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ORIGINAL ARTICLE

Perilesional emphysema as a predictor of risk of complications from computed tomography-guided transthoracic lung biopsy

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Abstract

Purpose This study evaluated whether or not patterns of emphysema and their qualitative and quantitative severity can predict the risk of complications with post-computed tomography (CT)-guided transthoracic lung biopsy (TTLB).

Materials and methods Three hundred and ninety-seven patients who underwent CT-guided TTLB in 2010–2018 were retrospectively reviewed. The severity of emphysema and presence of perilesional emphysema were assessed visually using the Fleischner Society classification. Ninety seven of the 397 patients underwent quantitative analysis of emphysema. Complications, including pneumothorax, chest tube insertion, and hemorrhage, were assessed by post-TTLB CT and radiographic imaging. The grade of hemorrhage was categorized into three groups. Independent risk factors for pneumothorax and hemorrhage were assessed by univariate and multivariate logistic regression analyses.

Results Pneumothorax occurred in 48.6% of cases and hemorrhage in 70.5%. Perilesional emphysema was significantly associated with pneumothorax (odds ratio 6.720; 95% confidence interval 3.265–13.831, $p < 0.001$) and hemorrhage (odds ratio 3.877; 95% confidence interval 1.796–8.367; $p = 0.001$). The severity of visual and quantitative emphysema was not a significant risk factor for pneumothorax or hemorrhage ($p > 0.05$). Perilesional emphysema was significantly associated with the grade of hemorrhage ($p < 0.001$).

Conclusion Perilesional emphysema can estimate the risk of iatrogenic complications from CT-guided TTLB.

Keywords Emphysema · Biopsy · Pneumothorax · Hemorrhage

Introduction

Many countries are now recommending low-dose computed tomography (CT) to screen for lung cancer, as the National Lung Screening Trial demonstrated that such screening can achieve a 20% reduction in lung-cancer mortality compared with chest radiography in persons at high risk for lung cancer [1, 2]. The increasing use of low-dose CT lung-cancer screening has led to an increase in the incidence of indeterminate nodules [3]. Percutaneous CT-guided transthoracic lung biopsy (TTLB) is a well-established method to evaluate peripheral lung nodules requiring pathological confirmation [4]. Recently, there has been an increase in the role of TTLB in the diagnosis of lung cancer and personalized medicine [5]. However, although TTLB has high diagnostic performance for malignant lesions, it has less sensitivity for evaluation of benign lesions [6].

Patients with chronic obstructive pulmonary disease (COPD) have a sixfold greater risk of developing lung cancer than matched smokers [7]. Emphysema, defined as irreversible enlargement of the airspaces and destruction of airway walls distal to the terminal bronchioles, is a phenotype of COPD that is associated with development of lung cancer [8, 9]. Pneumothorax and pulmonary hemorrhage are the most common complications of TTLB.

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The complication rate is influenced by a variety of factors, including emphysema, lesion size, pleura-to-lesion distance, needle size, number of specimens obtained, needle–pleural angle, and experience of the radiologist performing the biopsies [10]. Emphysema is a well-known risk factor for post-procedural pneumothorax [11]. Quantitative CT has been used to evaluate the extent of emphysema, and quantification of emphysema based on the Hounsfield unit (HU) threshold has been correlated with its histopathology, symptoms, and lung function [12–15]. The Fleischner Society has recently proposed patterns of emphysema, which can be assessed visually, and classified accordingly as centrilobular (trace, mild, moderate, confluent, and advanced destructive emphysema), panlobular, and paraseptal emphysema (mild and substantial paraseptal emphysema) [16]. A study reported that the visual severity of emphysema according to the Fleischner Society classification is associated with physiologic impairment and mortality, and is independent of the quantitative severity of emphysema [17]. The purpose of this study was to investigate whether or not these patterns of emphysema and their qualitative and quantitative severity can predict complications after TTLB.

