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The nodule-pleura relationship affects pneumothorax in CT-guided percutaneous transthoracic needle biopsy: avoiding to cross pleural tail sign may reduce the incidence of pneumothorax

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Abstract

Objectives To explore the role of nodule-pleural relationship, including nodule with pleural tail sign (PTS), nodule with pleural contact and nodule with pleural unrelated in CT-guided percutaneous transthoracic needle biopsy (PTNB)-induced pneumothorax, and whether employing different puncture routes has an impact on the incidence of pneumothorax in PTNB of nodules with PTS.

Methods Between April 1, 2019, to June 30, 2021, 775 consecutive PTNB procedures of pulmonary nodules in the Peking University Cancer Hospital were retrospectively reviewed. The univariate and multivariate regression analysis were used to identify the risk factors for pneumothorax in PTNB.

Results The nodule with pleural contact group has a lower incidence of pneumothorax than the nodule with PTS group ($p=0.001$) and the nodule with pleural unrelated group ($p=0.002$). It was observed that a higher incidence of pneumothorax caused by crossing PTS compared with no crossing PTS ($p<0.001$). Independent risk factors for pneumothorax included crossing PTS ($p<0.001$), perifocal emphysema ($p<0.001$), biopsy side up ($p<0.001$), longer puncture time ($p<0.001$), deeper needle insertion depth (intrapulmonary) ($p<0.001$) and nodules in the middle or lower lobe ($p=0.007$).

Conclusion Patients with crossing PTS, a nodule in the middle or lower lobe, longer puncture time, biopsy side up, deeper needle insertion depth (intrapulmonary), and perifocal emphysema were more likely to experience

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pneumothorax in PTNB. When performing the biopsy on a nodule with PTS, selecting a route that avoids crossing through the PTS may be advisable to reduce the risk of pneumothorax.

Keywords Computed tomography-guided percutaneous transthoracic needle biopsy, Pneumothorax, Nodule-pleural relationship, Crossing pleural tail sign

Introduction

In order to obtain the pathological diagnosis of pulmonary lesions, CT-guided percutaneous transthoracic needle biopsy (PTNB) was increasingly used. PTNB offered a sensitivity ranging from 85.7 to 97.4% and a specificity ranging from 88.6 to 100% for diagnosing malignancies [1]. Given that the reported incidence of pneumothorax in the literature ranged from 4.3 to 52.4% [2, 3], pneumothorax was one of the most common complications after PTNB.

A recent study suggested that pneumothorax was more likely to occur when performing PTNB on a nodule with pleural tail sign (PTS) [4]. Previous studies have reported that the tag result from thickening interlobular septa of the lung [5] or from pleural retraction [6]. The occurrence of PTNB-induced pneumothorax was related to the damage of visceral pleura [7] and that supported by studies of pleura-related variable including pleura angle [8–10]. Based on that, we hypothesized that the presence of PTS may cause the visceral pleura to be more vulnerable to damage for the biopsy of nodules with PTS, if our puncture path did not pass through the linear or striated pleural tags were visible and the pleura affected by the PTS, the extent of the pleural tear might decrease, so as to reduce the occurrence of pneumothorax.

Therefore, our study explored the role of nodule-pleural relationship that including nodule with pleural tail sign (PTS), nodule with pleural contact and nodule with pleural unrelated in PTNB-induced pneumothorax. Additionally, we aimed to assess whether employing different puncture routes for nodules with PTS had an impact on the occurrence of PTNB-induced pneumothorax.

Materials and methods

Patients and lesions

This study retrospectively included 775 consecutive PTNB procedures for pulmonary nodules conducted at Peking University Cancer Hospital from April 1, 2019, to June 30, 2021. The study encompassed lung nodules with a diameter of ≤3 cm. Exclusion criteria were as follows: (I) PTNB on the ipsilateral lung with surgical history; (II) Two nodules biopsied simultaneous; (III) Pre-existing pleural effusion at the puncture site; (IV) Puncture path passing through the mediastinum; (V)The chest wall or mediastinum invasion. On the basis of these criteria,33 cases were excluded (Fig. 1).

