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Complications of CT-Guided Percutaneous Lung Biopsy: A 1-Year Single-Center Experience in Iran

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Abstract

Background: Despite observing all precautions, complications are not uncommon during transthoracic needle biopsy (TTNB). We aimed to evaluate the complications associated with TTNB in patients with lung masses from 1 center in southern Iran.

Methods: In this retrospective cohort study, data on complication rates, types, and potential risk factors from 87 biopsies were collected. Complications were assessed through immediate post-biopsy computed tomography (CT) scans and follow-up chest X-rays, and their correlations were evaluated with patient demographics, lesion characteristics, and procedural factors. Chi-square and Wilcoxon rank-sum tests were used for univariable analysis, and multivariable binary logistic regression analyses were conducted to control for potential confounders.

Results: The overall complication rate was 37.9% (95% CI, 27.6%-48.3%), with pneumothorax being the most common, occurring in 26.4% (95% CI, 17.3%-35.6%) of cases, followed by perilesional hemorrhage (17.2%) (95% CI, 10.3%-25.3%), hemoptysis (3.3%), and pleural effusion (1.1%). All pneumothorax cases were identified via immediate post-biopsy CT, and only 1 patient required chest tube insertion. No significant correlations were found between age, sex, presence of emphysema, lesion size, location, and depth, or needle path and the incidence of pneumothorax. However, a significantly higher perilesional hemorrhage incidence was observed for smaller lesion size (26 mm [interquartile range, IQR], 13,40 vs 43 mm [IQR, 24,73]; $P = 0.019$), deeper lesion (10 mm [IQR, 0.17] vs 0 mm [IQR, 0.10]; $P = 0.041$), and longer needle path (17 mm [IQR, 9.29] vs 0 mm [IQR, 0.7]; $P < 0.001$). Furthermore, 47.8% of pneumothorax cases identified on postbiopsy CT showed no signs on follow-up chest X-ray 3 hours later.

Conclusion: TTNB is generally safe, with a manageable complication profile. Early detection and appropriate follow-up are crucial, particularly for pneumothorax, which often resolves spontaneously. The findings underscore the importance of considering lesion characteristics to minimize complications during biopsy procedures.

Keywords: Interventional radiology, Image-Guided Biopsy, Lung, Complications, Pneumothorax, Hemorrhage

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Introduction

Lung cancer incidence has surged significantly over recent decades. Given its associated high mortality rates, early detection is critical for improving patient outcomes. Pulmonary masses, especially those with unclear origins,

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↑What is "already known" in this topic:
Computed tomography (CT)-guided percutaneous lung biopsy carries significant complication risks, particularly pneumothorax, which may require chest tube drainage in approximately 5% to 20% of pneumothoraxes, and hemorrhage. Smaller lesion size, deeper location, and longer needle paths are their well-studied risk factors. Standard protocols recommend immediate postprocedural imaging and biopsy-side-down positioning to decrease complication risks.

→What this article adds:
This single-center Iranian study reports comparable complication rates after transthoracic needle biopsy (TTNB), but the chest tube insertion rate was among the lowest in the literature, which was attributed to immediate post-biopsy CT detection, standardized coaxial technique, and perpendicular pleural puncture for subpleural lesions. It quantifies perilesional hemorrhage risk in smaller and deeper lesions and longer needle path, but confirms all were self-limited, meaning that TTNB was safe with optimized technique.

pose a challenge for diagnosis using noninvasive imaging techniques. These lesions can stem from either benign or malignant processes, each requiring distinct therapeutic approaches. As such, accurate diagnosis is essential to guide appropriate treatment plans diagnosis (1).

Recent advancements in diagnostic imaging and interventional radiology, particularly through lung biopsies, have significantly increased the ability to diagnose pulmonary lesions. The widespread application of chest computed tomography (CT) has made it possible to identify more lung abnormalities—including small lesions, driving interest in the use of percutaneous CT-guided lung biopsies (2, 3). Various imaging modalities have been used for percutaneous needle biopsy, such as fluoroscopy, conventional CT, and, more recently, helical CT, which is becoming the preferred choice (4-6).

Among these, CT-guided transthoracic fine-needle aspiration (CT-FNA) has proven to be a highly effective, simple, and accurate method for evaluating pulmonary lesions, with successful tissue sampling in 74% to 100% of cases and a diagnostic accuracy ranging from 81% to 99% (7-9). In earlier studies, fine-needle aspiration dominated CT-guided lung biopsies, particularly for distinguishing between malignant and benign lesions (10-12). However, more recent approaches incorporate the use of tissue core biopsy with automated cutting needles, further improving diagnostic accuracy (12, 13). Transthoracic needle biopsy (TTNB) is now a commonly employed technique for diagnosing pulmonary nodules and masses (7). Among the various imaging-guided methods available, CT-guided TTNB has emerged as the most prevalent, offering high diagnostic accuracy (94%) and sensitivity (95%) for identifying malignancies. However, despite its effectiveness, TTNB carries certain risks, with pneumothorax being a frequent and potentially severe complication (14).

