted for age, gender, height, weight, chronic obstructive pulmonary disease (COPD), smoking status, alcohol consumption, systolic blood pressure (SBP), diastolic blood pressure (DBP), lesion location and diameter, needle-pleura angle, biopsy track length, number of pleural punctures and needle redirections, puncture through the interlobar fissure, puncture needle gauge, pulmonary hemorrhage along the needle path, operation duration, operator experience, and patient puncture position

parenchymal lung density of <-800 Hu were commonly observed in patients who experienced pneumothorax. However, the present study findings were not completely consistent with the previous study reports. It was found that the high CT attenuation values along the lung needle path did not exhibit a linear dose-dependent trend to reduce the pneumothorax risk, due to the presence of an inflection point. Few reports have studied the nonlinear relationship between the lung needle path CT attenuation values and immediate pneumothorax. Restricted cubic spline curves and piecewise linear regression models were used to identify and verify the nonlinear relationship between the lung needle path CT attenuation values and post-procedural immediate pneumothorax. The present study confirmed that a lower lung needle path CT attenuation value is an independent risk factor for the increased incidence of post-procedural immediate pneumothorax. Specifically, needle path CT attenuation values lower than −805 Hu are associated to higher risk of pneumothorax.

Lower needle path CT attenuation values may indicate a decrease in the mass of the pulmonary parenchyma or the abnormal enlargement of air spaces in the pulmonary parenchyma. These variations can lead to a decrease in vascular structures or impaired blood flow, which is often due to gravitational effects, resulting in higher air concentration and lesser blood flow in these areas. Furthermore, lower Hu is typically linked to compromised pulmonary function and illnesses, such as emphysema [30]. In this situation, the biopsy track may not easily seal, allowing air to enter the pleural cavity, and cause pneumothorax. Conversely, higher needle path CT attenuation values appear to provide a protective effect against pneumothorax. These elevated values are often associated to pulmonary hemorrhage along the needle track, which facilitates the sealing of the track, as well as other methods designed to increase needle track CT attenuation values. Pulmonary hemorrhage along the needle track, which is associated to the increase in needle path CT attenuation values, was reported to have a protective effect against pneumothorax in a study conducted on 904 patients [19]. Similarly, another study conducted by Luca et al. [31] reported a lower incidence of pneumothorax in patients with pulmonary hemorrhage along the needle track. This finding is consistent with the subsequent analyses in the present series of studies [32].

In the present study, several approaches were recommended to increase the needle path CT attenuation values, and reduce the risk of pneumothorax, These included positioning the patient biopsy-side down [20], removing the needle during expiration [33], sealing the biopsy track [18, 34, 35], and rapid rollover [29]. Post-procedural needle tract CT attenuation values represent a potential biomarker for effectively sealing needle tracts, thereby contributing to the improved management of post-biopsy pneumothorax.

Although the predictive efficacy of lung needle path CT attenuation values for pneumothorax remains a topic of ongoing investigation, the study conducted by Rothman A et al. [36], which involved 110 patients who underwent CT-guided transthoracic needle biopsy, indicated a high risk of major complications with higher Hu units of the targeted lesion. However, more recent research has suggested that an increase in CT attenuation values along the puncture route may potentially reduce the risk of biopsy-related pneumothorax [28].

The present study suggests that higher CT attenuation values along the lung needle path can be associated to reduced risk of post-procedural immediate pneumothorax. Several plausible mechanisms could underlie this association. Higher CT attenuation values may occur with alveolar shrinkage and airway closure adjacent to the needle path, thereby reducing the likelihood of air escaping into the pleural cavity. In addition, areas that exhibit higher attenuation may have poorer collateral ventilation on the dependent side, facilitating to isolate the puncture site and minimize the air leakage. Furthermore, elevated CT attenuation values might be associated to the reduction in alveolar-to-pleural pressure gradient at the puncture site, thereby ameliorating the driving force for air escape. Moreover, higher attenuation values could facilitate gravity-dependent blood collection in the needle track, which would help to seal the path, and prevent air leakage into the pleural space. The weight of the lung might enhance pleural apposition and compress the alveoli, effectively sealing the biopsy tract, and reducing the incidence of pneumothorax. The precise mechanisms underlying these observations remain unclear, and warrant further investigation.