Biopsy procedure

Our PTNB procedures were conducted on the outpatient basis. All PTNB procedures were carried out with a 64-detector row CT scanner (Optima CT 680; GE Healthcare) guidance by three attending radiologists (ML.C., YL.L., and HB.Z.), with 10, 5 and 4 years' experience in PTNB, respectively. The coaxial technique was performed with 17-gauge introducer needles and 18-gauge biopsy needles including automatic cutting biopsy needles (Argon Medical Devices) and semi-automatic cutting biopsy needles (Bard Magnum). The choice of biopsy needle type was made by the operators based on their experience and preference.

Before each biopsy, the relevant images were reviewed and the biopsy scheme was designed including the patient's position (biopsy side up or supine, prone) and the selection of the puncture path and depth. In the biopsy side up group, patients were placed in the supine or prone position with a pad placed under their body to elevate the lesion side or in the lateral decubitus position with the lesion side up. The key criteria for selecting the puncture path included avoiding fissure crossings, selecting larger pleural-needle angles, choosing the shorter distance that the needle traveled in the pulmonary and avoiding blood vessels and bronchi in the needle path. Local anesthesia was administered with 1% lidocaine into the subcutaneous tissue and pleural surface before the biopsy. The procedural complications (pneumothorax, pulmonary hemorrhage, hemothorax, and air embolism) were assessed by a chest CT scan after the biopsy. A routine upright chest radiograph was performed one hour after PTNB. Patients were discharged if there were no major complications requiring management.

Data collection

The electronic medical records and biopsy procedure details was reviewed. On the basis of previous literature and the experience of authors at our center, we collected the following potential risk factors for pneumothorax in PTNB. Collected data encompassed patient-related variables, nodule-related variables, technique-related variables, pleura-related variables, and procedural complications.

Patient-related variables included gender and age. Nodule-related variables included location, maximum diameter, diameter in the direction of needle insertion, nodule type (solid or non-solid). Perifocal emphysema was defined as the presence of emphysema in the area