Materials and methods

Study population

The medical records of 480 consecutive patients who underwent CT-guided TTLB with a coaxial technique at our institution between February 2010 and March 2018 were retrospectively reviewed. Data on clinical characteristics, histopathologic results, and findings on CT scans of the chest were collected. Indications for TTLB in our institution were as follows: (1) peripheral pulmonary lesions that cannot be localized with bronchoscopy or were non-diagnostic in previous bronchoscopies; (2) unidentified pleural masses with a high suspicion of cancer; (3) multiple nodules or masses in patients without a history of neoplastic disease; and (4) re-biopsy for targeted therapy in patients known to have malignancy. Eighty-three patients were excluded because of the absence of laboratory coagulation data ($n=26$) or no information on smoking history ($n=57$), leaving data for 397 patients available for analysis. Ninety seven of these 397 patients underwent quantitative analysis of emphysema on chest CT (Fig. 1).

The study protocol was approved by the institutional review board of Kangwon National University Hospital (IRB number 2018-07-001). The need for informed consent was waived in view of the retrospective observational nature of the research.

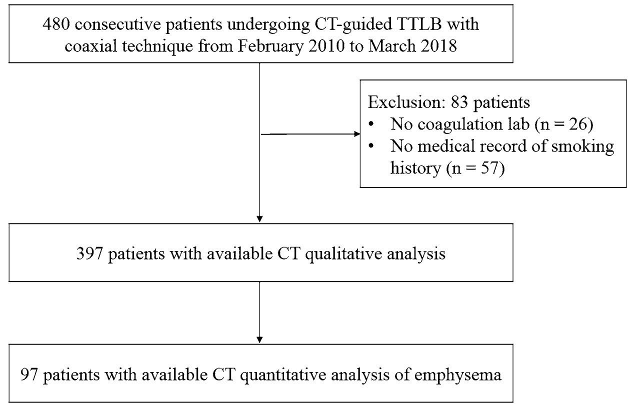

Fig. 1 Flowchart showing the enrolment process for the study populations. *CT* computed tomography, *TTLB* transthoracic lung biopsy

Analysis of procedural and post-procedural CT images

The procedural and post-procedural CT images were reviewed by two radiologists (DSL, SHB) who were blinded to all clinical information. Lesion-related variables assessed on procedural CT images included size, location, morphologic characteristics, and distance from the pleura. A pleural tag was defined as a linear opacity from the nodule surface to the pleural surface representing thickening of the interlobular septa [18]. Technique-related variables, including the number of needle passes and position, were assessed on the CT images. Complications, including pneumothorax, need for insertion of a chest tube, and hemorrhage, were assessed on the post-procedural CT images and on chest radiographs and positron emission tomography-CT scans acquired after TTLB. Pulmonary hemorrhage was defined as new consolidation or ground-glass opacity on post-procedural images. The severity of hemorrhage was graded as follows: grade 0, no pulmonary hemorrhage; grade 1, needle tract hemorrhage or hemorrhage with a width of ≤ 2 cm (mild); grade 2, hemorrhage with a width of > 2 cm, lobar hemorrhage, or hemothorax (severe; Online Resource 4) [5].

Evaluation of emphysema

All patients underwent chest CT within 30 days of TTLB. In all cases, the severity of emphysema was assessed visually by two radiologists using the Fleischner Society classification, including centrilobular emphysema (for no, trace, mild, moderate, confluent, advanced destructive, see Online Resource 1) and paraseptal emphysema (for no, mild, substantial, see Online Resource 2) [16].

Centrilobular emphysema was graded as follows: grade 1, no centrilobular emphysema; grade 2, trace or mild centrilobular emphysema; grade 3, moderate, confluent, or advanced destructive emphysema. Perilesional emphysema was defined as emphysema along the needle pathway (Fig. 2) [19]. Different interpretations of visual assessment of emphysema were resolved by consensus. Ninety seven of the 397 patients underwent volumetric noncontrast and inspiratory CT before TTLB. The quantitative analysis of emphysema was performed using an Aview® system (Coreline Soft Inc., Seoul, South Korea). The emphysema index was calculated as the percent of lung voxels below − 950 HU (Online Resource 3) [20].

