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Cone-Beam CT-Guided Percutaneous Transthoracic Needle Lung Biopsy of Juxtaphrenic Lesions: Diagnostic Accuracy and Complications

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Objective: To investigate the diagnostic accuracy and complications of cone-beam CT-guided percutaneous transthoracic needle biopsy (PTNB) of juxtaphrenic lesions and identify the risk factors for diagnostic failure and complications.
Materials and Methods: In total, 336 PTNB procedures for lung lesions (mean size ± standard deviation [SD], 4.3 ± 2.3 cm) abutting the diaphragm in 326 patients (189 male and 137 female; mean age ± SD, 65.2 ± 11.4 years) performed between January 2010 and December 2014 were included. The accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the PTNB procedures for the diagnosis of malignancy were measured based on the intention-to-diagnose principle. The risk factors for diagnostic failures and complications were evaluated using logistic regression analysis.
Results: The accuracy, sensitivity, specificity, PPV, and NPV were 92.7% (293/316), 91.3% (219/240), 91.4% (74/81), 96.9% (219/226), and 77.9% (74/95), respectively. There were 23 diagnostic failures (7.3%), and lesion sizes ≤ 2 cm (p = 0.045) were the only significant risk factors for diagnostic failure. Complications occurred in 98 cases (29.2%), including 89 cases of pneumothorax (26.5%) and 7 cases of hemoptysis (2.1%). The multivariable analysis showed that old age (> 65 years) (p = 0.002), lesion size of ≤ 2 cm (p = 0.003), emphysema (p = 0.006), and distance from the pleura to the target lesion (> 2 cm) (p = 0.010) were significant risk factors for complications.
Conclusion: The diagnostic accuracy of cone-beam CT-guided PTNB of juxtaphrenic lesions for malignancy was fairly high, and the target lesion size was the only significant predictor of diagnostic failure. Complications of cone-beam CT-guided PTNB of juxtaphrenic lesions occurred at a reasonable rate.
Keywords: *Lung; Biopsy; Image-guided biopsy; Cone-beam computed tomography*

INTRODUCTION

Percutaneous transthoracic needle biopsy (PTNB) is widely used as a diagnostic procedure to identify malignancy in pulmonary lesions. The accuracy of PTNB for the diagnosis of malignancy has been reported to be as high as 90–99% [1-9]. Cone-beam CT-guided PTNB with virtual guidance has been established as a highly accurate and safe tissue sampling technique [1-4]. However, diagnostic failure and complications inevitably occur in at least a small proportion of PTNBs. The reported risk factors for diagnostic failure of PTNB include a small target lesion, a benign final diagnosis, and the use of fine-needle aspiration (FNA) as the diagnostic method [4-6]. A lower lobar location of the target lesion is also known to be associated with both diagnostic failure and the occurrence of pneumothorax [4,8-12]. However, the relationships between diagnostic failure or complications and the abutment of the diaphragm by the target lesion have not yet been established,

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although in practice, radiologists find the procedure more challenging when the target lesion is located adjacent to the diaphragm because it is strongly affected by respiratory motion. There is a risk of abdominal solid organ injury, and needle trajectory planning is limited. Some lesions are not sufficiently visible on fluoroscopy [12,13]. Patel et al. [12] investigated the impact of target lesion proximity to the diaphragm on biopsy yield and pneumothorax risk, but in their study, the mean distance of target lesions from the diaphragm was 8.3 cm, which was far from a juxtaphrenic location. To the best of our knowledge, the diagnostic accuracy and complication rate of PTNB for juxtaphrenic lesions have not been evaluated in prior studies.

Thus, the purpose of our study was to investigate the diagnostic accuracy and complications of cone-beam CT-guided PTNB of juxtaphrenic lesions and identify the risk factors for diagnostic failure and complications.

MATERIALS AND METHODS

Study Design and Population

This retrospective study was approved by the Institutional Review Board of Seoul National University Hospital, and the requirement for written informed consent was waived (IRB No. 2006-065-1131).

