

Development of a Nomogram Model to Predict the Risk of Pneumothorax after CT-guided Coaxial Core Needle Lung Biopsy: A Cross-sectional Study

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ABSTRACT

Introduction: A sharp increase in the incidence of chest tumours has led to an increased demand for Computed Tomography (CT)-guided lung biopsy. Pneumothorax remains the most common complication of CT-guided coaxial core needle lung biopsy. Pneumothorax triggers shortness of breath and chest pain, which leads to prolonged inpatient stay. To reduce the incidence of pneumothorax, a predictive model in the form of nomogram was developed using the potential risk factors to identify patients at high-risk for pneumothorax.

Aim: To investigate the risk factors of pneumothorax and develop a nomogram model using the independent risk factors to predict pneumothorax after CT-guided coaxial core needle lung biopsy and to validate the prediction model in a test population.

Materials and Methods: A cross-sectional time-bound study was done at Barnard Institute of Radiology, Madras Medical College, and Rajiv Gandhi Government General Hospital in Chennai, Tamil Nadu, India from October 2023 to October 2024. The study included 335 patients who were referred to the Department of interventional radiology for CT-guided coaxial core needle lung biopsy to diagnose lung nodules or masses suspected of malignancy in chest CT. A total of 28 variables were assessed, which included baseline patient characteristics, primary pulmonary diseases, target lesion image characteristics, and biopsy-related variables. Of the total sample size of 335

patients, 233 (70%) were part of the development group, and 102 patients were included in the validation group (30%). Multivariate and univariate logistic regression analysis methods were used to identify the independent risk factors of pneumothorax, which were used to develop the nomogram risk prediction model. The prediction model was validated in a test population of 102 patients.

Results: A total of 51 (21.88%) patients developed pneumothorax post CT-guided lung biopsy among the development group, and 20 (19.60%) patients among the validation group also developed pneumothorax. Seven independent risk factors were determined among the assessed variables using multivariate logistic regression analysis, which included age, emphysema, pleural thickening, fissure traversed, patient position, size grade, and lesion depth. The seven factors were used to construct a nomogram risk prediction model. Receiver Operating Characteristic (ROC) curves were used to validate the nomogram model. In the development group, Area Under Curve (AUC) was 0.921, and in the validation group, AUC was 0.897.

Conclusion: A nomogram risk prediction model for pneumothorax was developed using the seven independent risk factors and has proven to be accurate and statistically valid. The nomogram model can thus help predict pneumothorax in clinical practice, assisting interventional radiologists in avoiding risk factors.

Keywords: Computed tomography, Lung biopsy complications, Prediction model, Pneumothorax risk, Risk prediction

INTRODUCTION

Computed Tomography (CT)-guided lung biopsy is universally used for the histological diagnosis of lung lesions and has the advantage of providing an accurate diagnosis [1,2]. With technological advancements in CT, it is now the preferred guiding modality for Percutaneous Transthoracic Needle Biopsy (PTNB) [1,2]. The CT-guided PTNB is an effective, accurate, and safe procedure for diagnosing suspicious lung lesions [1].

Core needle biopsy has been shown to have a high overall sensitivity, specificity, and accuracy of 89%, 97%, and 93%, respectively [1]. It is a widely accepted procedure and is less invasive compared to surgical biopsy. However, it is inevitably accompanied by procedural and postprocedural complications [1,2].

Historically, transthoracic needle biopsy was conducted with a single needle. The current trend is to adopt a coaxial approach, since it delivers good diagnostic accuracy for intrathoracic lesions with acceptable low rates of complications [3]. Recent studies have focused on determining the diagnostic accuracies and complication rates associated with coaxial approach and

demonstrated that coaxial technique is safer than alternative biopsy techniques [3,4].

Coaxial Core Needle Biopsy (CCNB) is a sort of PTNB in which operators pierce the target lesion with a coaxial needle, then draw out the needle core while leaving the needle sheath in the lung. This allows the core biopsy needle to be repeatedly inserted and removed from the lung tissue for sampling purposes. Using a coaxial needle sheath reduces the need for multiple passes into the pleura, allowing for more efficient sampling [3].