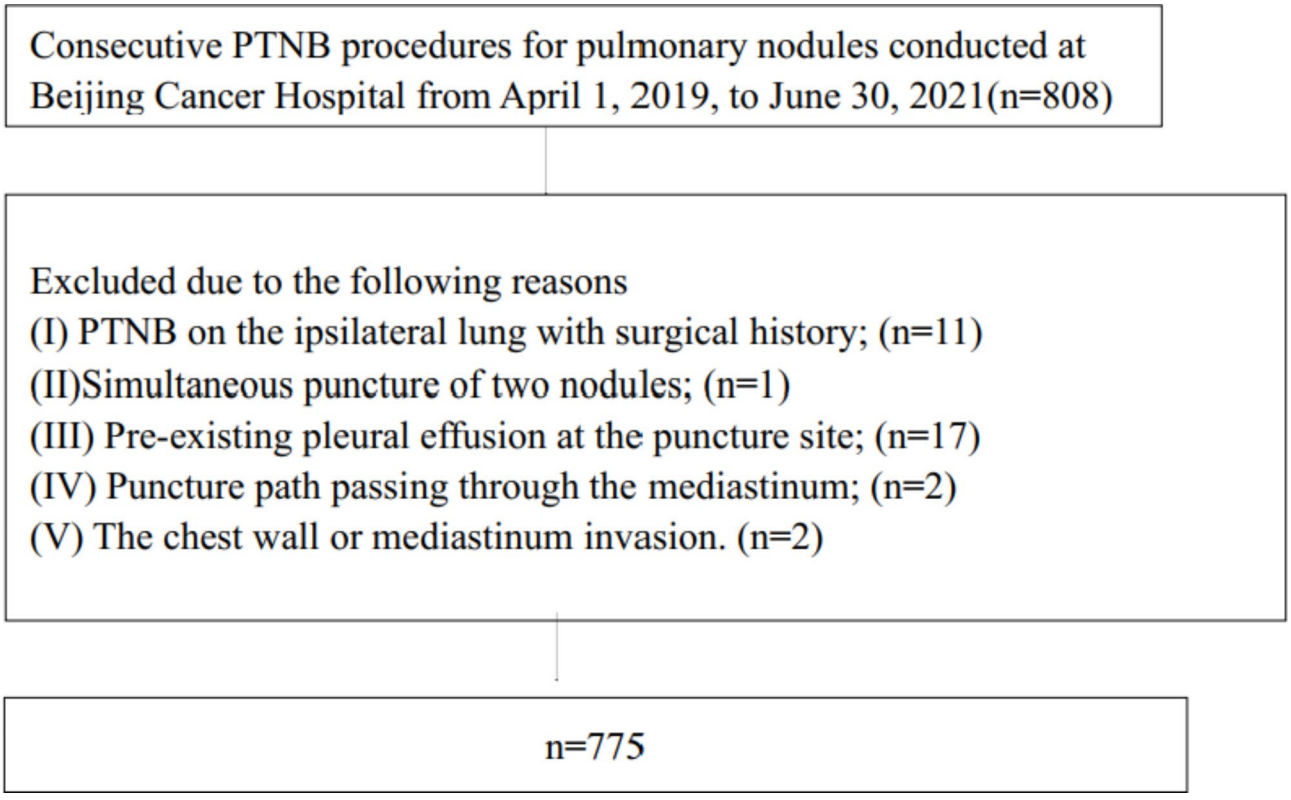

Fig. 1 Inclusion and exclusion criteria

of lung tissue around the lesion with a diameter of 2 cm. Technique-related variables included the time taken of puncture, biopsy needle type, position, needle insertion depth (intrapulmonary and overall), and pleura-needle angle, which was the acute angle formed by the tangent line of the pleura at the puncture point and the needle. Nodules were divided into three kinds on their relationship with the pleura: nodules with PTS, nodules with pleural contact and nodules with pleural unrelated. In the nodules with PTS group, the puncture routes were divided into two categories: crossing PTS (passing through visible linear or striated pleural tags affected by PTS) and no crossing PTS (Fig. 2, 3).

Procedural complications were mainly documented as pneumothorax on chest CT after PTNB. The volume of pneumothorax was measured by the distance between the chest wall and pleura, and the distance larger than 1 cm was defined as the meaningful pneumothorax. We also documented the occurrence of other complications, including pulmonary hemorrhage and gas embolism. We referred to the pulmonary hemorrhage grading criteria proposed by Ryan Tai et al. and documented instances of high-grade pulmonary hemorrhage defined by their criteria [11].

Statistical analysis

Normally distributed continuous variables were described using mean and standard deviation (SD), while non-normally distributed continuous variables were described using the median with interquartile range. Categorical variables were presented as frequencies. The potential risk factors (p-values less than 0.1) for pneumothorax were identified by univariate logistic regression analysis. In the multivariate logistic regression analysis, we calculated the independent risk factors from above potential risk factors. Before multivariate logistic regression analysis, variables of the nodule-pleura relationship and the puncture routes were adjusted according to the results of univariate analysis. Statistical significance was set at $P<0.05$, and all statistical analysis were carried out with IBM SPSS Statistics 26.0.

Results

Patient demographics

A total of 775 biopsies were conducted on 764 lung nodules, with a mean nodule size of 21.9±5.6 mm, involving 681 patients. PTS was detected in 456 nodules (59.7%) out of the 764 lesions. Of these biopsy procedures, 406 (52.4%) were male and a mean age was 62.1±10.4 year. There were 348 nodules (44.9%) in the middle or lower lobe. The mean diameter in the direction of needle insertion was 16.5±5.4 mm. The mean length of the