As the number of lung biopsies has risen in recent years, there is a need to weigh the associated morbidity and mortality risks against the benefits of the procedure. Even with strict precautions in place, complications may still occur, making early identification and management crucial. Pneumothorax, hemoptysis, hemothorax, infection, and air embolism are some of the complications that can arise, with pneumothorax being the most common (15). The incidence of these complications varies widely across studies, and their occurrence may lead to increased hospitalization rates. As a result, reducing the incidence of such complications remains a key priority (16). This study was designed and conducted to investigate the frequency and associated factors of complications due to CT-guided percutaneous lung biopsies over 1 year at a single center in Iran.

Methods

Study Setting and Patients

This single-center retrospective cohort study was performed to evaluate the prevalence of complications related to TTNB among patients with lung masses. A total of 87 eligible patients who were referred for TTNB to the Faghihi Teaching Hospital, affiliated with Shiraz University of Medical Sciences, Shiraz, Southern Iran, between March 20, 2016, and March 19, 2017, were included in the study. The study protocol was approved by the Local Ethics Committee of Shiraz University of Medical Sciences (Ethics Code: IR.SUMS.MED.REC.1396.s223). All procedures were conducted following the Declaration of Helsinki, and informed consent was obtained from all patients before the procedure.

All patients had previously undergone chest CT scans, which identified and characterized the lung lesions. The TTNB procedures were performed under CT guidance using a 2-slice MDCT scanner (Siemens). The referring physician, who was either an oncologist or a surgeon, determined the indication for TTNB based on the patient's medical history and imaging results, which the radiologist later confirmed. Patients were excluded from the study if they required a second TTNB due to an inadequate initial biopsy. Additionally, any patient with a history of lung resection surgery (due to potential protection against pneumothorax from postsurgical adhesions) or inadequate coagulation status (INR >1.4 or platelet count <70,000 mL) was excluded. Anticoagulant and antiplatelet treatments were paused in accordance with hematologist guidelines before the procedure. Patients with poor respiratory function or those who were uncooperative during the procedure were also excluded.

Procedure

All patients received a thorough verbal explanation of the biopsy procedure, including potential complications. Informed consent was obtained in writing, including permission to use anonymized clinical data for scientific purposes.

TTNB was performed by an experienced interventional radiologist using a coaxial system with an 18-G True-Cut biopsy needle (TSK, Japan). Patients were positioned supine, prone, or in lateral decubitus based on lesion location to optimize access and minimize pleural trauma. For pleural puncture, a perpendicular trajectory was employed for subpleural lesions, and an oblique angle (30°-45°) was used for deeper lesions to avoid traversing interlobar fissures or vascular structures. The ideal needle trajectory was determined based on lesion location to minimize interference from anatomical structures. Lesion centering was carried out on the axial slice of the image stack that presented the most significant extension of the lesion, and the presence of anatomical structures less hampered needle access. The lesion was scanned with 13 to 15 slices at 2.5 mm thickness to adequately document the needle track.

Postprocedural complications were primarily evaluated by a chest CT scan immediately after the biopsy to assess for pneumothorax and perilesional hemorrhage, followed by a chest X-ray (CXR) 3 hours later to detect overt pneumothorax or its progression. The postprocedural chest CT protocol was identical to that of the chest CT performed for TTNB. Pneumothorax depth and width were measured if detected. Any signs of respiratory distress and shortness of breath prompted chest tube placement. Pneumothorax was defined as the presence of air between the lung and pleura. Perilesional hemorrhage was charac-

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terized by increased lung attenuation along the needle path while bronchial and vascular margins were preserved. Hemoptysis was defined as blood expectoration from the lower respiratory tract, ranging from small streaks of blood to significant bleeding; pleural effusion as the fluid accumulation in the pleural space that can be identified on follow-up CT scans; and pericardial effusion as excess fluid within the pericardial sac, detectable on imaging or clinical examination. Moreover, air emboli were defined as the presence of gas bubbles inside the venous or arterial system, identified by imaging studies. Supplemental oxygen was administered via nasal cannula to patients diagnosed with pneumothorax on CT or CXR. All patients would be informed of emergency contact information and instructed to stay in Shiraz, where the centers are located, for 72 hours post-procedure in case of any potential delayed complications. Telephone follow-ups were conducted at 24 and 72 hours to monitor such complications.

Imaging and Data Collection

The CT-guided TTNB procedures were performed using a 2-slice Lightspeed CT system (Siemens Medical Systems). Scanning was conducted from the lung apex to the base during a single inspiratory breath-hold with the following parameters: slice thickness 2.5 mm, collimation 10 mm, field of view 320 to 360 mm, pitch 1.75, 120 kV, with standard reconstruction filters and a lung window. All images (ie, prebiopsy, biopsy, and postbiopsy axial CT slices, and postbiopsy chest radiographs) were analyzed by 1 expert radiologist using a digital reading workstation (Extended Brilliance Workspace, Infinite Medical Systems) (Figure 1A). The CT images were examined for lesion size, lesion location (i.e., upper, middle, or lower right lobe and upper or lower left lobe), lesion depth, and distance to pleura measured along the needle path.