We enrolled 3558 consecutive cone-beam CT-guided PTNBs that were performed at a single tertiary referral hospital between January 2010 and December 2014. We included 348 PTNBs that satisfied the selection criterion of the target lesion abutting the diaphragm on a sagittal scan of preprocedural cone-beam CT (Fig. 1). Twelve PTNBs that underwent repeat biopsies of the same target lesion within a week were excluded; post-procedural pneumothorax or pulmonary hemorrhage may affect the results or complications of repeat biopsies. Finally, 336 PTNBs in 326 patients were included in the study. With respect to the diagnostic performance analysis, 20 PTNBs that did not fulfill the predefined criteria for determining the final diagnosis were excluded. The patient cohort of our study has also been included in previous multi-institutional studies that reported the malignancy risk demonstrated by non-diagnostic results from PTNBs and the diagnostic accuracy and complications of PTNBs [1,14,15]. However, no analysis has been conducted on PTNBs with a focus on

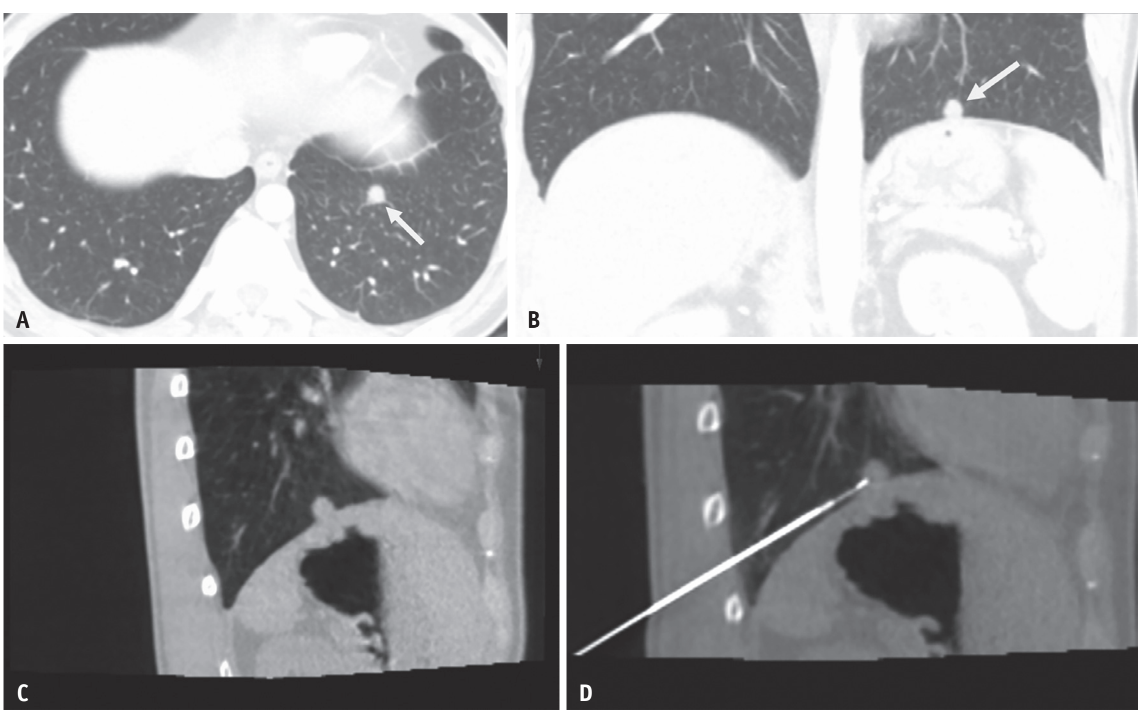

Fig. 1. Cone-beam CT–guided PTNB of a lung nodule in the juxtaphrenic location in a 39-year-old male with hepatocellular carcinoma.
A, B. Diagnostic CT image shows a 1.3-cm nodule (arrows) in the left lower lobe abutting the diaphragm on axial **(A)** and coronal **(B)** images. **C.** On the sagittal scan of preprocedural cone-beam CT, the shortest distance between the target lesion and diaphragm is 0 cm. **D.** After confirming the location of the needle tip on cone-beam CT, PTNB was performed. The nodule was confirmed as poorly differentiated carcinoma on biopsy. The nodule increased in size on follow-up CT (not shown). PTNB = percutaneous transthoracic needle lung biopsy

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juxtaphrenic lesions yet.