Statistical analysis

Parametric variables are summarized as the mean ± standard deviation and nonparametric variables as the number (percentage). Univariate and multivariate logistic regression analyses were performed to identify risk factors for pneumothorax and hemorrhage. All variables with a p value ≤ 0.10 in univariate analysis were selected for multivariate logistic regression analysis. The Kruskal–Wallis test was used to compare the variables according to the grade of hemorrhage (none, mild, or severe). All analyses were performed using SPSS for Windows (version 23.0; IBM Corp., Armonk, NY, USA). A p value < 0.05 was considered statistically significant.

Results

Patient characteristics

The mean patient age was 70.1 (range 16–94) years; 72.3% were male and 65.8% were current or ex-smokers. Two hundred and fifteen of the 397 patients had lesions located in the upper or middle lobes and 182 had lesions in the lower lobes. The mean lesion size was 4.4 ± 2.6 (range 0.7–17.0) cm. Pneumothorax occurred in 48.6% of cases (with insertion of a chest tube required in 6.0%) and hemorrhage in 70.5%. Severe hemorrhage occurred after TTLB in 83 (20.9%) of the 397 cases, sublobar hemorrhage with a width of > 2 cm in 82, and hemothorax in 1. The patient and lesion characteristics are summarized in Table 1.

Risk factors for pneumothorax

In univariate logistic regression analysis, age ($p = 0.094$), lesion size ($p < 0.001$), perifissural nodule ($p < 0.001$), pleural tag ($p = 0.002$), paraseptal emphysema ($p = 0.012$–0.076), perilesional emphysema ($p < 0.001$), distance from the pleura ($p < 0.001$), and number of passages ($p < 0.001$) were identified as risk factors for pneumothorax (Online Resource 5). Multivariate logistic regression analysis revealed perilesional emphysema (odds ratio [OR] 6.720; 95% confidence interval [CI] 3.265–13.831; $p < 0.001$) to be a significant independent risk factor for pneumothorax (Fig. 3). However, the visual grade of centrilobular emphysema was not a significant risk factor for pneumothorax. Lesion size (OR 0.985; 95% CI 0.974–0.997; $p = 0.014$), a perifissural nodule (OR 22.402; 95% CI 5.061–99.150; $p < 0.001$), paraseptal emphysema (mild [OR 0.210; 95% CI 0.096–0.460; $p < 0.001$] and substantial [OR 0.235; 95% CI 0.074–0.742; $p = 0.014$] paraseptal emphysema), distance from the pleura (OR 1.017; 95% CI 1.003–1.030; $p = 0.016$), and number of passages (OR 2.173; 95% CI 1.316–3.587; $p = 0.002$) were associated with development of pneumothorax (Table 2). Furthermore, in a subgroup analysis of 97 patients in whom quantitative analysis of emphysema was performed, the emphysema index was not a significant risk factor for pneumothorax in univariate or multivariate analyses ($p > 0.050$).

In addition, multivariate logistic regression analysis showed that perifissural nodules (OR 8.360; 95% CI 2.479–28.198; $p = 0.001$), perilesional emphysema (OR 9.421; 95% CI 1.919–46.253; $p = 0.006$), and distance from the pleura (OR 1.017; 95% CI 1.003–1.051; $p = 0.026$) are significant independent risk factors for pneumothorax requiring chest tube insertion (Table 3).