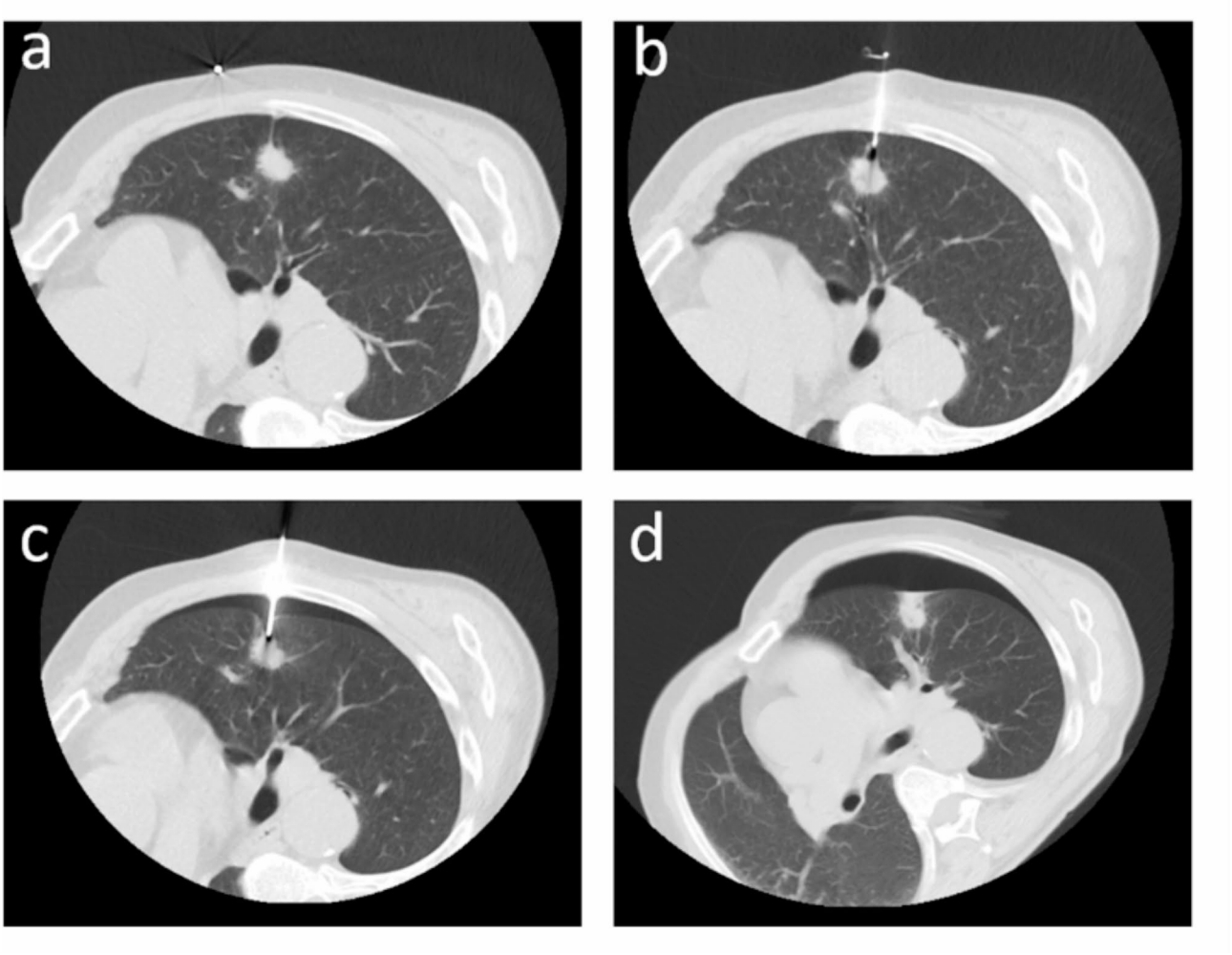

Fig. 2 A PTNB procedure on a nodule with PTS in a 63-year-old male patient. (**a**) A chest CT image shows a nodule with PTS in the left upper lobe. (**b-c**) Our puncture path passed through the linear tags and the pleura affected by the PTS. (**d**) Postoperative CT revealed pneumothorax in the left thoracic cavity