Cone-Beam CT-Guided PTNB Procedures

Cone-beam CT–guided PTNBs were primarily performed by thoracic radiologists who had performed at least 100 PTNBs, but residents and fellows in training were involved under the supervision of experienced thoracic radiologists (with 15 years and 7 years of experience in image-guided PTNB). The PTNBs were performed using two different cone-beam CT systems (Axiom Artis dTA/VB30 flat-panel detector with a 2048 x 1538 element, Siemens; Allura Xper FD20 flat-panel detector with a 2480 x 1920 element, Philips Healthcare) with virtual guidance software (iGuide, Siemens Medical Solutions; XperGuide, Philips Healthcare). Preprocedural cone-beam CT and the insertion and extraction of the biopsy needle were performed when patients held their breath at the end of expiration.

Data Collection

One radiologist (5 years of clinical experience) and a trained radiology technician (1 year of research experience in chest CT) retrospectively reviewed preprocedural CT images of the PTNBs using a picture archiving and communication system station. On the sagittal scans of preprocedural cone-beam CT, the shortest distance between the target lesion and diaphragm was measured. PTNBs with a distance of 0 cm were included in the study.

Variables related to patients, target lesions, and biopsy procedures were collected from our PTNB data registry. The patient variables included age, sex, and presence of pulmonary emphysema on CT images. The target characteristics were lesion size (long-axis diameter on a diagnostic CT image), location, and distance from the pleura to the target. The biopsy procedural information consisted of patient position, biopsy method (FNA or core needle biopsy [CNB]), and the number of tissue samples. Complications, including pneumothorax, pneumothorax requiring drainage catheter insertion, and hemoptysis, were recorded after reviewing the procedure records, medical charts, and follow-up images.

Based on the pathologic reports for the biopsy specimen, the cone-beam CT-guided PTNB results were categorized as positive, negative, or non-evaluable due to insufficient specimens, and the final diagnosis was blinded. Malignancy, atypical cells suggestive of malignancy, atypical cells suspicious for malignancy, and atypical cells of indeterminate malignancy were considered positive, based on previous research [15]. Specific benign diagnoses, such as hamartoma and tuberculosis, and nonspecific benign pathologic results, including granulomatous inflammation, abscess, or organizing pneumonia, were considered negative. The results were considered non-evaluable when the cone-beam CT-guided PTNB reports indicated that the specimens were insufficient or inadequate for diagnosis due to cellular paucity.

Reference Standards

For each lesion biopsied, the final diagnosis was classified as malignant or benign, and the reference standard for each lesion was established in one of the following four ways [4,8]. First, the final diagnosis was based on a surgical pathologic report if the lesion was surgically resected. Second, if the PTNB revealed a malignant or specific benign diagnosis and the target lesion was not surgically resected, the final diagnosis was based on a pathologic analysis of the PTNBs. Atypical cell results were not used to determine the final diagnosis. Third, the lesion was considered benign if its size decreased by 20% or more or remained stable for at least 2 years without treatment. Fourth, the lesion was identified as malignant if its clinical behavior showed obvious malignant processes. Lesions that did not fulfill the above criteria were classified as having incomplete reference standards and excluded from the diagnostic performance analysis.

Statistical Analysis

The accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the diagnosis of malignancy were calculated with 95% confidence intervals (CIs) on a per-lesion basis. Based on the intention-to-diagnose principle, non-evaluable results due to insufficient specimens were considered to be false negatives when calculating sensitivity and false positives when calculating specificity [1,16].

The cone-beam CT-guided PTNB results were categorized into two groups: the diagnostic success group and the diagnostic failure group. The diagnostic success group consisted of true-positive and true-negative results. The diagnostic failure group consisted of false-positive, false-negative, and non-evaluable results due to insufficient specimens. To determine the risk factors for diagnostic failure, the statistical significance of the differences between the diagnostic success and failure groups was analyzed using the Pearson chi-squared test or Fisher's exact test, as appropriate. Variables with $p < 0.010$ during the univariable analysis were used as input variables for multivariable logistic regression analysis to identify independent factors. In the multivariable logistic regression analysis, a backward stepwise conditional method was used.

The rates of overall complications, pneumothorax, pneumothorax requiring drainage catheter insertion, hemoptysis, and other rare complications were calculated. The risk factors for overall complications and pneumothorax were investigated as aforementioned.

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 24.0 (IBM Corp.). A p value of less than 0.05 was considered to indicate statistical significance.