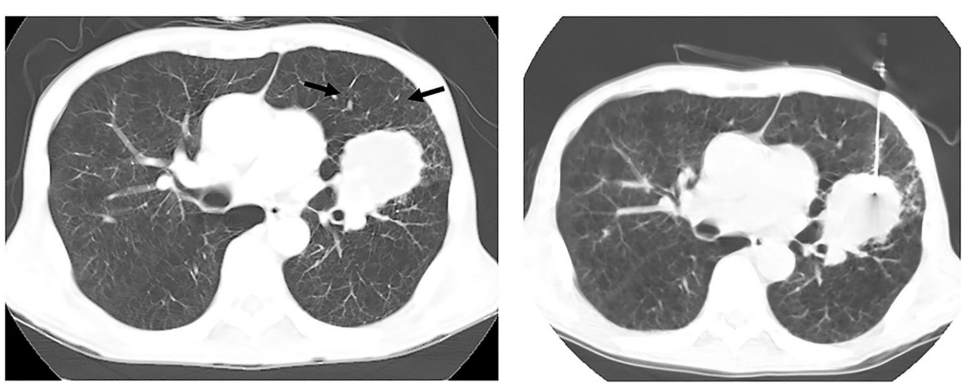

Fig. 2 Perilesional emphysema. Perilesional emphysema is defined as the presence of emphysema (arrows) along the needle pathway

Table 1 Demographics, radiologic findings, lesion characteristics, and iatrogenic complications of transthoracic lung biopsy in 397 patients

Characteristic	
Age, years	70.1 ± 11.0
Male sex	287 (72.3)
Smoking history	
Never	136 (34.2)
Former	144 (36.3)
Current	117 (29.5)
Pathology	
Malignant	299 (75.3)
Benign	98 (24.7)
Location	
RUL[a]	99 (24.9)
RML[b]	28 (7.1)
RLL[c]	99 (24.9)
LUL[d]	88 (22.2)
LLL[e]	83 (20.9)
Lesion	
Solid	383 (96.5)
Part-solid	11 (2.8)
Ground-glass opacity	3 (0.7)
Lesion size (mm)	43.8 ± 25.6
Centrilobular emphysema	
None	214 (53.9)
Trace	57 (14.4)
Mild	66 (16.6)
Moderate	43 (10.8)
Confluent	16 (4.0)
Advanced, destructive	1 (0.3)
Paraseptal emphysema	
None	288 (72.6)
Mild	83 (20.9)
Substantial	26 (6.5)
Pneumothorax	
No	204 (51.4)
Yes	193 (48.6)
Chest tube	24 (6.0)
Hemorrhage	
None	117 (29.5)
Mild	197 (49.6)
Severe	83 (20.9)

The data are mean ± standard deviation or as the number (percentage)

[a]Right upper lobe

[b]Right middle lobe

[c]Right lower lobe

[d]Left upper lobe

[e]Left lower lobe

Risk factors for hemorrhage

Univariate logistic regression analysis identified the following risk factors for hemorrhage: age ($p = 0.044$), international normalized ratio ($p = 0.032$), activated partial thromboplastin time (aPTT; $p = 0.019$), platelet count ($p = 0.002$), location of lesion ($p = 0.043$–0.929), lesion size ($p < 0.001$), pleural tag ($p = 0.061$), perilesional emphysema ($p < 0.001$), distance from the pleura ($p < 0.001$), and number of passages ($p < 0.001$; Online Resource 6). In multivariate logistic regression analysis of these factors, there was a significant association of perilesional emphysema (OR 3.877; 95% CI 1.796–8.367; $p = 0.001$) with development of hemorrhage (Fig. 3). In contrast, visual grades of centrilobular and paraseptal emphysema were not significant risk factors for hemorrhage ($p > 0.050$). The aPTT (OR 0.941; 95% CI 0.898–0.986; $p = 0.010$), lesion size (OR 0.982; 95% CI 0.970–0.995; $p = 0.007$), and distance from the pleura (OR 1.083; 95% CI 1.058–1.109; $p < 0.001$) were significant independent risk factors for hemorrhage (Table 4). In the subgroup analysis of the 97 patients in whom quantitative analysis of emphysema was performed, the emphysema index was not a significant risk factor for hemorrhage in univariate or multivariate analyses ($p > 0.050$).

There were significant differences in age ($p = 0.046$), smoking status ($p = 0.016$), international normalized ratio ($p = 0.018$), aPTT ($p = 0.008$), platelet count ($p = 0.001$), lesion morphology ($p = 0.041$), lesion size ($p < 0.001$), pleural tag ($p = 0.029$), perilesional emphysema ($p < 0.001$), distance from the pleura ($p < 0.001$), and number of passages ($p < 0.001$) according to grade of hemorrhage (Table 5).