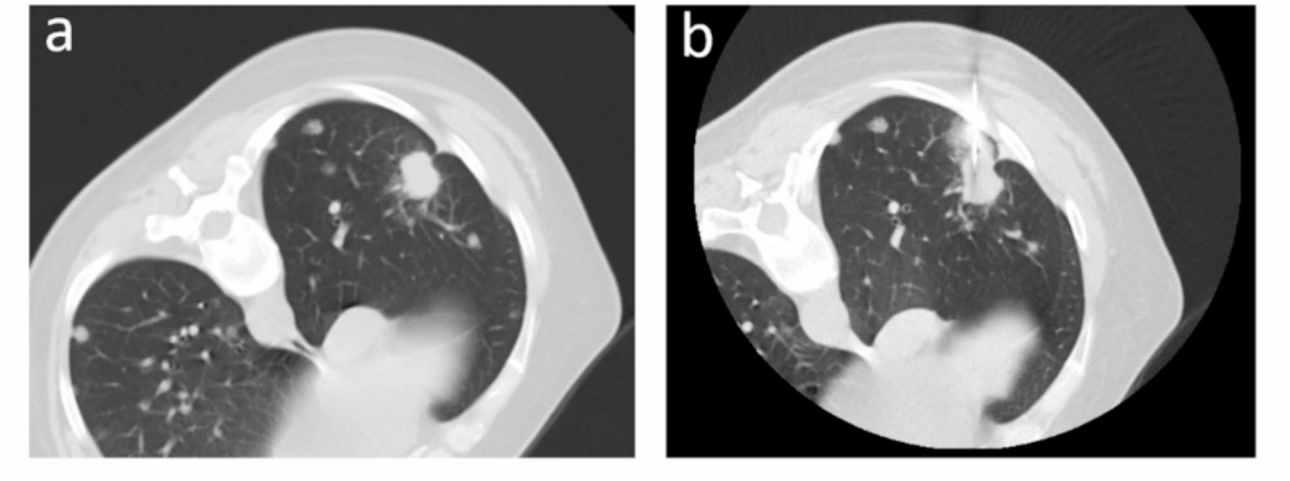

Fig. 3 A PTNB procedure on a nodule with PTS in a 41-year-old female patient. (**a**) A chest CT image shows multiple nodules in both lungs and the bigger one with PTS is in right lower lobe. (**b**) Our puncture path avoided the tags and the pleura affected by the PTS. There was no pneumothorax in Postoperative CT

Table 1 Univariate analyses to determine the risk factors for immediate pneumothorax

	Pneumothorax (*n* = 171)	No pneumothorax(*n* = 604)	*p*
Female sex	72	297	0.102
Age (y)	63.0 ± 10.3	61.8 ± 10.4	0.189
Biopsy side up	94	220	0.000
Pleura-needle angle(°)	68.8 ± 15.5	66.8 ± 16.6	0.170
Time taken for puncture (min)	23.4 ± 11.7	20.1 ± 8.7	0.000
Nodule type(non-solid)	36	110	0.402
Location (the middle or lower lobe)	88	260	0.051
Perifocal emphysema	36	61	0.000
Maximum diameter of nodules (mm)	22.0 ± 5.5	21.9 ± 5.7	0.915
Diameter of nodules in the direction of needle insertion (mm)	16.0 ± 5.5	16.7 ± 5.3	0.200
Needle insertion depth(intrapulmonary) (mm)	23.8 ± 16.1	19.5 ± 14.0	0.000
Needle insertion depth (overall) (mm)	62.6 ± 18.8	59.7 ± 19.9	0.094
Automatic cutting biopsy needle	113	415	0.515
Crossing PTS (vs. No PTS + No crossing PTS)	96	240	0.000
Pleural contact (vs. No pleural contact)	19	143	0.000
Fissure crossed	5	8	0.153

PTS, pleural tail sign;

needle within the pulmonary and overall was respectively 20.4±14.5 mm and 60.4±19.7 mm. The median pleural puncture angle was 67.3±16.4 °. The mean time taken for puncture was 22.0±10.3 min. The comparison of the two groups with and without pneumothorax was shown in Table 1.