RESULTS

Patient Demographics and Lesions

In total, 326 patients underwent 336 cone-beam CT-guided PTNBs, and their mean age was 65.2 ± 11.4 years (age range, 30–86 years). After excluding 20 cases with incomplete reference standards, the diagnostic performance of 316 cone-beam CT-guided PTNBs in 306 patients with a mean age of 65.5 ± 11.2 years (age range, 33–86 years) was analyzed. The characteristics of the patients, lesions, and procedures are shown in Table 1.

Diagnostic Accuracy

Of the 316 cone-beam CT-guided PTNBs, 221 (69.9%) showed positive results, 90 (28.5%) showed negative results, and 5 (1.6%) were non-evaluable due to insufficient specimens. According to the final diagnosis, 235 (74.4%) lesions were confirmed as malignant, and 81 (25.6%) lesions were confirmed as benign. The final diagnosis of malignancy was based on surgical pathology (n = 59), specific malignant biopsy results (n = 168), and clinical malignant behavior (n = 8). Benignity was confirmed based on surgical pathology (n = 9), specific benign biopsy results (n = 8), and a significant decrease or stability in size for at least 2 years (n = 64).

Table 1. Characteristics of Patients, Lesions, and Procedures

	Analysis of Diagnostic Performance	Analysis of Complications
Total no. of procedures	316	336
Total no. of patients	306	326
Sex		
Male	174 (56.9)	189 (58.0)
Female	132 (43.1)	137 (42.0)
Age, year		
Mean ± SD	65.5 ± 11.2	65.2 ± 11.4
Range	33–86	30–86
Position		
Supine	42 (13.3)	45 (13.4)
Prone	274 (86.7)	291 (86.6)
Biopsy needle		
FNA only	9 (2.8)	11 (3.3)
CNB or combined	307 (97.2)	325 (96.7)
No. of tissue samples		
≤ 3	250 (79.1)	265 (78.9)
≥ 4	66 (20.9)	71 (21.1)
Lesion size, cm		
Mean ± SD	4.3 ± 2.4	4.3 ± 2.3
Range	1.0–13.9	1.0–13.9
Presence of pulmonary emphysema on CT		
Yes	55 (17.4)	57 (17.0)
No	261 (82.6)	279 (83.0)
Distance from pleura to target, cm		
Mean ± SD	1.9 ± 1.9	1.9 ± 1.9
Range	0–9.3	0–9.3

Data are presented as n (%) unless specified otherwise. CNB = core needle biopsy, FNA = fine-needle aspiration, SD = standard deviation

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The overall accuracy, sensitivity, specificity, PPV, and NPV for the diagnosis of malignancy were 92.7% (293 of 316; 95% CI, 89.3–95.3%), 91.3% (219 of 240; 95% CI, 86.9–94.5%), 91.4% (74 of 81; 95% CI, 83.0–96.5%), 96.9% (219 of 226; 95% CI, 93.9–98.5%), and 77.9% (74 of 95; 95% CI, 70.0–84.2%), respectively (Fig. 2). The diagnostic categories stratified by lesion size are presented in Table 2.

Diagnostic Failure and Risk Factors

The diagnostic failure group included 7.3% cone-beam CT-guided PTNBs (95% CI, 4.4–10.1%; 23 PTNBs). Table 3 summarizes the results of the univariable analysis comparing the diagnostic success and failure groups. There was a significant difference in lesion size (≤ 2 cm vs. > 2 cm) (p = 0.037). Logistic regression analysis revealed that a lesion size of ≤ 2 cm was significantly associated with diagnostic failure (odds ratio [OR], 2.78; 95% CI, 1.02–7.55; p = 0.045). The other variables did not significantly differ in the two groups.

Cone-Beam CT-Guided PTNB-Related Complications

Cone-beam CT-guided PTNB-related complications occurred after 29.2% (95% CI, 24.1–33.9%; 98 PTNBs) of the 336 PTNBs. Pneumothorax occurred after 26.5% of the PTNBs (95% CI, 21.7–31.3%; 89 PTNBs), and drainage catheter insertion was, subsequently, required for 2.1% (95% CI, 0.6–3.9%; 7 PTNBs). Hemoptysis occurred after 2.1% of the PTNBs (95% CI, 0.6–3.9%; 7 PTNBs). Other rare complications included hemothorax after 0.9% (95% CI, 0.0–2.1%; 3 PTNBs), all of which resolved without