Discussion

This study showed that perilesional emphysema was a significant predictor of pneumothorax and hemorrhage after CT-guided TTLB. Moreover, perilesional emphysema was associated with the severity of hemorrhage. In contrast, the qualitative and quantitative severity of emphysema measured in the whole lung was not associated with iatrogenic complications of TTLB.

In the present study, pneumothorax and pulmonary hemorrhage occurred in 48.6% and 70.5% of patients after CT-guided TTLB, respectively. This complication rate in the present study was higher than that in other studies, which demonstrated that the incidence of pneumothorax after CT-guided TTLB varied from 4 to 62% [21]. The 2003 American College of Chest Physicians guideline reported that TTLB plays no role in patients with resectable solitary lesion [22]. Unnecessary TTLB could result in increased complications and hospital stays. However, in our country, 70% of radiologists have initially performed TTLB for

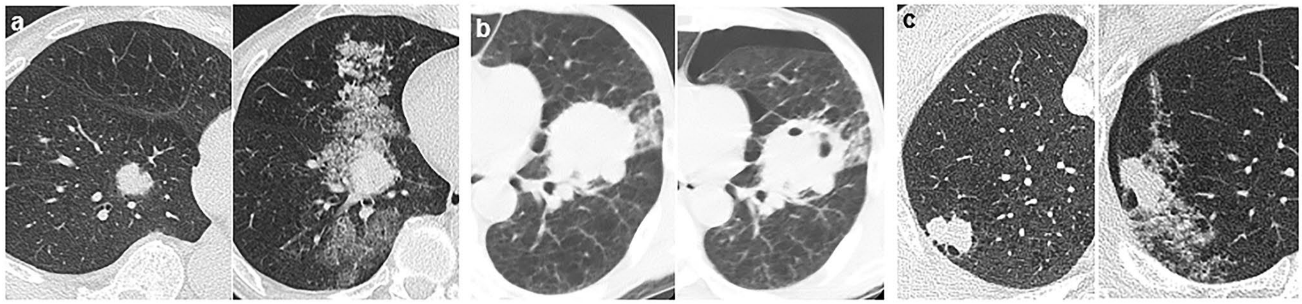

Fig. 3 CT-guided TTLB of a solitary lesion with perilesional emphysema. **a** A 73-year-old man with a nodule in the right lower lobe. Severe pulmonary hemorrhage occurred after CT-guided TTLB. **b** A 62-year-old man with a nodule in the left upper lobe. Pneumothorax occurred after CT-guided TTLB. **c** A 54-year-old man with a nodule in the right upper lobe. Pulmonary pneumothorax and hemorrhage occurred after CT-guided TTL. *CT* computed tomography, *TTLB* transthoracic lung biopsy

Table 2 Multivariate logistic regression analysis of risk factors for pneumothorax

Variable	*p* value	OR[a]	95% CI[b]
Age	0.531	0.993	0.971–1.015
Lesion size	**0.014**	0.985	0.974–0.997
Perifissural nodule			
No	Reference		
Yes	**< 0.001**	22.402	5.061–99.150
Pleural tags			
No	Reference		
Yes	0.080	1.667	0.940–2.958
Paraseptal emphysema			
No	Reference		
Mild	**< 0.001**	0.210	0.096–0.460
Substantial	**0.014**	0.235	0.074–0.742
Perilesional emphysema			
No	Reference		
Yes	**< 0.001**	6.720	3.265–13.831
Distance	**0.016**	1.017	1.003–1.030
Number of passages			
1	Reference		
≥ 2	**0.002**	2.173	1.316–3.587

Bold values indicate statistically significant

[a]Confidence interval

[b]Odds ratio

Table 3 Multivariate logistic regression analysis of risk factors for pneumothorax requiring chest tube insertion