The most commonly observed complications, including pneumothorax, perilesional hemorrhage, hemothorax, hemoptysis, and pleural effusion, were documented. Rare complications, such as neoplastic cell seeding along the

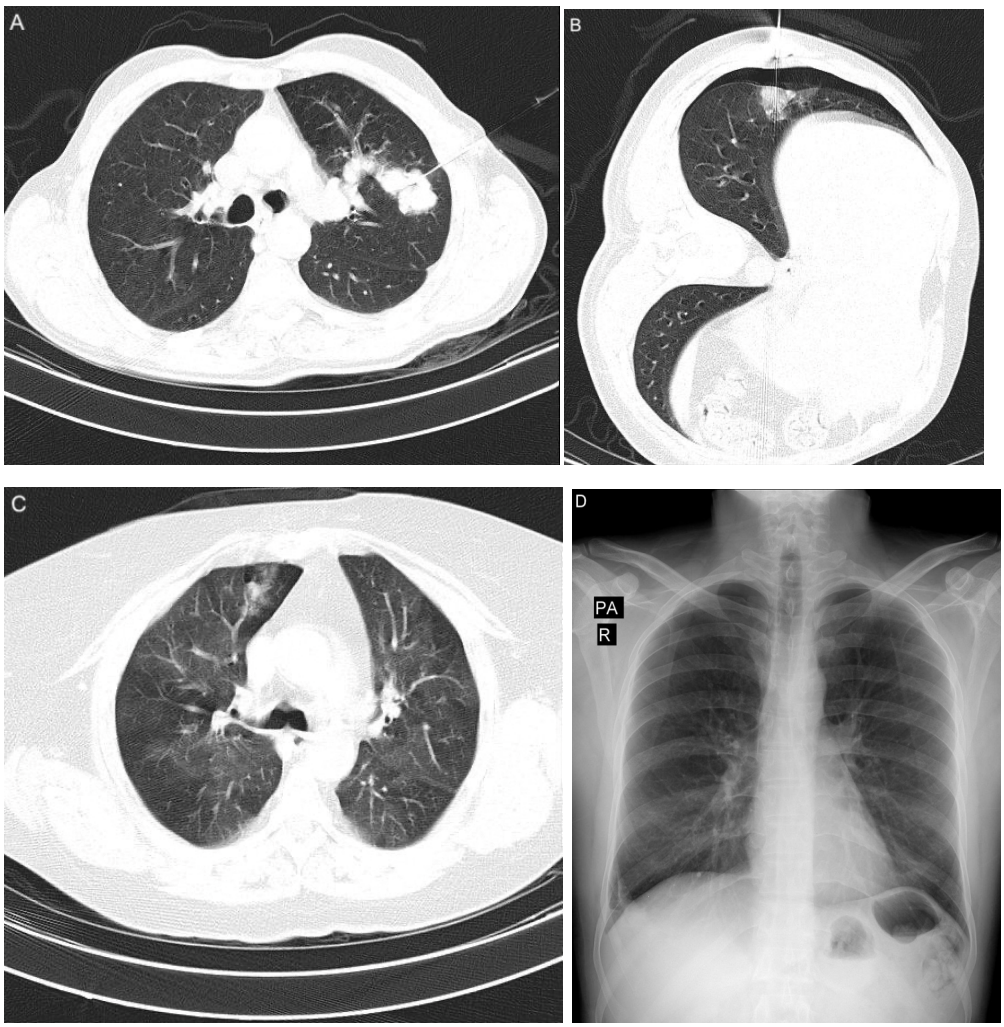

Figure 1. Transthoracic Needle Biopsy (TTNB) Findings: (A) TTNB of a pulmonary nodule without complications. (B) TTNB resulting in pneumothorax, the most common complication. (C) TTNB leading to perilesional hemorrhage, the second most common complication. (D) Right-sided pneumothorax diagnosed on chest X-ray (CXR) performed 3 hours post-procedure

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needle path, pericardial effusion, air emboli, and pulmonary infections, were also considered. Patient characteristics such as age, sex, and presence of emphysema were also documented.

Management of pneumothorax was carried out based on the severity of the condition as observed through post-procedural imaging. In cases of mild pneumothorax, defined as the presence of a small amount of air between the pleura and lung without respiratory distress, air was aspirated using a needle. This procedure was performed under sterile conditions and monitored for immediate resolution. In instances where severe pneumothorax occurred, characterized by a significant accumulation of air leading to respiratory distress, a chest tube was inserted to evacuate the air and restore lung expansion. The insertion of the chest tube was performed according to standard protocols, with continuous monitoring to ensure adequate drainage and prevent further complications.

Statistical Analysis

Statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 19.0 (SPSS Inc). Baseline characteristics were presented as mean ± standard deviation or median (IQR) for continuous variables, and as percentages for categorical variables. The chi-square test and the Wilcoxon rank-sum test were employed to evaluate correlations between various factors (ie, patient age and sex, emphysema, needle path, and lesion site, size, and depth) and the presence of complications (eg, pneumothorax, hemorrhage, and hemoptysis). Potential outliers in lesion size, lesion depth, and needle path length were assessed using boxplot visualization and the Tukey method. However, outliers were retained in the analysis, as they represented biologically plausible measurements. To handle these outlier values and their accompanying non-normal distributions, we used non-parametric tests. Besides, sensitivity analyses excluding outliers (ie, lesion size >100 mm, lesion depth >50 mm, and needle path length >30 mm) confirmed the stability of associations for the outcomes. To control for potential confounders, multivariable binary logistic regression analyses were performed. The regression models adjusted for age, sex, and the presence of emphysema. Results were presented as adjusted odds ratios (aOR) with 95% confidence intervals (CI).