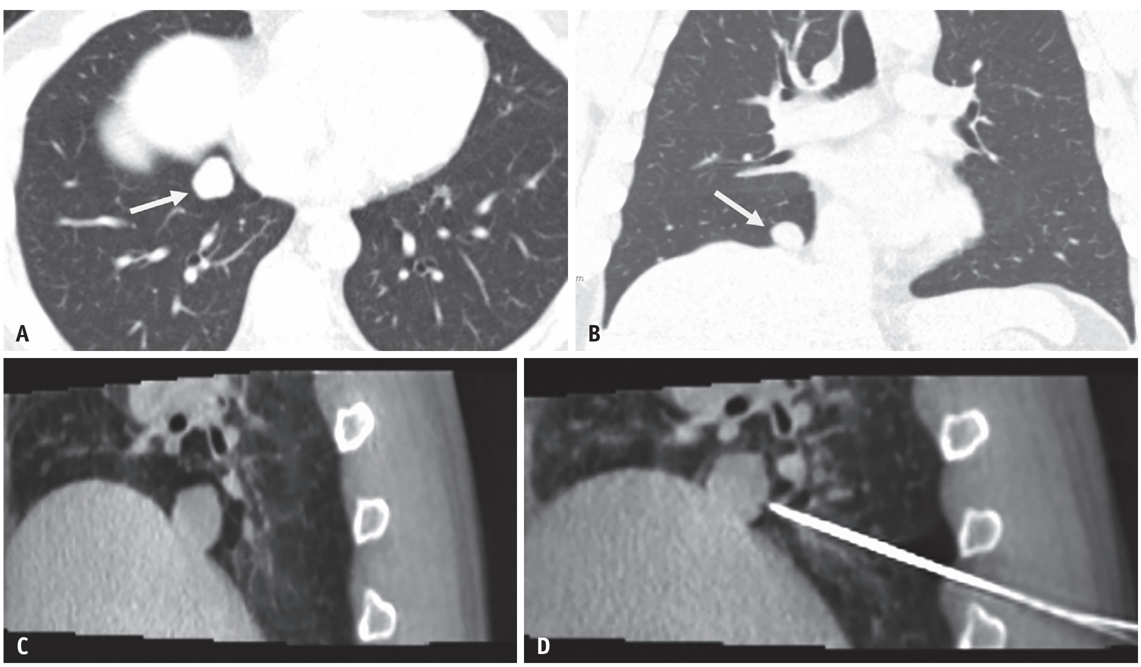

Fig. 2. Cone-beam CT–guided PTNB in a 55-year-old male with a solitary pulmonary nodule in the juxtaphrenic location.
A, B. Diagnostic CT image shows a 2.2-cm nodule (arrows) in the right lower lobe abutting the diaphragm on axial **(A)** and coronal **(B)** images. **C.** On the sagittal scan of a preprocedural cone-beam CT, the shortest distance between the target lesion and the diaphragm is 0 cm. **D.** After confirming the location of the needle tip on cone-beam CT, PTNB was performed. The nodule was confirmed as chondroid hamartoma on biopsy. PTNB = percutaneous transthoracic needle lung biopsy

Table 2. Diagnostic Categories for Malignancy according to Lesion Size

Diagnostic Categories	Lesion Size (cm)				
	≤ 2.0 (n = 39)	2.1–4.0 (n = 143)	4.1–6.0 (n = 70)	> 6.0 (n = 64)	Overall (n = 316)
True-positive	26 (66.7)	91 (63.6)	53 (75.7)	49 (76.6)	219 (69.3)
True-negative	7 (17.9)	41 (28.7)	15 (21.4)	11 (17.2)	74 (23.4)
False-positive	1 (2.6)	0 (0.0)	1 (1.4)	0 (0.0)	2 (0.6)
False-negative	1 (2.6)	10 (7.0)	1 (1.4)	4 (6.3)	16 (5.1)
Non-evaluable	4 (10.3)	1 (0.7)	0 (0.0)	0 (0.0)	5 (1.6)

Data are presented as n (%).