Complications associated with CT-guided lung biopsy encompass pneumothorax, haemoptysis, infections, and air embolism [1,2]. Pneumothorax is the most common complication following PTNB and can become potentially fatal if not identified and managed immediately [1-4]. Pneumothorax causes chest pain, dyspnoea, and hypoxia, and therefore increases the rates of chest tube drainage and prolonged hospitalisation [5].

Several studies have found that age, emphysema, lesion size, lesion location, needle insertion through fissures, patient position, and needle path distance from pleura to lesion are predictors of pneumothorax

[6-13]. Other predictors found in different studies include pleural thickening [6], lobulation sign [6], lesions not in contact with the pleura [7], longer procedure duration, and the use of a 19 G needle [14].

A number of studies have developed nomogram models for predicting pneumothorax following CT-guided CCNB [6,7,11]. Some of these studies applied the predictive nomograms to validate and calibrate the results [6,11].

Hence, present study was conducted to further investigate the risk factors of pneumothorax and to develop a nomogram model using the independent risk factors to predict pneumothorax post CT-guided CCNB and to validate the model in a test population.

MATERIALS AND METHODS

A cross-sectional, time-bound study was conducted at Barnard Institute of Radiology, Madras Medical College, and Rajiv Gandhi Government General Hospital, Chennai, Tamil Nadu, India from October 2023 to October 2024. Institutional Ethical Committee approval was obtained (16092023). Consent to participate in the study was obtained from each patient before included in the study.

Inclusion criteria: Patients referred for CT-guided lung biopsy to evaluate single or multiple lung nodules or masses suspected to be malignant based on diagnostic CT chest imaging.

Exclusion criteria:

- Cases with poor image quality where data cannot be collected.
- Patients who had already had pneumothorax before the lung biopsy.

Sample size: Of present total sample size of 335 patients, 233 (70%) were part of the development group, while the validation group included 102 patients (30%).

Study Procedure

All CT-guided lung biopsies performed at the Institute were CCNBs. CT examinations were performed using a Siemens 16-slice helical CT machine. The biopsy procedure was conducted with the patient in a supine or prone position, depending on the lesion's location and plan of entry. The patient was positioned on the biopsy table so that the skin entry site was placed upright. The CT fluoroscopic images were used to guide the coaxial needle placement. Settings used were: scanning speed- 0.5 seconds per rotation (360°); tube voltage- 120 kVp; current- 70 to 80 mA; collimation- 1 mm; and section thickness- 2 mm. A 17G coaxial needle was used to perform the biopsies in all cases. Once the position of the tip of the needle was confirmed to be within the lesion, tissue specimens were extracted using a semi-automated or automated biopsy gun and placed into a 10% formaldehyde solution for pathological examination. In most cases, five passes were made to obtain five cores of biopsy tissue, which was considered adequate. Post-procedure, all patients were observed and monitored for at least six hours with periodic recording of the vital signs and were discharged if a control chest radiograph was clear.

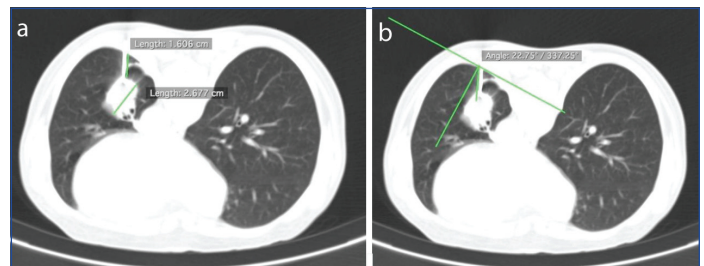
Image analysis and Data collection: The image interpreters were not involved in the biopsy procedures and were unaware of any occurrences of pneumothorax. The clinicopathologic information collected included 28 factors:

- 1) Baseline patient demographics such as age, sex, blood pressure, and laboratory values were recorded.
- 2) The presence or absence of lung pathology, such as bullae, emphysema, pleural thickening, hydrothorax, and pulmonary fibrosis.
- 3) Target lesion image characteristics: lesion size, size grade (≤ 3.0 cm, >3.0 cm), lesion location, spiculated margins, pleural indentation, lesion calcifications, perifocal inflammation, and biopsy diagnostic results (malignant, benign, or inconclusive).
- 4) Biopsy-related factors: lesion depth from pleura, needle insertion angle, patient position (supine or prone), number of

tissue cores extracted, whether the fissure was traversed or not, and operator experience (procedure performed by Junior Resident (JR) or Senior Resident (SR)).