Post-hoc Power Analysis

Since this study was observational and included all consecutive eligible patients, a post-hoc power analysis was conducted using G*Power software (version 3.1.9.7) to assess the achieved power for detecting significant associations observed in our primary outcomes in multivariable binary logistic regression analysis. For the model analyzing any complication (37.93% incidence) and the lesion size being its key predictor (OR = 0.976, $P = 0.007$, $\alpha = 0.05$, N = 87), the achieved power was 92% in detecting a small-to-medium effect size (Cohen's $f^2 = 0.15$). Similarly, for the model analyzing perilesional hemorrhage (17.24% incidence), which found a significant independent association with needle path length (OR = 1.125, $P < 0.001$, $\alpha = 0.05$, N = 87, $f^2 = 0.18$), the model achieved 85% power. Both of these calculations confirmed adequate power (>80%) for the primary statistically significant findings.

Results

All 87 patients who underwent TTNB met the inclusion criteria, and none were excluded, resulting in a final cohort of 87 patients. The mean age of the patients was 56.5 ± 18.3 years, ranging from 10 to 89 years, with 28.7% (n = 25) of the patients being female and 71.3% (n = 62) male. Emphysema was identified in 10.3% (n = 9) of patients. The average lesion size was 47.5 ± 32.4 mm, ranging from 5 to 140 mm. Regarding the location of the lesions, 29.9% (n = 26) were in the right upper lobe (RUL), 20.7% (n = 18) in the right lower lobe (RLL), 2.3% (n = 2) in the right middle lobe or lingula, 25.3% (n = 22) in the left upper lobe (LUL), and 21.8% (n = 19) in the left lower lobe (LLL). The minimum distance from the lesion to the pleura ranged from pleural-based lesions to a maximum distance of 101 mm, with a mean distance of 9.4 ± 17.9 mm. The mean needle path length was 6.8 ± 11.0

Table 1. Describing patients, lesions, and procedures

Characteristic	Value
Age, years (M±SD [range])	56.5 ± 18.3 [10-89]
Sex (N, %)	
Female	25 (28.7)
Male	62 (71.3)
Emphysema (N, %)	
Yes	9 (89.7)
No	78 (10.3)
Lesion size, mm (M±SD [range])	47.5 ± 32.4 [5-140]
Lesion location distribution (N, %)	
RUL	26 (29.9)
RLL	18 (20.7)
RML or lingula	2 (2.3)
LUL	22 (25.3)
LLL	19 (21.8)
Lesion depth, mm (M±SD [range])	9.4 ± 17.9 [0-101]
Needle path, mm (M±SD [range])	6.8 ± 11.0 [0-54]
Needle size (N, %)	
18G	87 (100)
Other	0 (0)

Abbreviations: SD, standard deviation; G, gauge; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe.

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mm. All procedures were performed using an 18-G needle (Table 1).

A total of 33 (37.9% [95% CI, 27.6%-48.3%]) of biopsies developed at least 1 complication. The most frequent complication was pneumothorax, observed in 26.4% (95% CI, 17.3%-35.6%) of patients (n = 23) (Figure 1B). Among those with pneumothorax, 4.3% (n = 1) required chest drain placement, representing 1.1% of the total cohort. No patient was diagnosed with delayed pneumothorax, as all were diagnosed immediately after the procedure on post-biopsy CT scans. That is, of the patients who developed pneumothorax on post-procedure CT scans, 52.2% (n = 12) still had pneumothorax visible on the follow-up CXR (Figure 1D). No new cases of pneumothorax were detected on the CXR that were not already identified on the immediate post-procedure CT scan. The second most frequent complication was perilesional hemorrhage, occurring in 17.2% (95% CI, 10.3%-25.3%) of the patients (n = 15) (Figure 1C). Hemoptysis was documented in 3.3% of cases (n = 3), appearing either immediately or within hours after the biopsy, all of which were self-limited. Pleural effusion occurred in 1.1% of patients (n = 1). Importantly, no patients developed pericardial effusion or air emboli (Table 2).