Variable	*p* value	OR[a]	95% CI[b]
Perifissural nodule			
No	Reference		
Yes	**0.001**	8.360	2.479–28.198
Centrilobular emphysema			
No	Reference		
Trace and mild	0.607	0.669	0.145–3.090
Moderate, confluent, advanced	0.396	2.001	0.403–9.926
Paraseptal emphysema			
No	Reference		
Mild	0.089	0.319	0.086–1.190
Substantial	0.730	1.301	0.292–5.808
Perilesional emphysema			
No	Reference		
Yes	**0.006**	9.421	1.919–46.253
Distance	**0.026**	1.017	1.003–1.051

Bold values indicate statistically significant

[a]Confidence interval

[b]Odds ratio

resectable lesion [4], and the present study included numerous biopsy cases for resectable lesions. The majority of our patients are elderly and smokers and, thus, have COPD as an underlying disease. However, since video-assisted thoracoscopic surgery could not be performed in our hospital for a while, TTLB had to be performed on patients with a high risk for diagnosis [21]. In addition, the incidence of complications may vary depending on the detection method used, i.e., chest radiograph or CT [6]. We confirmed complications by post-procedural CT with chest radiography in all patients and by positron emission tomography-CT images taken for staging within a few days of TTLB in patients with lung cancer. Therefore, we included very minor pneumothorax and hemorrhage along the needle tract on post-procedural CT as a complication (Online Resource 4a). Therefore, for various reasons, the complication rate in this study is higher than that in other studies.

Emphysema is a well-known risk factor for pneumothorax [23]. Studies have shown that the presence of emphysema along the needle pathway is associated with post-procedural pneumothorax and chest tube placement for symptomatic

Table 4 Multivariate logistic regression analysis of risk factors for hemorrhage

Variable	*p* value	OR[a]	95% CI[b]
Age	0.345	0.967	0.960–1.014
INR[c]	0.304	0.266	0.021–3.331
aPTT[d]	**0.010**	0.941	0.898–0.986
PLT[e]	0.054	0.997	0.995–1.000
Location			
RUL[f]	Reference		
RML[g]	0.735	1.244	0.350–4.426
RLL[h]	0.647	0.830	0.374–1.841
LUL[i]	0.537	1.318	0.548–3.170
LLL[j]	0.537	1.318	0.548–3.170
Lesion size	**0.007**	0.982	0.970–0.995
Pleural tags			
No	Reference		
Yes	0.157	0.583	0.277–1.231
Perilesional emphysema			
No	Reference		
Yes	**0.001**	3.877	1.796–8.367
Distance from the pleura	**< 0.001**	1.083	1.058–1.109
Passages			
1	Reference		
≥ 2	0.129	1.603	1.603–2.947

Bold values indicate statistically significant

[a]Confidence interval

[b]Odds ratio

[c]International normalized ratio

[d]Activated partial thromboplastin time

[e]Platelet

[f]Right upper lobe

[g]Right middle lobe

[h]Right lower lobe

[i]Left upper lobe

[j]Left lower lobe

pneumothorax [19, 24]. In our study, perilesional emphysema was a significant predictor of pneumothorax as in previous reports. The effect of perilesional emphysema on the occurrence of pneumothorax can be explained by the fact that disruption of dilated air spaces may result in increased airway pressure that prevents the rapid sealing of the air leak [19, 25]. In addition, emphysema may decrease the pulmonary reserve and increase the need for chest tube insertion by increasing the likelihood of symptomatic pneumothorax [23, 25]. The present study also demonstrated that perilesional emphysema is an important risk factor for chest tube placement. Emphysema can be measured by quantifying the area of low attenuation using a selected HU density threshold [20]. Zang et al. [21] showed that a lung radiodensity along the needle passage of − 850 HU or less was an independent risk factor for pneumothorax. Furthermore, several studies in whole lungs found that quantitative emphysema was a significant predictor of pneumothorax post-procedure and that the risk of pneumothorax increased by 7.4% per unit increase in quantitative emphysema [26, 27]. In contrast, the present study showed that quantitative emphysema was not associated with post-procedural pneumothorax. Moreover, the visual grade of emphysema was not associated with pneumothorax. Some studies, like ours, found no correlation between emphysema and pneumothorax [28–30]. Many studies have shown that emphysema is a significant risk factor for pneumothorax, but our results are inversely related. The variability in patients, populations, lesion sizes, and radiologist's assessments could explain the different results obtained in our study compared to other studies. Patients without emphysema could have had an impact on the incidence of pneumothorax, because the nodule size was smaller (without emphysema: 3.9 cm) than that in patients with emphysema (trace and mid emphysema: 4.8 cm, and moderate/confluent/advanced destructive emphysema: 5.0 cm). Patients with confluent and advanced destructive emphysema exhibited a very low rate of 4.3%, indicating that some of the patients with emphysema had no emphysema along the needle pathway, which may have affected this result. In addition, radiologists performed procedures more carefully in patients with severe emphysema.