Biopsy complications

The overall incidence of pneumothorax was 22.1% (171 out of 775). 10 cases required hospitalization for observation and treatment. Among these, 7 of the hospitalized patients had pneumothorax, with 3 requiring oxygen inhalation and 4 needing chest tube placement. 2 patients were hospitalized due to hemothorax, while another was hospitalized because of a sudden drop in blood pressure following the procedure. 4 patients were found to have gas in the left heart cavity after the operation, but the gas was absorbed after adjusting their position, and both patients were eventually discharged. Details of complications other than pneumothorax were shown in supplementary Table 1.

Table 3 Results of multivariate logistic regression analysis to determine the risk factors for immediate pneumothorax

Variable	OR	CI	*p*
Biopsy side up	2.117	1.458–3.073	0.000
Time taken for puncture	1.033	1.016–1.050	0.000
Location (the middle or lower lobe)	1.656	1.145–2.395	0.007
Crossing PTS	2.566	1.710–3.851	0.000
Needle insertion depth(intrapulmonary) (mm)	1.031	1.017–1.045	0.000
Perifocal emphysema	2.637	1.618–4.298	0.000

PTS, pleural tail sign; OR, odds ratio; CI, confidence interval

Analysis of nodule-pleura relationship

The incidence of pneumothorax in the PTS group, the pleural contact group and the pleural unrelated group was respectively 24.7%, 13.3% and 25.2%. The Table 2 showed the analysis of the association between pneumothorax and nodule-pleura relationship, significant differences were observed between the PTS group and the pleural contact group (p=0.001), as well as between the pleural contact group and the pleural unrelated group (p=0.002). However, no significant differences were found between the PTS group and the pleural unrelated group (p=0.904). Therefore, for multivariate logistic regression analysis, the PTS group and the pleural unrelated group were combined as the no pleural contact group. In the subgroup analysis of the PTS group (Table 2), it was observed that Crossing PTS resulted in a higher incidence of pneumothorax compared with No crossing PTS (p=0.002). Therefore, we attempted to merge the No crossing PTS, the pleural contact group

Table 2 Correlation analysis between nodules-pleura relationship and pneumothorax and subgroup analysis for the nodules with PTS group

	Pneumothorax (*n* = 171)	No pneumothorax (*n* = 604)	*p* (vs. pleural contact)	*p* (vs. pleural unrelated)	*p*
PTS	114	348	0.001*	0.904*	
Crossing PTS	96	240	/	/	0.002
No crossing PTS	18	108	/	/	
Pleural contact	38	113	/	0.002*	
Pleural unrelated	19	143	/	/	

*For pairwise comparisons among the three groups, a p value of less than 0.0167 was needed to be statistically significant

PTS, pleural tail sign

and the pleural unrelated group into the No PTS/No crossing PTS group. The incidence of pneumothorax was compared between the Crossing PTS group and No PTS/No crossing PTS group and significant differences ($p<0.001$) were observed (Table 1).

Univariate and Multivariate Analysis

Univariate analysis (Table 1) revealed that the incidence of pneumothorax was significantly higher with perifocal emphysema ($p<0.001$), biopsy side up ($p<0.001$), longer puncture times ($p<0.001$), deeper needle insertion depth (intrapulmonary) ($p<0.001$), Crossing PTS ($p<0.001$) and Pleural contact ($p<0.001$). Multivariate analysis (Table 3) identified independent risk factors for pneumothorax, which included Crossing PTS (OR 2.566, 95% CI 1.710–3.851, $p<0.001$), perifocal emphysema (OR 2.637, 95% CI 1.618–4.298, $p<0.001$), biopsy side up (OR 2.117, 95% CI 1.458–3.073, $p<0.001$), longer puncture time (OR 1.033, 95% CI 1.016–1.050, $p<0.001$), deeper needle insertion depth (intrapulmonary) (OR 1.031, 95% CI 1.017–1.045, $p<0.001$),and nodules located in the middle or lower lobe (OR 1.656, 95% CI 1.145–2.395, $p=0.007$).