The lesion's size was measured as the maximum diameter on axial CT-chest images in lung window [Table/Fig-1a], location of the lesion was categorised as situated in the upper or Lower Lobes (LL) of left lung, or upper, lower, or Middle Lobes (ML) of right lung.

Lesion's depth from the pleura was calculated as the length of the needle tract between the point where the needle punctures the pleura and the location of the lesion [Table/Fig-1a]. Needle insertion angle was measured as the acute angle formed between the direction of the needle and a perpendicular line drawn to the pleura at the point where the needle enters the pleura [Table/Fig-1b].



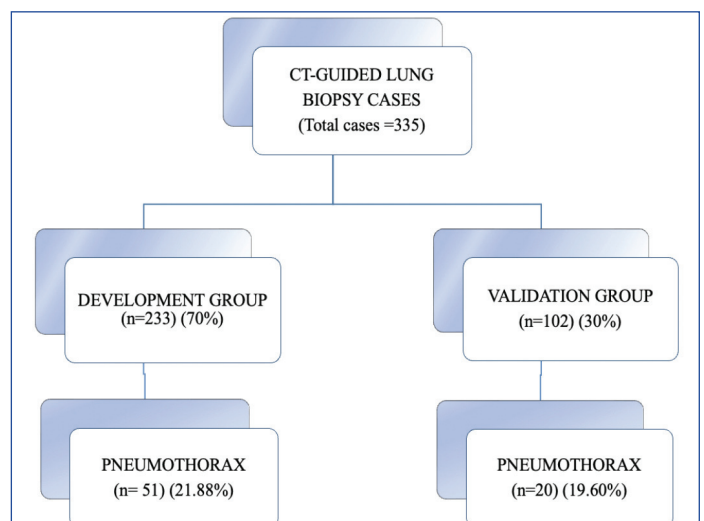
[Table/Fig-1]: Axial CT images in lung window: a) Lesion in lower lobe of left lung with lesion depth from pleura 1.6 cm and size of the lesion is 2.677 cm; b) Needle insertion angle is 22.75 degrees and biopsy performed in prone position.

STATISTICAL ANALYSIS

The collected data was analysed using IBM Statistical Packages of Social Sciences (SPSS) statistics software for Windows, version 25.0. Univariate and multivariate logistic regression analyses were performed. Variables with $p < 0.05$ in univariate logistic regression analysis were included in the multivariate logistic regression model. Based on the regression coefficients of the independent risk factors, an individualised nomogram risk prediction model of pneumothorax was developed. ROC curves were derived for both groups using the predicted probabilities of pneumothorax and were analysed with IBM SPSS statistics software for Windows version 25.0.

RESULTS

A total of 335 patients were included in the study. Pneumothorax occurred in 51 of 233 biopsy procedures (21.88%) in the development group and in 20 of 102 biopsies (19.60%) in the validation group [Table/Fig-2]. The data of baseline patient characteristics in the development and validation groups has been depicted in [Table/Fig-3]. Of the 335 patients included in present study, three patients underwent chest tube placement for clinically significant pneumothorax.



[Table/Fig-2]: Flowchart demonstrating the outcomes of pneumothorax after CT-guided coaxial core needle lung biopsy in the development and validation groups.