There have been fewer studies on the effect of emphysema on hemorrhage than on pneumothorax after TTLB. Yeow et al. [30] demonstrated that emphysema seen on CT were not associated with post-procedural hemorrhage. However, another study reported that emphysema was associated with a higher grade of hemorrhage [5]. As with pneumothorax, the evidence for an effect of emphysema on post-procedural hemorrhage is mixed. We classified our patients by subtype of emphysema according to the Fleischner Society statement and performed quantitative analyses in some patients to investigate the effect of emphysema on hemorrhage. There appear to be few such studies in the literature. According to our findings, neither the quantitative nor quantitative degree of emphysema was associated with hemorrhage. In contrast with the grade of emphysema in the whole lung, emphysema around the target lesion was significantly associated with pulmonary hemorrhage, including higher grade hemorrhage. Perilesional emphysema has been considered to increase the risk of hemorrhage because of the lack of effective tamponade by adjacent tissue and pulmonary hypertension [31, 32].

The results of our study show an increasing rate of pneumothorax and hemorrhage with greater lesion depth and smaller lesion size. The increased complication rate in patients with small nodules reflects the increased technical difficulties, i.e., more need for needle correction and sampling of tissue from adjacent aerated lung that cannot provide

Table 5 Distribution of variables according to grade of hemorrhage

Grade of hemorrhage ($n = 397$)				
Characteristic	None ($n = 117$)	Mild ($n = 197$)	Severe ($n = 83$)	p value
Sex				0.083
Male	83 (70.9)	136 (69.0)	68 (81.9)	
Female	34 (29.1)	61 (31.0)	15 (18.1)	
Age, years	71.8 ± 10.6	69.7 ± 11.0	68.5 ± 11.5	**0.046**
Smoking status				**0.016**
Non-smoker	37 (31.6)	78 (39.6)	21 (25.3)	
Ex-smoker	50 (42.7)	67 (34.0)	27 (32.5)	
Current smoker	30 (25.7)	52 (26.4)	35 (42.2)	
INR[a]	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	**0.018**
aPTT (sec)[b]	36.0 ± 5.6	34.2 ± 6.0	35.2 ± 5.1	**0.008**
PLT ($\times 10^3$/μL)[c]	290.3 ± 105.3	248.3 ± 80.5	258.8 ± 147.9	**0.001**
Pathology				0.511
Malignant	89 (76.1)	144 (73.1)	66 (79.5)	
Benign	28 (23.9)	53 (26.9)	17 (20.5)	
Location				0.087
RUL[d]	22 (18.8)	51 (25.9)	26 (31.3)	
RML[e]	6 (5.1)	16 (8.1)	6 (7.2)	
RLL[f]	35 (29.9)	43 (21.8)	21 (25.3)	
LUL[g]	25 (21.4)	45 (22.9)	18 (21.7)	
LLL[h]	29 (24.8)	42 (21.3)	12 (14.5)	
Lesion				**0.041**
Solid	117 (100)	188 (95.4)	78 (94.0)	
Part-solid	0 (0)	7 (3.6)	4 (4.8)	
Nodule with ground-glass opacity	0 (0)	2 (1.0)	1 (1.2)	
Lesion size (mm)	58.8 ± 30.4	39.6 ± 20.9	32.8 ± 18.1	**< 0.001**
Perifissural nodule				0.581
No	108 (92.3)	177 (89.8)	73 (88.0)	
Yes	9 (7.7)	20 (10.2)	10 (12.0)	
Pleural tag				**0.029**
No	99 (84.6)	144 (73.1)	69 (83.1)	
Yes	18 (15.4)	53 (26.9)	14 (16.9)	
Centrilobular emphysema				0.357
None	66 (56.4)	109 (55.3)	39 (47.0)	
Trace and mild	31 (26.5)	63 (32.0)	29 (34.9)	
Moderate, confluent, advanced	20 (17.1)	25 (12.7)	15 (18.1)	
Paraseptal emphysema				0.068
No	82 (70.1)	152 (77.1)	54 (65.1)	
Mild	25 (21.4)	37 (18.8)	21 (25.3)	
Substantial	10 (8.5)	8 (4.1)	8 (9.6)	
Perilesional emphysema				**< 0.001**
No	105 (89.7)	142 (72.1)	43 (51.8)	
Yes	12 (10.3)	55 (27.9)	40 (48.2)	
Position				0.163
Supine	39 (33.3)	82 (41.6)	36 (43.4)	
Prone	73 (62.4)	110 (55.8)	47 (56.6)	
Lateral	5 (4.3)	5 (2.6)	0 (0.0)	
Distance from the pleura (mm)	6.4 ± 12.0	21.6 ± 16.3	35.6 ± 20.1	**< 0.001**
Passages				**< 0.001**
1	88 (75.2)	103 (52.3)	36 (43.4)	