The occurrence of pneumothorax and perilesional hemorrhage was further analyzed in relation to various patient and lesion characteristics (Table 3). Development of pneumothorax or perilesional hemorrhage was not associated with age (P = 0.229, 0.783), sex (P = 0.435, 0.350), emphysema (P = 1.000, 1.000), and lesion location (P = 0.103, 0.952). Additionally, when location was generally stratified into upper and lower lesions, no statistically significant difference in upper and lower locations was observed for both of pneumothorax (24% vs 29.7%, $P_{\text{Fisher's exact test}}$ = 0.626) and perilesional hemorrhage (16% vs. 18.9%, $P_{\text{Fisher's exact test}}$ = 0.770). However, the rates were slightly higher for the lower lesions. Moreover, lesion depth and needle path were not significantly associated with pneumothorax occurrence (P = 0.804, P = 0.244). Of note, pneumothorax was more frequent in patients with smaller lesion sizes, although the association was not statistically significant (28 mm [IQR, 20-38] vs 47 mm [IQR, 26-73]; P = 0.070). However, perilesional hemorrhage was significantly associated with smaller lesion size (26 mm [IQR, 13-40] vs. 43 mm [IQR: 24, 73]; P = 0.019), deeper lesions (10 mm [IQR: 0, 17] vs. 0 mm [IQR, 0-10]; P = 0.041), and longer needle path length (17 mm [IQR, 9-29] vs. 0 mm [IQR, 0-7]; P <0.001) (Table 3). Furthermore, the adjusted binary logistic regression analyses confirmed the abovementioned nonsignificant univariable analyses for pneumothorax. However, for perilesional hemorrhage, significant univariable associations was remained statistically significant only for the needle path length (adjusted OR [aOR] = 1.125 [95% CI, 1.057-

Table 2. Complications associated with CT-guided TTNB

Complication	Value (N, %)	95% confidence interval [1]
Pneumothorax	23 (26.4)	17.3, 35.6
Perilesional hemorrhage	15 (17.2)	10.3, 25.3
Hemoptysis	3 (3.3)	NA
Pleural effusion	1 (1.1)	NA
Pericardial effusion	0 (0)	NA
Air emboli	0 (0)	NA
Complication rate	33 (37.9)	27.6, 48.3

[1] 95% confidence intervals were estimated using the bootstrap method.

Table 3. Association of patient and lesion characteristics with complications following TTNB

Variable	Pneumothorax			Perilesional hemorrhage			Any complication		
	Yes (n = 23)	No (n = 64)	*P*	Yes (n = 15)	No (n = 72)	*P*	Yes (n = 33)	No (n = 54)	*P*
Age [1]	61 [51, 74]	57 [44, 69]	0.229	56 [44, 72]	58 [46, 71]	0.783	60 [48, 72]	57 [42, 68]	0.300
Sex [2]									
Female	5 (21.7)	20 (31.3)	0.435	6 (40)	19 (26.4)	0.350	10 (30.3)	15 (27.8)	0.812
Male	18 (78.3)	44 (68.8)		9 (60)	53 (73.6)		23 (69.7)	39 (72.2)	
Emphysema [2]									
Yes	2 (8.7)	7 (10.9)	1.000	1 (6.7)	8 (11.1)	1.000	3 (9.1)	6 (11.1)	1.000
No	21 (91.3)	57 (89.1)		14 (93.3)	64 (88.9)		30 (90.9)	48 (88.9)	
Lesion size [1]	28 [20, 38]	47 [26, 73]	0.070	26 [13, 40]	43 [24, 73]	0.019	26 [16, 39]	52 [29, 80]	0.001
Lesion location [3]									
RUL	7 (30.4)	19 (29.7)	0.103	4 (26.7)	22 (30.6)	0.952	9 (27.3)	17 (31.5)	0.421
RLL	5 (21.7)	13 (20.3)		2 (20.0)	15 (20.8)		7 (21.2)	11 (20.4)	
RML or lingula	2 (8.7)	0 (0)		0 (0)	2 (2.8)		2 (6.1)	0 (0)	
LUL	3 (13.0)	19 (29.7)		4 (26.7)	18 (25.0)		7 (21.2)	15 (27.8)	
LLL	6 (26.1)	13 (20.3)		4 (26.7)	15 (20.8)		8 (24.2)	11 (20.4)	
Lesion depth [1]	0 [0, 11]	0 [0, 13]	0.804	10 [0, 17]	0 [0, 10]	0.041	2 [0, 12]	0 [0, 12]	0.363
Needle path [1]	2 [0, 14]	0 [0, 11]	0.244	17 [9, 29]	0 [0, 7]	<0.001	9 [0, 17]	0 [0, 1]	0.001

[1] Reported as median [IQR], compared using the Wilcoxon rank-sum test.
[2] Reported as frequency (%), compared using the Fisher's exact test.
[3] Reported as frequency (%), compared using the Chi-square test.
Abbreviations: SD, standard deviation; G, gauge; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; IQR, interquartile range.

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Table 4. Adjusted association between lesion characteristics with complications following TTNB using the multivariable binary logistic regression models [1]

Variable	Pneumothorax			Perilesional hemorrhage			Any complication		
	aOR	95% CI	*P*	aOR	95% CI	*P*	aOR	95% CI	*P*
Lesion size	0.986	0.969, 1.003	0.114	0.980	0.958, 1.003	0.087	0.976	0.959, 0.993	0.007
Lesion location									
RUL, reference category	-	-	-	-	-	-	-	-	-
RLL	0.848	0.209, 3.445	0.818	1.204	0.222, 6.535	0.830	1.119	0.307, 4.073	0.864
RML or lingula	NA	NA	NA	NA	NA	NA	NA	NA	NA
LUL	0.375	0.082, 1.718	0.207	1.216	0.258, 5.730	0.804	0.805	0.235, 2.758	0.730
LLL	1.237	0.328, 4.673	0.753	1.461	0.309, 6.916	0.632	1.408	0.408, 4.863	0.589
Lesion depth	0.984	0.954, 1.016	0.326	1.011	0.983, 1.041	0.438	0.988	0.961, 1.015	0.365
Needle path	1.020	0.978, 1.064	0.354	1.125	1.057, 1.197	<0.001	1.070	1.021, 1.121	0.004

[1] Models were adjusted for age, sex, and presence of emphysema.
Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe.