Table 3. Results of Univariable Analysis of Risk Factors for Diagnostic Failure

Variable	Diagnostic Success (n = 293)	Diagnostic Failure (n = 23)	*P*
Sex			0.653
Male	167 (57.0)	12 (52.2)	
Female	126 (43.0)	11 (47.8)	
Age, year			0.530
≤ 65	133 (45.4)	12 (52.2)	
> 65	160 (54.6)	11 (47.8)	
Position			0.971
Supine	39 (13.3)	3 (13.0)	
Prone	254 (86.7)	20 (87.0)	
Biopsy needle			0.133
FNA only	7 (2.4)	2 (8.7)	
CNB or combined	286 (97.6)	21 (91.3)	
No. of tissue samples			0.917
≤ 3	232 (79.2)	18 (78.3)	
≥ 4	61 (20.8)	5 (21.7)	
Target size			0.037
≤ 2 cm	33 (11.3)	6 (26.1)	
> 2 cm	260 (88.7)	17 (73.9)	
Emphysema			0.392
Yes	53 (18.1)	2 (8.7)	
No	240 (81.9)	21 (91.3)	
Pneumothorax			0.664
Yes	77 (26.3)	7 (30.4)	
No	216 (73.7)	16 (69.6)	
Hemoptysis			1.000
Yes	6 (2.0)	0 (0)	
No	287 (98.0)	23 (100)	
Distance from pleura to target lesion			0.520
≤ 2 cm	173 (59.0)	12 (52.2)	
> 2 cm	120 (41.0)	11 (47.8)	
Final diagnosis			0.584
Benign	74 (25.3)	7 (30.4)	
Malignant	219 (74.7)	16 (69.6)	

Data are presented as n (%). CNB = core needle biopsy, FNA = fine-needle aspiration

additional procedures, and vasovagal syncope after 0.3% (95% CI, 0.0–0.9%; 1 PTNB). There were no cases of abdominal solid organ injuries, air embolism, or mortality.

Regarding the risk factors for complications, there were significant differences in patient age (≤ 65 years vs. > 65 years) (p = 0.002), lesion size (≤ 2 cm vs. > 2 cm) (p = 0.014), presence of emphysema (p = 0.001), and distance from the pleura to the target lesion (≤ 2 cm vs. > 2 cm) (p = 0.014). Multivariable logistic regression analysis revealed that an age of > 65 years (OR, 2.36; 95% CI, 1.38–4.03; p = 0.002), lesion size of ≤ 2 cm (OR, 2.93; 95% CI, 1.44–5.96; p = 0.003), presence of emphysema (OR, 2.39; 95% CI, 1.29–4.44; p = 0.006), and lesion distance of > 2 cm from the pleura (OR, 1.92; 95% CI, 1.16–3.18; p = 0.010) were associated with the occurrence of complications. Table 4 summarizes the results of the multivariable analyses for the risk factors of complications.

With respect to pneumothorax, patient age (≤ 65 years vs. > 65 years) (p = 0.001), presence of emphysema (p = 0.001), and the distance from the pleura to the target lesion (≤ 2 cm vs. > 2 cm) (p = 0.007) significantly differed in the PTNBs with pneumothorax and those without pneumothorax. The multivariable logistic regression analysis showed that patient age of > 65 years (OR, 2.78; 95% CI, 1.59–4.88; p = 0.001), lesion size of ≤ 2 cm (OR, 2.50; 95% CI, 1.20–5.24; p = 0.015), presence of emphysema (OR,

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Table 4. Results of Univariable and Multivariable Logistic Regression Analysis of Risk Factors for Complications

Variable	No Complication (n = 238)	Complication (n = 98)	Univariable Analysis	Multivariable Analysis	
			P	AOR (95% CI)	*P*
Sex			0.188		
Male	132 (55.5)	62 (63.3)			
Female	106 (44.5)	36 (36.7)			
Age, year			0.002		0.002
≤ 65	125 (52.5)	33 (33.7)		Reference	
> 65	113 (47.5)	65 (66.3)		2.360 (1.382–4.030)	
Position			0.271		
Supine	35 (14.7)	10 (10.2)			
Prone	203 (85.3)	88 (89.8)			
Biopsy needle			0.736		
FNA only	7 (2.9)	4 (4.1)			
CNB or combined	231 (97.1)	94 (95.9)			
No. of tissue samples			0.932		
≤ 3	188 (79.0)	77 (78.6)			
≥ 4	50 (21.0)	21 (21.4)			
Target size			0.014		0.003
≤ 2 cm	23 (9.7)	19 (19.4)		2.930 (1.439–5.964)	
> 2 cm	215 (90.3)	79 (80.6)		Reference	
Emphysema			0.001		0.006
Yes	30 (12.6)	27 (27.6)		2.391 (1.288–4.437)	
No	208 (87.4)	71 (72.4)		Reference	
Distance from pleura to target lesion			0.014		0.010
≤ 2 cm	151 (63.4)	48 (49.0)		Reference	
> 2 cm	87 (36.6)	50 (51.0)		1.924 (1.163–3.181)	