Table 5 (continued)

Grade of hemorrhage ($n=397$)				
Characteristic	None ($n=117$)	Mild ($n=197$)	Severe ($n=83$)	p value
≥ 2	29 (24.8)	94 (47.7)	47 (56.6)	

The data are shown as the mean ± standard deviation or as the number (percentage)

Bold values indicate statistically significant

[a]International normalized ratio

[b]Activated partial thromboplastin time

[c]Platelet

[d]Right upper lobe

[e]Right middle lobe

[f]Right lower lobe

[g]Left upper lobe

[h]Left lower lobe

adequate tamponade [10, 33]. This finding is consistent with the previous reports of increased rates of pneumothorax and hemorrhage in patients with deeper and smaller lesions [23, 25, 30, 34]. Furthermore, our study showed that perifissural nodules can increase the risk of pneumothorax. Ko et al. [35] found that lesions along the fissure were associated with a higher rate of pneumothorax and need for placement of a chest tube. In the case of perifissural nodules, although the introducer needle does not pass through the fissure, the cutting needle is likely to pass through the fissure and cause injury [35].

Our study has some limitations. The first is its retrospective design, which may have introduced a degree of bias. Between February 2010 and March 2018, TTLBs were performed by any one of three radiologists, whose may have differed in their selection of target lesions and needle paths. Second, we performed quantitative analysis of emphysema in 97 of 397 cases. Quantitative analysis could not be performed for TTLBs performed before 2015, because a precontrast image with thin section was not obtained before the procedure. Therefore, given that quantitative analysis of emphysema was performed in only a small number of patients, it seems inappropriate to generalize our findings to all patients. However, the results of the quantitative analysis can be considered representative because of their similarity to those quoted for visual assessment in the Fleischner Society statement. Third, we did not perform an external validation of our results. Therefore, a larger prospective study is now needed to validate our findings.

In conclusion, perilesional emphysema, but not the severity of emphysema, may be used to estimate the risk of iatrogenic complications before CT-guided TTLB. Preprocedural patient selection and planning of TTLB are very important to minimize complications post-procedure. The results of this study could be important in establishing risk stratification and pre-interventional planning in patients with COPD.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics statement This article does not contain any studies with human participants or animals performed by any of the authors.

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