1.197], $P < 0.001$) and the lesion's size and depth associations with perilesional hemorrhage were not statistically significant (aOR = 0.980 [95% CI, 0.958-1.003], P = 0.087; aOR = 1.011 [95% CI, 0.983-1.041], P = 0.438) (Table 4).

Moreover, when assessing complications altogether, developing any complication was statistically associated with smaller lesion size (26 mm [IQR, 16-39] vs 52 mm [IQR, 29-80]; P < 0.001) and longer needle path length (9 mm [IQR, 0-17] vs 0 mm [IQR, 0-1]; P = 0.001) (Table 3). These associations were still statistically significant in multivariable logistic regression analysis (aOR = 0.976 [95% CI, 0.959-0.993], P = 0.007; aOR = 1.070 [95% CI, 1.021-1.121], P = 0.004) (Table 4).

Discussion

In this study, we evaluated the complications associated with TTNB in a cohort of 87 patients with lung masses. Our findings showed a complication rate of 37.9%, with pneumothorax being the most prevalent, occurring in 26.4% of cases. Other complications included perilesional hemorrhage (17.2%), hemoptysis (3.3%), and pleural effusion (1.1%). Notably, all of the pneumothorax cases were identified immediately post-biopsy via CT, and only 1 patient required a chest drain. Additionally, we observed a significant correlation between lesion size, lesion depth, and needle path regarding the incidence of perilesional hemorrhage; however, no such correlation was found for pneumothorax. Furthermore, the incidences of both perilesional hemorrhage and pneumothorax were not associated with age, sex, presence of emphysema, or lesion location.

Our findings showed a complication rate of 37.9%, with pneumothorax being the most frequent, occurring in 26.4% of cases, followed by perilesional hemorrhage (17.2%), hemoptysis (3.3%), and pleural effusion (1.1%). Pneumothorax and hemorrhage after TTNB are consistently reported as complications in the literature. Pneumothorax, in particular, is the most common complication, especially in CT-guided procedures (17). The reported incidence of pneumothorax in large series generally varies between 5% and 30% (6, 12, 16, 17), with an average of approximately 20% (18). However, higher rates, up to 60%, have also been documented in some studies (19). Hemorrhage is considered the second most frequent complication after TTNB. The estimated incidence of perilesional hemorrhage varies widely in the literature, ranging from 1% to 66%, likely due to differences in defining hemorrhage. This variation may stem from the use of different diagnostic criteria, such as code-based diagnostic algorithms, clinical definitions based on patient-reported symptoms, or radiographic clues (20, 21). Additionally, hemoptysis is reported in up to 20% of cases (22). A meta-analysis by Heerink et al (23), evaluating complication rates in CT-guided TTNB across 8133 core biopsy procedures and 4620 FNA procedures, reported pooled complication rates of 38.8% for core biopsy and 24% for FNA. Specifically, the rate of pneumothorax was 25.3% for core biopsy, while pulmonary hemorrhage occurred in 18% of cases, and hemoptysis in 4.1%. Similarly, an extensive retrospective cohort study by Vachani et al (24) showed a complication rate of 25% among patients undergoing TTNB, with pneumothorax being the most common complication (23.3%), followed by hemorrhage (3.6%), and a rare occurrence of air embolism.

In our study, we did not observe any significant correlation between factors such as age, sex, presence of emphysema, needle path, lesion location, size, and depth, and the incidence of pneumothorax. This aligns with some previous reports, which have yielded conflicting results on the influence of these factors on TTNB complications, particularly pneumothorax. Many studies have explored the relationship between various patient-, lesion-, and procedure-related factors and complication rates, but predicting the occurrence of pneumothorax remains challenging, unlike hemorrhage, which typically occurs immediately following TTNB. While there is debate, lesion size and depth are among the factors that have been reported to associate with an increased risk of pneumothorax (23, 25).