Biopsy outcomes

There were 5 cases lacked pathological reports. Of the cases with available pathology reports, 640 were diagnosed as definitively malignant, 21 were diagnosed as atypical cells and repeat puncture or the follow-up should be performed. Additionally, 21 cases were diagnosed as specific benign lesions (e.g., hamartoma), and 78 cases were diagnosed as normal tissues, with or without other components (e.g., inflammatory cells or fibrosis). In 10 cases, a diagnosis could not be established due to insufficient or necrotic tissue. Detailed biopsy pathological results were shown in the Supplemental Table 2.

Discussion

In our study, the incidence of pneumothorax was 22.1% which was similar to the pooled overall pneumothorax incidence of 25.9% in meta-analysis [2]. We examined the impact of the nodule-pleura relationship during PTNB on pneumothorax incidence in our study. The results indicated that the PTS group had a similar pneumothorax incidence compared pleural unrelated which was different from previous study [4]. In our study, the pleural unrelated group had a deeper intrapulmonary puncture depth than the PTS group (29.2±15.0 mm vs. 19.5±12.8 mm, $p<0.001$). We thought that this factor may have masked the difference that the PTS group had higher incidence of pneumothorax than the pleural unrelated group. Our study concluded that the depth of needle insertion (intrapulmonary) was an independent risk factor for pneumothorax similar to previous studies [2–4, 12, 13].

B. Peng et al. proposed that PTS causes local pleural deformation and increased tensile stress, reducing the lung parenchyma's elastic properties resembling the emphysematous pulmonary tissue [4]. However, this theory can't fully explain the above situation that no crossing PTS but pulmonary tissue nearby did not increase the incidence of pneumothorax. By the way, our study also identified perifocal emphysema as an independent risk factor for pneumothorax, in line with prior researches [14, 15].

The occurrence of pneumothorax may be related to the local pleura affected by PTS. PTS was characterized by linear pleural tags resulting from pleural retraction [6] and thickening of interlobular septa by either localized edema, tumor extension within or outside of lymphatic vessels, inflammatory cells or fibrosis [5]. Some studies have suggested that specific aspects of PTS, such as the "pit-fall sign" and "bridge tag sign," may be associated with a higher risk of visceral pleural invasion [6, 16]. For part of patients with primary spontaneous pneumothorax, "pleural porosity" may be the reason: the air leakage into the pleural space at the visceral pleura where the inflammatory elastofibrotic layer with porosity replaced disrupted mesothelial cells [17]. Similarly, for the nodules with PTS, visceral pleural integrity and elasticity may be compromised, making the visceral pleura more susceptible to tearing when the needle penetrated the visceral pleura. Subgroup analysis of the PTS group and multivariate logistic regression analysis further confirmed this observation with a higher pneumothorax incidence in the crossing PTS group. In addition, we thought that due to the impact of PTS, the local visceral pleura tensile stress increased like a string straightened and easily torn by the tip of the needle.

Some studies have suggested that a smaller pleura-needle angle was a risk factor for pneumothorax in PTNB [8–10]. Ko JP et al. suggested that when the pleura was punctured at a shallow angle, the created pleural hole may elongate, potentially increasing the risk of pneumothorax [10]. However, in our study, we found the pleura-needle angle was not an independent risk factor consistent with other studies [4, 18]. Chunhai Li et al. proposed that their preference for larger pleura-needle angles may be the reason why they did not find the correlation between pleura-needle angle and pneumothorax [18]. We concurred with their perspective that there may be bias in our study due to our awareness of this risk factor and our attempts to avoid it. In previous studies, parietal pleura-needle angle was the default for pleural-needle angles [8–10] and visceral pleura-needle angles were rarely mentioned. However, when we chose the puncture route of crossing PTS, the visceral pleura-needle angle may be shallower in our path selection criteria including selecting larger parietal pleural-needle angles.