Variables	Development group (n=233)	Validation group (n=102)	p-value
Pneumothorax (%)	51 (21.88%)	20 (19.60%)	
Age (years) (mean±SD)	58.58±9.36	57.53±8.80	0.914
Gender (%)			
Male	161 (69.1%)	73 (71.6%)	0.650
Female	72 (30.99%)	29 (28.4%)	
Blood pressure (mean±SD)			
SBP	124.64±9.28	124.80±9.20	0.878
DBP	80.9±7.63	81.08±7.57	0.845
Smoke index (mean±SD)	255.54±119.04	243.21±124.97	0.391
RBC ×10 ⁶ (mean±SD)	4.41±0.61	4.37±0.62	0.545
WBC ×10 ⁴ (mean±SD)	6.09±1.77	6.14±1.76	0.828
Platelet ×10 ⁶ (mean±SD)	3.21±0.97	3.22±0.96	0.928
Prothrombin time (seconds) (mean±SD)	14.15±1.80	14.27±1.73	0.554
Emphysema (%)	38 (16.3%)	14 (13.7%)	0.548
Bullae (%)	15 (9.49%)	23 (6.95%)	0.326
Pulmonary fibrosis (%)	14 (6%)	7 (6.9%)	0.767
Hydrothorax (%)	38 (16.3%)	17 (16.7%)	0.935
Pleural thickening (%)	54 (23.2%)	25 (24.5%)	0.791
Lesion location (%)			
UL	99 (42.5%)	41 (40.2%)	0.919
LL	113 (48.5%)	10 (9.8%)	
ML	21 (9%)	51 (50%)	
Size (cm)	5.25 (2.64)	5.49 (2.84)	0.456
Size grade (%)			
<3 cm	47 (20.2%)	17 (16.7%)	0.453
>3 cm	186 (79.8%)	85 (83.3%)	
Spiculation	59 (25.32%)	29 (28.4%)	0.998
Pleural indentation (%)	84 (36.1%)	41 (40.2%)	0.470
Calcification (%)	22 (9.4%)	10 (9.8%)	0.917
Perifocal inflammation (%)	21 (9%)	8 (7.8%)	0.927
Vessel convergence (%)	41 (17.6%)	14 (13.7%)	0.917
Biopsy result (%)			
Malignant	203 (87.1%)	86 (84.3%)	0.521
Specific benign	21 (9%)	7 (6.9%)	
Non diagnostic	9 (3.9%)	9 (8.8%)	
No. of samplings (%)			
5	201 (86.3%)	90 (82.2%)	0.867
6	25 (10.7%)	9 (8.8%)	
7	7 (3%)	3 (2.9%)	
Patient position (%)			
Supine	129 (55.4%)	63 (61.8%)	0.276
Prone	104 (44.6%)	39 (38.2%)	
Lesion depth (cm) (mean±SD)	1.59±1.38	1.44±1.37	0.371
Needle angle (mean±SD)	62.44±14.37	61.66±15.53	0.656
Fissure traversed			
Yes	34 (14.6%)	13 (12.7%)	0.654
No	199 (85.4%)	89 (87.3%)	
Operator experience (%)			
JR	142 (60.9%)	61 (59.8%)	0.868
SR	91 (39.1%)	41 (40.2%)	

[Table/Fig-3]: The baseline characteristics of patients in the development and validation groups.

The continuous variables are displayed as the mean and Standard deviation; The categorical variables are displayed as number and percentage; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; UL: Upper lobe; LL: Lower lobe; ML: Middle lobe; JR: Junior resident; SR: Senior resident

Univariate analysis and multivariate analysis: Univariate logistic regression analysis of the 28 variables after CT-guided coaxial core needle lung biopsy in the development group showed nine factors age, emphysema, pleural thickening, patient position, fissure traversing, size grade, lesion depth, lesion location, and hydrothorax- as independent risk factors [Table/Fig-4,5]. Age, emphysema, pleural thickening, fissures traversed, patient position, size grade, and lesion depth were found to be independent risk factors using the multivariate logistic regression analysis [Table/Fig-4,5].

Nomogram development: An individualised prediction model was developed to predict pneumothorax after CT-guided coaxial core needle lung biopsy has been depicted in [Table/Fig-6].

Discrimination of the model: The predicted probability of pneumothorax and the actual incidence of pneumothorax were analysed using the ROC curves. AUC of the predictive model was 0.921 (95% CI=0.885-0.957) [Table/Fig-7], while that of the validation group was 0.897 (95% CI=0.846-0.947) [Table/Fig-8].

DISCUSSION

Pneumothorax is the most common complication of CT-guided lung biopsy [1,4,13]. When large, pneumothorax can cause lung collapse, and the risk to patients increases drastically when this occurs in an outpatient setting. The ability to predict the probability of pneumothorax pre-procedurally will be extremely useful when performing a CT-guided lung biopsy.

A total of seven independent risk factors for pneumothorax were identified based on multivariate logistic regression analysis: age, emphysema, patient position, pleural thickening, traversing of the fissure, size grade, and lesion depth.