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The impact of nodule size on diagnostic accuracy and pneumothorax risk remains controversial. Smaller lesion sizes have been previously linked to a higher pneumothorax risk (26-28), with rates ranging from 33% to 60% for lesions under 2 cm in some studies, while others found no significant difference based on lesion size (25, 29-31). Smaller lesions present technical challenges, often requiring longer procedures and more needle adjustments, increasing the likelihood of complications. Similar to our findings, Ernst et al (32) observed comparable pneumothorax rates in patients with small and large nodules, with no statistically significant difference. Likewise, Swischuk et al (33) showed that TTNB procedures carried a pneumothorax frequency of 26.9%, with no significant difference in rates between smaller and larger lesions. In addition, lesion depth and needle path length have also been associated with pneumothorax risk, although this remains debated (11, 34). Longer needle paths, especially when targeting deeper lesions, may complicate the procedure, prolonging biopsy times and increasing the risk of pneumothorax. Studies have also shown that greater pleura-to-lesion distances are associated with higher pneumothorax rates (28, 35-37). Moreover, one known patient-related risk factor is the presence of emphysema or chronic obstructive pulmonary disease (COPD), which might increase the pneumothorax rate after TTNB in patients with moderate-to-severe emphysema or following core biopsy. However, while some earlier reports have shown a higher pneumothorax risk in COPD patients (28, 35, 38-42), others have not found such a significant correlation between pneumothorax and emphysema, as well as abnormal pulmonary function test results (26, 36, 43, 44). Furthermore, age has also been suggested as a factor that increases the likelihood of TTNB-related pneumothorax in some studies (16, 45). However, our findings are consistent with those of others who found no correlation between age or gender and pneumothorax incidence (6, 27).

We observed a significant correlation between lesion size, lesion depth, and needle path with the incidence of perilesional hemorrhage. However, significant associations for lesion size and depth disappeared when adjusted for the baseline patients' characteristics. Additionally, similar to the occurrence of pneumothorax, no correlation was found between hemorrhage and factors such as age, sex, presence of emphysema, or lesion location. Moreover, developing any complication was significantly associated with a smaller lesion size and a longer needle path. Several studies have shown that smaller lesion sizes, deeper lesion locations, and longer biopsy paths are associated with a higher risk of bleeding complications (23, 46). The increased risk during the biopsy of smaller lesions may be due to the involvement of adjacent aerated lung tissue, as the cutting needle often includes a part of aerated lung, along with less ability of the aerated lung to exert a tamponade effect compared to solid tissues. Additionally, the technical difficulty in accessing small lesions often results in more needle adjustments and extended procedure times, further elevating the bleeding risk (26, 31, 47). Moreover, deeply located tumors increase the likelihood of the needle passing through more aerated lung tissue and pulmonary vessels, thereby raising the chances of pulmonary hemorrhage (48, 49). Centrally located pulmonary vessels tend to be more crowded and larger. In contrast, peripheral lesions are less likely to involve major pulmonary vessels, and any vessel traversed is expected to be smaller, reducing the risk of severe hemorrhage. Lesion depth has been specifically linked to bleeding risk, with lesions more than 2 cm from the pleural surface having a 10-fold higher risk of bleeding compared to those abutting the pleural surface (26, 41). Consistent with our findings, other studies have shown that factors such as needle size, the number of biopsy specimens, pleural puncture site, post-biopsy positioning, lung lesion location, patient age, and the presence of emphysema on CT do not significantly affect the risk of bleeding (25, 31). Furthermore, Yeow et al (26) reported a six-fold increase in bleeding complications among patients with lesions ≤2 cm compared to those with lesions larger than 4 cm, emphasizing the challenges in smaller lesion biopsies.

In this study, all pneumothorax cases identified on CXRs 3 hours post-procedure had already been diagnosed on the immediate post-biopsy CT scans, and no new cases of pneumothorax were found during the later CXRs. Additionally, 47.8% of the patients who developed pneumothorax according to the evidence from post-biopsy CT scan showed no signs of pneumothorax on the CXR taken 3 hours later. This could be due to either the resolution of pneumothorax or the lower sensitivity of CXR in detecting it. Early detection of pneumothorax after TTNB is crucial, as it can help prevent complications. Although a simple CXR is commonly used to identify pneumothorax, it has limitations when performed immediately after TTNB. The detection of pneumothorax using posteroanterior (PA) CXR can be delayed because it usually takes time for the pneumothorax to develop fully (16, 50). Byrd and Roy (51) suggested that a CT scan taken immediately after TTNB could reliably predict the occurrence of pneumothorax, making routine follow-up with CXR potentially unnecessary. They further recommended instructing patients to seek medical attention only if symptoms of pneumothorax develop.

The finding that only one (1.1%) of patients in our cohort required chest tube insertion for pneumothorax represents a remarkably low rate compared to literature reports of 1% to 15% (12, 25, 27, 29, 31, 39, 44, 45). In addition, this is substantially lower than the 6.9% pooled incidence in a meta-analysis of 23,104 patients (52) and the 5.9% rate reported in extensive contemporary studies (53). Notably, according to the American College of Radiology (ACR) Appropriateness Criteria, pneumothorax is the most frequent complication requiring intervention, occurring in 10% to 30% of CT-guided percutaneous lung biopsies, in which 20% to one-third of patients require intervention. In most cases, pneumothorax after TTNB resolves conservatively or spontaneously (52, 54). Our chest tube rate constituted just 4.2% of pneumothorax cases (1 out of 23) versus the typical 20% to 33% (52, 54). Several factors might explain this observation: first, immediate detection was allowed in our study as the protocol of post-biopsy CT enabled same-procedure identification of all

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pneumothoraxes, as well as early intervention; second, we used perpendicular pleural puncture for subpleural lesions and coaxial technique, which might decrease pleural injury (52, 53, 55, 56); third, lesions in our cohort were predominantly peripheral (median depth of 0 mm) and the fissure traverse was less happened (52). Moreover, variations in chest tube insertion rate are attributed to baseline characteristics, biopsy techniques, and analytical methods (55). Recent studies reported significantly higher requirements for chest tube insertion with anterior biopsy approaches, supine position, emphysema, or deep lesions (52, 53, 54); however, we found no such associations, possibly due to our standardized technique. Recently, it has been proposed that machine-learning algorithm development can predict the risk of post-lung biopsy pneumothorax, which may require chest tube insertion, using readily available preprocedural information such as lesion character, COPD (ie, emphysema), lesion depth, and age (56).