So we should pay attention to both parietal and visceral pleural-needle angles in the following biopsy procedures and future research.

Furthermore, previous studies have observed a lower incidence of pneumothorax in CT-guided biopsies of lesions with pleural contact similar to our study [4, 19, 20]. However, in our study, nodule with pleura contact was not a protective factor against pneumothorax in the multivariate analysis. On the one hand, the shallow depth of needle insertion may mask its protective effect on pneumothorax. On the other hand, the introducer needles may not always penetrate the nodule itself but instead stay in the extra-pleural space due to the small nodules. When obtaining tissue samples with the cutting biopsy needle, the pleura may be incised. In addition, the needle tip might scratch the pleura with respiratory movement. This pleural damage could exceed the small pinhole created by the guide needle, increasing the likelihood of pneumothorax.

We found the correlation between pneumothorax and patient position. Drumm O et al. have suggested that positioning the patient with the biopsy side down during PTNB reduced the incidence of pneumothorax [21], while Leger T et al. didn't reach the same conclusion [22]. In our institution, we did not adopt this specific positioning strategy but the biopsy side up position for easier control according to operator preference. Therefore, we cannot discuss this controversial indicator. However, our study revealed that the incidence of pneumothorax increased in patient with biopsy side up position compared to supine or prone during PTNB. Zidulka et al. hypothesized that in the biopsy side down position, the alveoli around the needle path decrease in size, airway closure occurs, and collateral ventilation in the dependent lung encounters greater resistance, reducing the alveolar-to-pleural pressure gradient at the puncture site [23]. When the patient was positioned biopsy side up and the alveolar-to-pleural pressure gradient increased, it was easier for gas to enter the pleural cavity from the pleura at the puncture point.

Regarding the interlobar fissure, numerous studies have suggested the passage of the needle through the interlobar fissure was a risk factor for pneumothorax [12, 19]. In our study, only 13 cases involved needle passage through the interlobar fissure, and out of these, 5 cases resulted in pneumothorax. However, we did not observe any statistically significant differences in our study. We attributed this lack of statistical significance to the few cases. Given that passing through the interlobar fissure is a recognized risk factor, operators at our hospital made conscious efforts to avoid this needle trajectory.

There are several limitations to this study. Firstly, it is a retrospective single-center study, which may introduce biases, such as the choice of route on crossing PTS and crossing the pleura with nodule. Further prospective studies are needed. Secondly, the sample size of this study is relatively small. Although the number of 775 patients is large, the number in our subgroup analysis is small. Thirdly, to minimize the interference of other confounding factors, our study only explored pulmonary nodules with the diameter of 3 cm or less and did not analyze large lesions; therefore, the study was mainly applicable to pulmonary nodules and larger lesions should be further investigated.

In conclusion, patients with crossing PTS, a nodule in the middle or lower lobe, longer puncture time, biopsy side up, deeper needle insertion depth (intrapulmonary), and perifocal emphysema were more likely to experience pneumothorax in PTNB. When performing the biopsy on a nodule with PTS, selecting a route that avoids crossing through the PTS may be advisable to reduce the risk of pneumothorax.

Abbreviations

PTNB	CT guided percutaneous transthoracic needle biopsy
PTS	Pleural tail sign
SD	Standard deviation
OR	Odds ratio
CI	Confidence interval

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-024-03307-z.

Supplementary Material 1

Author contributions

Conception and design: XB.D., L.X., ML.C., YS.S. Collection and assembly of data: XB.D., L.X. Development of methodology: XB.D., L.X., XT. L., ML.C., YS.S. Data analysis and interpretation: XB.D., L.X., ML.C., YS.S. Manuscript writing: All authorsFinal approval of manuscript: All authors.

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Data availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This retrospective study was approved by review board of Peking University Cancer Hospital (2021KT04) and the requirement for informed patient consent was waived.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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