The increased risk of pneumothorax in elderly individuals following lung biopsy may be due to the fact that lung tissue and pleura are more likely to be ripped by the needle [6,13]. Emphysema was found to be an independent risk factor. Emphysematous lungs are hyperinflated and have decreased lung elasticity, weakening the surrounding supportive interstitium. This decrease in tensile strength can lead to inadequate lung retraction after the needle is withdrawn, making it difficult for the lung to seal the air leak quickly once the needle is removed [6,7]. Pleural thickening was also a significant factor and worked as protective force against pneumothorax. This could be attributed to the fact that thickened pleura cannot tear easily [6,8].

Traversing of fissure was another independent risk factor. When the fissure is crossed by the needle, shearing takes place at the puncture sites along the fissure, causing each lobe to move independently during breathing. The needle remains fixed within each lobe, resulting in multiple pleural punctures. This creates several possibilities for air leakage and increases the risk of developing a pneumothorax [11].

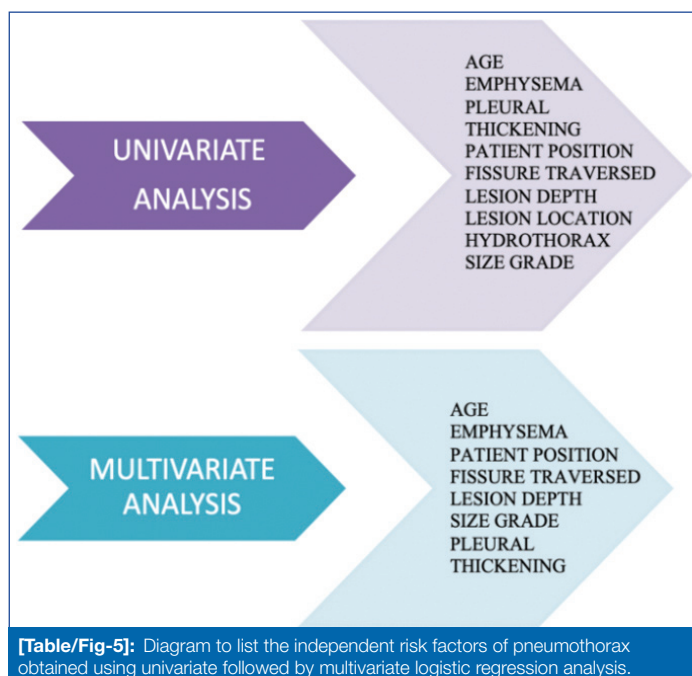
It was determined that lesions smaller than 3 cm in size (size grade) had a higher risk of developing pneumothorax in present study. Several studies found that the smaller the lesion, the higher the risk of post-puncture pneumothorax [6,10]. One probable explanation for this mechanism is that with smaller lesions, the point of the needle is less stable, causing back-and-forth motions during free breathing, which results in significant disruption of the neighbouring lung parenchyma [6]. Another explanation is that approaching smaller lesions may result in prolonged and more difficult operations [11]. However, the threshold lesion size for assessing biopsy risk remains controversial [10].

Lesion depth was determined to be a significant risk factor; as the depth of the lesion increases from the pleura, the risk of

Variables	Univariate analysis			Multivariate analysis		
	Coefficient	OR (95% CI)	p-value	Coefficient	Adj. OR (95% CI)	p-value
Age	0.11	1.11 (1.07,1.16)	<0.001*	0.03	1.03 (1.02,2.06)	0.036*
Emphysema						
No	1			1		
Yes	2.02	7.56 (3.56,16.05)	<0.001*	0.97	2.64 (1.23,7.21)	0.024*
Pleural thickening						
No	1			1		
Yes	-1.86	0.16 (0.05,0.52)	0.003*	-1.53	0.216 (0.14,0.96)	0.043*
Lesion location						
Upper lobe of left lung	1			1		
Lower lobe of left lung	-2.85	0.06 (0.02,0.17)	<0.001*	0.725	2.06 (0.32,2.64)	0.069
Upper lobe of right lung	-0.85	0.43 (0.19,0.96)	0.039*	0.67	1.49 (0.53,7.25)	0.268
Middle lobe of right lung	-21.55	1.52 (0.76,3.59)	0.635	1.08	2.94 (0.88,8.64)	0.357
Lower lobe of right lung	-21.55	1.36 (0.98,7.63)	0.584	0.24	1.27 (0.24,10.56)	0.686
Size grade						
</=3	1			1		
>3	-2.87	0.06 (0.03,0.12)	<0.001*	-1.68	0.19 (0.063,0.55)	0.002*
Patient position						
Prone	1			1		
Supine	-1.47	4.35 (2.15,8.81)	<0.001*	-0.53	1.69 (1.03,8.09)	0.001*
Lesion depth	0.68	1.97 (1.51,2.56)	<0.001*	0.23	1.24 (1.05,1.92)	0.004*
Hydrothorax						
No	1			1		
Yes	0.43	1.53 (0.70,3.34)	0.028*	0.32	1.37 (0.23,5.32)	0.299
Fissure traversed						
No	1			1		
Yes	3.29	26.85 (10.58,68.11)	<0.001*	2.19	8.9 (3.26,11.26)	<0.001*