Data are presented as n (%). AOR = adjusted odds ratio, CI = confidence interval, CNB = core needle biopsy, FNA = fine-needle aspiration

2.51; 95% CI, 1.34–4.71; p = 0.004), and lesion distance of > 2 cm from the pleura (OR, 2.16; 95% CI, 1.28–3.63; p = 0.004) were associated with pneumothorax. The risk factors for pneumothorax are summarized in Table 5.

DISCUSSION

In this study, we evaluated the diagnostic accuracy of cone-beam CT-guided PTNB for juxtaphrenic lung lesions based on the intention-to-diagnose principle and analyzed the cone-beam CT-guided PTNB-related complications. The accuracy for the diagnosis of malignancy was 92.7%, and target size was the only significant predictor of diagnostic failure. Complications occurred after 29.2% of cone-beam CT-guided PTNBs of juxtaphrenic lesions, with pneumothorax occurring in 26.5%.

The sensitivity and specificity of the cone-beam CT-guided PTNBs were 91.3% and 91.4%, respectively, and diagnostic failure occurred after 7.3%. Although the technique we used in our study is limited to cone-beam CT with virtual guidance, the results of our study are comparable to those of prior studies that analyzed the overall diagnostic accuracy of PTNB [1-4,6-9,17,18]. In a previous multicenter study, Lee et al. [1] reported that the sensitivity, specificity, and accuracy of PTNB with various types of imaging guidance, including cone-beam CT, CT, and fluoroscopy, were 92.5%, 86.5%, and 91.1%, respectively. The diagnostic accuracy of PTNB under cone-beam CT guidance has been reported to be equivalent or slightly higher in previous studies [1-4,17,18]. Considering this, the diagnostic accuracy of this study is reasonable for clinical situations where a biopsy is required to differentiate malignant tumors from benign lesions. The specificity recorded in our study was lower than that of previous studies, which ranged from 98–100% [2-9,18]. This discrepancy can be explained by the fact that non-evaluable results were considered as false positives in our study according to the intention-to-diagnose principle, whereas in previous studies, non-evaluable results were excluded or regarded as negative biopsy results [1-9,18].

A target lesion size of ≤ 2 cm was the only independent

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Table 5. Results of Univariable and Multivariable Logistic Regression Analysis of Risk Factors for Pneumothorax

Variable	No Pneumothorax (n = 247)	Pneumothorax (n = 89)	Univariable Analysis	Multivariable Analysis	
			P	AOR (95% CI)	*P*
Sex			0.098		0.704
Male	136 (55.1)	58 (65.2)		1.116 (0.633–1.967)	
Female	111 (44.9)	31 (34.8)		Reference	
Age, year			0.001		0.001
≤ 65	131 (53.0)	27 (30.3)		Reference	
> 65	116 (47.0)	62 (69.7)		2.782 (1.586–4.880)	
Position			0.289		
Supine	36 (14.6)	9 (10.1)			
Prone	211 (85.4)	80 (89.9)			
Biopsy needle			0.490		
FNA only	7 (2.8)	4 (4.5)			
CNB or combined	240 (97.2)	85 (95.5)			
No. of tissue samples			0.718		
≤ 3	196 (79.4)	69 (77.5)			
≥ 4	51 (20.6)	20 (22.5)			
Target size			0.068		0.015
≤ 2 cm	26 (10.5)	16 (18.0)		2.504 (1.197–5.235)	
> 2 cm	221 (89.5)	73 (82.0)		Reference	
Emphysema			0.001		0.004
Yes	31 (12.6)	26 (29.2)		2.510 (1.339–4.706)	
No	216 (87.4)	63 (70.8)		Reference	
Distance from pleura to target lesion			0.007		0.004
≤ 2 cm	157 (63.6)	42 (47.2)		Reference	
> 2 cm	90 (36.4)	47 (52.8)		2.157 (1.280–3.634)	