The strengths of the present study included the following: (1) to the best of our knowledge, the present study was the first to explore the nonlinear relationship between the lung needle track CT attenuation values and post-procedural immediate pneumothorax, and the optimal inflection point of the needle path CT values was identified; (2) strict statistical adjustments were applied to remove residual confounders, and a variety of nonlinear models were constructed and verified with each other to make the results more robust; (3) different standard linear and nonlinear binomial logistic models (the smooth curve fitting model and restricted cubic spline model) were constructed to explore the relationship between the lung needle track CT attenuation values and post-procedural immediate pneumothorax, and the present analysis had greater clinical implications.

Nevertheless, the present study had several limitations: (1) The retrospective design of the present study could have missed some of the potential confounders, and underestimated the complications. (2) The study participants were selected from a single hospital in China, thereby requiring further investigations to determine whether these results can be generalized to other patient populations, and whether these results need to be validated for other medical facilities. (3) The present study did not provide a quantitative measurement of the volume of the pneumothorax. The post-procedural immediate pneumothorax was diagnosed based on the CT scan, while the delayed pneumothorax was assessed mostly by X-ray. The diagnosis for delayed pneumothorax might not be as accurate as that for immediate pneumothorax. In addition, the study failed to analyze the association between needle path CT attenuation and delayed pneumothorax, since merely a small size of patients (only 10 patients) was detected. (4) CT scans were used to diagnose the post-procedural immediate pneumothorax in the present study. Patients detected with a scanty amount of pneumothorax might not require special treatment. Patients with clinically meaningful pneumothorax might be more appropriate targets for the study. (5) The lesion characteristics were not considered in the present study. Lesion characteristics, such as solid, cystic, or cavity lesions, might impact the pneumothorax development. (6) The present study evaluated the association between needle path CT values and postoperative pneumothorax. However, the causal relationship between these requires further investigation. Despite some potential limitations, the present study provides reliable evidence, and was the first to reveal the nonlinear relationship between the needle path CT attenuation values and post-procedural immediate pneumothorax, which has never been reported in previous regression models.

Conclusion

There is a nonlinear relationship between the needle path CT attenuation values and post-procedural immediate pneumothorax in adults undergoing CT-LB, with an inflection point. This nonlinear relationship should be considered when selecting the optimal preoperative lung puncture path, in order to reduce the risk of immediate pneumothorax caused by CT-LB. Future prospective studies are warranted to verify these present research findings.

Abbreviations

BP	blood pressure
CI	confidence interval
COPD	chronic obstructive pulmonary disease
CT	computed tomography
GAM	generalized additive model
Hu	Hounsfield units
OR	odds ratio
ROC	region of interest
SD	standard deviation

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions

SQZ: conceptualization, methodology, investigation, data curation, writing-original draft, visualization, and project administration, writing-review and editing. FL: conceptualization, formal analysis, writing-original draft review and editing. KL: supervision; writing-review and editing. XR: methodology, investigation, data analysis, validation, writing-review and editing. JY: investigation, data curation, writing-review and editing. FRL: writing-review and editing, supervision. Final approval of manuscript: all authors.

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Data availability
The data that support the findings of the study are available from the corresponding author upon reasonable request. The data are not publicly available due to privacy or ethical restrictions.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the hospital institutional review board (Ethics 28 Committee of Chongqing General Hospital, ID: XJS S2022-052-01), and all methods were carried out in accordance to relevant guidelines and regulations. The requirement for informed consent was waived, and this was approved by the Ethics 28 Committee of Chongqing General Hospital due to the retrospective design of the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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