[Table/Fig-4]: Risk factors identified using univariate and multivariate logistic regression analysis in the development group.

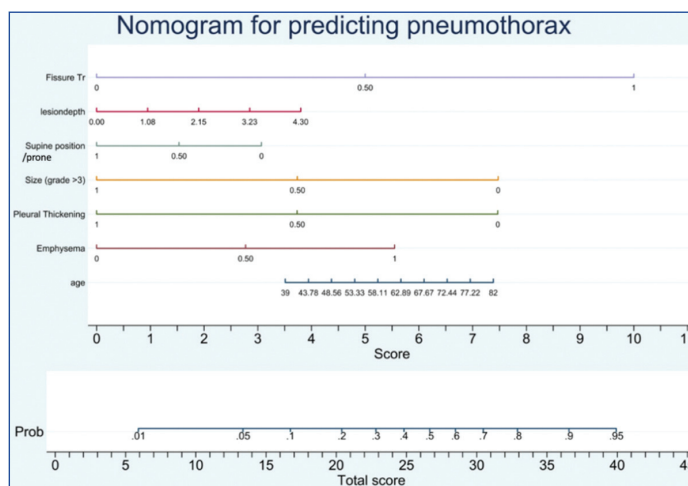
(*) indicates statistical significance



[Table/Fig-5]: Diagram to list the independent risk factors of pneumothorax obtained using univariate followed by multivariate logistic regression analysis.

pneumothorax also increases. A longer needle pathway can result in tearing of the pleura and surrounding lung parenchyma as the patient breathes during the procedure, potentially increasing the volume of air leakage [11, 14].

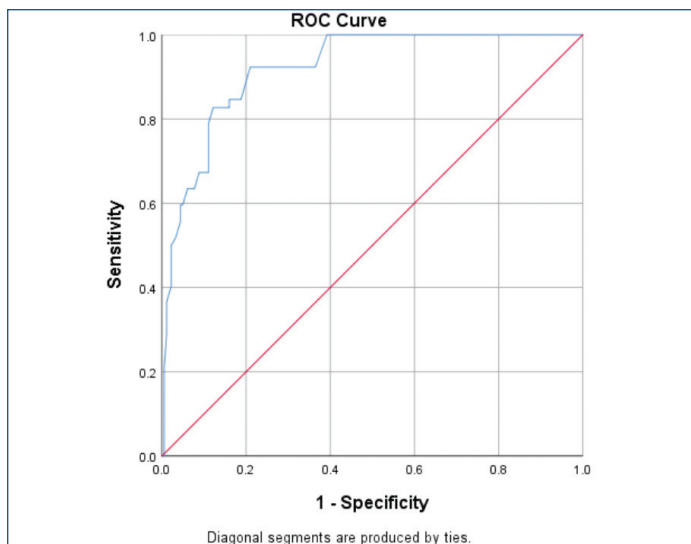
With regard to patient position in present study, prone position was found to be associated with higher rates of pneumothorax, which contradicts studies that found the prone position to be associated with a lower risk of pneumothorax compared to non prone positions