For small lesions, we confirmed significantly higher hemorrhage risk, which is consistent with literature implicating size and trajectory as key determinants (52, 54). To minimize the risk and manage this, we advocated preprocedural planning using thin-slice CT to map vessels and fissures, in addition to the attempt to reduce needle path length (median 0 mm in complication-free cases). Also, with the use of coaxial systems, repunctures were avoided, and immediate manual aspiration was available if hemorrhage occurred, although no interventions were needed, as all perilesional hemorrhages were self-limited. For pneumothorax, our protocol of mandatory post-biopsy CT and CXR enabled 100% immediate detection, which might critically support immediate CT as a best practice that potentially minimizes progression to drain-requiring pneumothorax, and the 24- and 72-hour telephone follow-up ensured no delayed cases.

Since all procedures in our study were performed using an 18-G needle, we were unable to assess its correlation with the incidence of complications. It is generally believed that the risk of pneumothorax rises with increasing needle diameter; however, some studies suggest no significant difference in pneumothorax rates between larger and smaller needles (33, 45). Notably, larger cutting needles, such as 14G, have been associated with higher complication rates, while smaller needles, like 18G, do not appear to increase complication rates, compared to FNAB (57-59).

Our study had several limitations. First, our findings were obtained from a single-center study; hence, these may reflect institution-specific practices, as well as patient population characteristics, which limit generalizability to other settings. Second, the relatively small sample size of 87 patients might reduce the statistical power and reliability of the findings. Although we confirmed adequate power to detect the significant associations in logistic regression models, a larger sample size would have been required to detect clinically relevant differences with higher confidence. Additionally, the low incidence of complications in specific subcategories of independent variables might have contributed to the lack of statistically significant associations in the multiple logistic regression analysis. Third, to minimize operator variability, all procedures were performed by a single experienced interventional radiologist; however, on the other hand, this practice might introduce bias due to the experience of the radiologist. Fourth, as a retrospective study, the sample size was restricted to the available eligible cases, which is a recognized limitation in this context. The retrospective design also constrained the availability of certain confounding variables, such as smoking status and detailed respiratory health history, which could have influenced the outcomes. While multivariable binary logistic regression analyses were performed to adjust for age, sex, and the presence of emphysema, the lack of more comprehensive data on potential confounders might have introduced bias into the results. The absence of data on key baseline characteristics limited the comprehensiveness of our analysis. Although strict exclusion criteria were applied to mitigate bias (eg, excluding patients with poor respiratory function), the lack of these specific baseline data restricted the ability to evaluate confounding factors fully. Fifth, since all patients underwent a single needle pass, the role of the number of passes in the occurrence of complications was not feasible to be assessed. Sixth, the unavailability of rapid on-site evaluation (ROSE) might have influenced the sampling process, as inadequate samples requiring subsequent procedures were excluded. Seventh, all procedures were performed using an 18-G needle, which prevented an assessment of the correlation between needle size and complication rates. While it is generally believed that larger needle diameters may increase the risk of complications such as pneumothorax, some studies have shown no significant difference between the complication rates of larger and smaller needles. Eighth, the study was limited by the absence of long-term follow-up, and future studies might consider more extended follow-up periods to evaluate the long-term outcomes of complications. Additionally, due to data unavailability, we were not able to perform stratified analysis for patient positioning (prone vs. supine) during TTNB. Finally, although we implemented a 72-hour telemedicine follow-up protocol for patients, the absence of systematic imaging beyond such immediate post-procedural follow-up might lead to possible missing of significantly delayed complications (ie, >72 hours).

Conclusion

TTNB remains a valuable diagnostic tool for lung masses, with an acceptable complication rate and minimal need for intervention in most cases. While pneumothorax was the most frequent complication, the majority were detected early through post-biopsy CT and resolved without requiring chest tube placement. Perilesional hemorrhage was significantly associated with lesion size and depth, reflecting the need for precision in targeting deeper or smaller nodules. Overall, our findings suggest that TTNB is a relatively safe procedure when performed under appropriate clinical conditions and with vigilant post-procedural follow-up.

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Authors' Contributions

Conception and designing of study (M.R.S.); data collection (M.P.); data analysis (M.P.); manuscript drafting (M.P.); draft editing (M.R.S.); critical revision (M.R.S. & M.P.); final approval (M.R.S. & M.P.); manuscript supervision (M.R.S.); supervision of work (M.R.S.).

Ethical Considerations

The study protocol was approved by the Local Ethics Committee of Shiraz University of Medical Sciences (Ethics Code: IR.SUMS.MED.REC.1396.s223).

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Conflict of Interests

The authors declare that they have no competing interests.

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