Data are presented as n (%). AOR = adjusted odds ratio, CI = confidence interval, CNB = core needle biopsy, FNA = fine-needle aspiration

risk factor for diagnostic failure in our study. Although cone-beam CT-guided PTNB is known to be an accurate diagnostic method for even small lung nodules [2,3], adequate and safe tissue acquisition for small juxtaphrenic lesions requires high proficiency and expertise. Avoiding passing the needle through the diaphragm is technically challenging, particularly when the lesion is small because this location is strongly influenced by respiratory motion. Small juxtaphrenic lesions of ≤ 2 cm are more difficult for PTNB and have a higher diagnostic failure rate than larger lesions, but radiologists can expect successful diagnosis from a cone-beam CT-guided PTNB for larger lesions within the juxtaphrenic location. Other variables, including the final diagnosis and biopsy method (FNA or CNB), were not associated with diagnostic failure in this study, unlike in previous reports [1,5,8,9]. However, only 2.8% (9 of 316) of PTNBs were performed with FNA in our study, and more cases of FNA would be necessary for a confirmatory evaluation.

The complication rate of cone-beam CT-guided PTNB of juxtaphrenic lesions was 29.2% in this study. Pneumothorax occurred after 26.5% of PTNBs, which is within the previously reported range of 16.2–38.4% [2,4,11,12,14,18-20]. Significant risk factors for pneumothorax were old age, presence of emphysema, small target size, and deep location, all of which are consistent with prior studies [4,9,10,14,21-23]. Regarding the association between a lower lobar location and the occurrence of pneumothorax, several studies have reported that a lower lobar location was related to the increased incidence of pneumothorax [4,9-11,17]. As our study evaluated only juxtaphrenic lesions, we did not investigate whether pneumothorax was correlated with a lobar location or abutment to the diaphragm. However, the incidence of pneumothorax in juxtaphrenic lesions was within the acceptable range in this study. Moreover, only 2.1% of cases required drainage catheter insertion, which is lower than the previously reported incidence, ranging from 2.4% to 15% [4,9,10,14,21]. We suggest that a juxtaphrenic location is unlikely to have a major influence on the occurrence of

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pneumothorax.

In this study, the hemoptysis rate was 2.1%, which was within the previously reported range of 2.0–6.9% but in the lower range [4,9,10,14,18,22]. This can be explained by the fact that juxtaphrenic lesions are located in the periphery of the lung and have a lower chance of bronchovascular injuries along the needle course [24]. Furthermore, as no major complications, such as liver or spleen injury, air embolism, or mortality were noted, cone-beam CT-guided PTNB for juxtaphrenic lesions is a relatively safe procedure.

Our study had several limitations. First, this study had a retrospective design with unknown biases. Second, preprocedural cone-beam CT was performed at the end of expiration. However, diagnostic chest CT images are mostly performed when patients hold their breath after inspiration. The location of juxtaphrenic lesions may change according to respiration, and lesions located slightly apart from the diaphragm on diagnostic CT may have been included in this study. Nevertheless, the procedure was carried out during expiration, and this issue likely did not have a significant impact on the results. Third, our study did not compare the diagnostic accuracy and complications of juxtaphrenic lesions with those of lesions located farther from the diaphragm. Further studies are necessary to confirm the impact of lesions abutting the diaphragm. Lastly, the surgeons in our institution had already had experience and were familiar with cone-beam CT-guided PTNB. It is not certain that our results can be reproducible where surgeons were skilled with different methods such as CT or CT fluoroscopy and were not familiar with cone-beam CT guidance.

In conclusion, the accuracy of cone-beam CT-guided PTNB of juxtaphrenic lesions for the diagnosis of malignancy was fairly high, and the target size was the only significant predictor of diagnostic failure. Complications of cone-beam CT-guided PTNB of juxtaphrenic lesions occurred at a reasonable rate.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Chang Min Park. Data curation: Wonju Hong, Soon Ho Yoon. Formal analysis: Wonju Hong. Investigation: Wonju Hong, Chang Min Park. Methodology: Chang Min Park. Project administration: Chang Min Park. Supervision: Chang Min Park, Jin Mo Goo. Writing—original draft: Wonju Hong. Writing—review & editing: Soon Ho Yoon, Jin Mo Goo, Chang Min Park.

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