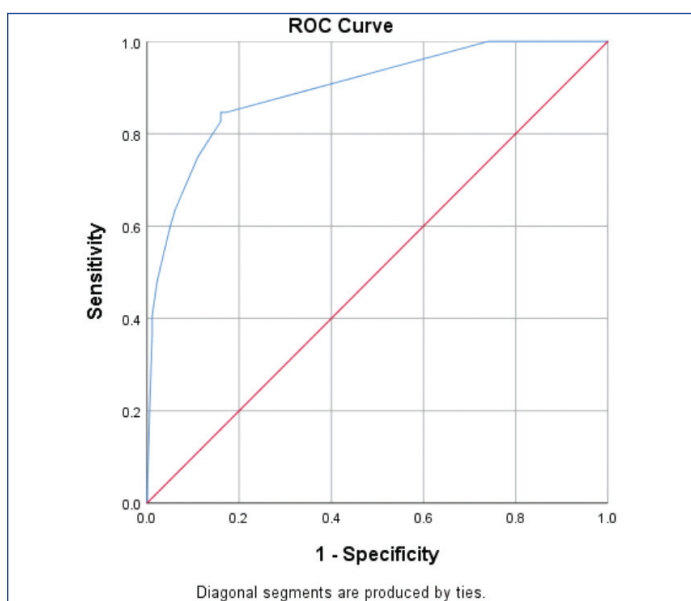
[Table/Fig-6]: The nomogram model used to predict the probability of pneumothorax after CT-guided lung biopsy. Firstly, score for each of the variables of a patient are determined on the uppermost rule; then all points are added together to calculate the "total score"; finally find the corresponding predicted probability of pneumothorax on the lowest rule based.

[15]. The impact of body position on the risk of pneumothorax is hard to explain. In a different study [12], the prone position was found to be associated with a higher risk of pneumothorax and was also identified as an independent risk factor of pneumothorax. Most other studies have not analysed the influence of body position on pneumothorax. Among those that did, the results varied. Thus, precise role of body position can be understood by further research.

Lesion location was found to be a significant risk factor in the univariate analysis but was not statistically significant in the



[Table/Fig-7]: Graph shows ROC curve for validating the discrimination of the nomogram model in the development group: AUC=0.921 (95% CI=0.885-0.957).



[Table/Fig-8]: Graph shows ROC curve for validating the discrimination of the nomogram model in the validation group: AUC=0.897 (95% CI=0.846-0.947).

multivariate logistic regression analysis; hence, it was not included in present nomogram model. Zhao Y et al., established lesion location as an independent risk factor in their study, demonstrated that due to the greater respiratory motion in the lower lung field, lesions in that area were at a higher risk for pneumothorax than the lesions in upper, upper-middle, middle, and middle-lower lung fields [11]. This was debated in another study by Weon J et al., who contradicted this finding by establishing that lesions in the upper lobe posed a higher risk of pneumothorax [7].

A risk prediction model was established based on seven independent risk factors and showed favourable predictive performance in present research, with AUCs of 0.921 and 0.897 in the development and validation groups, respectively. These findings demonstrated that the predictive model performed well in distinguishing between pneumothorax and non-pneumothorax following lung biopsy.

Limitation(s)

First, an external validation was not conducted; this was a single-centre study. Second, risk factors like pulmonary function and lateral positioning were not included in this study. Lateral positioning during biopsy procedure can increase the risk of developing pneumothorax, as shown in previous studies. This may be due to

the separation of the parietal and visceral pleural layers when the lung being biopsied is positioned upward in the lateral decubitus position, in comparison to the supine or prone positions where the biopsied lung is dependent. As a result, air is more likely to enter the pleural cavity when the needle is withdrawn. But patient's position in the lateral position was not considered in present study due to the minimal number of cases performed in this position in the course of present study. Third, authors utilised the most commonly used 17 G biopsy needle; and hence needle size as a risk factor was not assessed. Previous studies have demonstrated that needle size is an important risk factor for pneumothorax [14].

CONCLUSION(S)

Pneumothorax is a relatively common complication of CT-guided lung biopsy. Independent risk factors for pneumothorax include age, emphysema, traversing fissures, size grade of the lesion, pleural thickening, patient's position, and the depth of the lesion from pleura. The nomogram predictive model developed in present study was accurate and showed good predictability for pneumothorax. Therefore, it can provide clinicians and Interventional Radiologists with a method to predict a patient's probability of pneumothorax after CT-guided CCNB of the lung.

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