Original Article

Diagnostic value and safety of endobronchial ultrasonography with a guide sheath transbronchial biopsy for diagnosing peripheral pulmonary lesions in patients with interstitial lung disease

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Background: Radial endobronchial ultrasonography transbronchial biopsy with and without a guide sheath is a useful method for diagnosing peripheral pulmonary lesions (PPLs). However, the diagnostic yield and complications of radial endobronchial ultrasonography transbronchial biopsy for PPLs remains elusive in patients with interstitial lung disease (ILD).

Methods: We retrospectively analysed 431 patients (69 with and 362 without ILD) who underwent radial endobronchial ultrasonography with a guide sheath transbronchial biopsy (EBUS-GS TBB) for PPLs from April 1, 2011, to March 31, 2020. We investigated the diagnostic yield and complications of the procedure for PPLs and compared them between patients with and without ILD. We also evaluated the factors contributing to successful diagnosis.

Results: The diagnostic yield of radial endobronchial ultrasonography in patients with ILD was significantly lower than in those without ILD (62.3% *vs.* 75.4%, P=0.024). Multivariate analysis showed that the presence of ILD as background lung [odds ratio (OR) =0.517], probe position within the lesion (OR =4.654), and the presence of solid lesion (OR =1.946) significantly affected the diagnostic yield of PPLs. There was a significant difference in the rate of pneumothorax between the patients with ILD and those without ILD (4.3% *vs.* 0.6%, P=0.031).

Conclusions: The presence of ILD as the background lung significantly affected the diagnostic yield of PPLs with radial EBUS-GS TBB. Regarding the complications, pneumothorax occurred more frequently in patients with ILD than in those without ILD.

Keywords: Bronchoscopy; endobronchial ultrasound (EBUS); interstitial lung disease (ILD); lung cancer; transbronchial lung biopsy

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Introduction

Low-dose computed tomography (LDCT) has been reported to facilitate the early detection of lung cancer and contribute to a reduction in the mortality rate (1). Therefore, it is gradually being adopted in clinical practice. Preclinical or asymptomatic interstitial lung disease (ILD) is sometimes detected by LDCT. ILD was reported to be highly associated with lung cancer (2-4).

All peripheral pulmonary lesions (PPLs) encountered in patients with ILD were not always malignant lesions (5). Therefore, these lesions were required for pathological diagnosis of whether the lesions were malignant or not. Furthermore, in determining the treatment policy in patients with lung cancer co-existing with idiopathic pulmonary fibrosis (IPF), anti-cancer therapies including radiotherapy, chemotherapy and surgical therapy have the possibility of causing acute exacerbation of ILD and/or fatal complications (6,7). Therefore, accurate diagnosis is more important to present treatment plan to patients with ILD. PPLs, including peripheral lung cancer, can be diagnosed based on bronchoscopy, transthoracic needle biopsy (TTNB) and surgical lung biopsy (SLB). According to previous reports on the diagnostic yield and complications, bronchoscopy can be an initial option for diagnosing PPLs (7,8). For the diagnosis of PPLs via bronchoscopy, radial endobronchial ultrasonography with a guide sheath transbronchial biopsy (EBUS-GS TBB) has improved the diagnostic yield of PPLs, including small PPLs (8-13).

Several studies have reported that the factors affecting the diagnostic yield based on EBUS-GS TBB were the probe position relative to the lesion, the bronchus sign, (represents a bronchus directly leading to the lesion) on computed tomography (CT), the lesion size, and its segment (14,15). Few reports have assessed the diagnostic yield of EBUS-GS TBB in lungs with a background pathology. In particular, regarding the presence of pulmonary emphysema influencing the diagnostic yield of EBUS-GS TBB, although the diagnostic yield varied depending on the severity of emphysema, the presence of emphysema itself has not been reported to reduce the yield. Furthermore, the presence of usual interstitial pneumonia (UIP) pattern on CT in patients with IPF considerably affected the EBUS-GS TBB results (16,17). Additionally, a previous study reported that the diagnostic yield of EBUS-GS TBB for PPLs in patients with ILD was reported to be lower, about 60%, as compared with the diagnostic yield of about 70% as described on the previous meta-analysis report, which might be related to the small sample size (15,18). Thus, there has been limited data assessing the association of patients with ILD regarding the diagnostic yield and complications of EBUS-GS TBB. In patients with IPF, honeycomb structures have been reported to show a patchy combination of hyper- and hypoechoic patterns on radial endobronchial ultrasonography in autopsied lungs. Therefore, these changes might prevent the recognition of lesions by radial endobronchial ultrasonography (19).

We hypothesised that the diagnostic yield of EBUS-GS TBB for PPLs in patients with ILD might be lower than that in patients without ILD. Hence, we evaluated the utility and safety of EBUS-GS TBB for PPLs in patients with ILD in the background lung, along with the factors affecting the diagnostic yield of EBUS-GS TBB. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-809/rc).

Methods

Patient enrolment

We performed a retrospective analysis of consecutive patients who underwent EBUS-GS TBB for PPLs at Nagoya University Hospital from April 1, 2011, to March 31, 2020. The PPLs were defined as lesions surrounded by normal lung parenchyma or interstitial lung area and were not visible on bronchoscopy (20). We excluded patients with endobronchial lesions and only pulmonary emphysema without ILD. A pneumonologist (T.I.) and an experienced radiologist (S.I.) identified ILD based on high-resolution CT (HRCT) images before performing bronchoscopy, as described below. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Nagoya University Hospital Institutional Review Board (No. 2021-0272). The requirement for patient consent was waived because of the retrospective nature of the study.

Bronchoscopy procedure

Spirometry was performed a day prior to the bronchoscopy in 64.0% cases. Before the procedure, all patients were locally anaesthetised with a 1% lidocaine spray, and an intravenous bolus of midazolam was administered. A thin bronchoscope (BF-P260F; Olympus, Tokyo, Japan) with a guide sheath (K-201; Olympus; external diameter,

1.95 mm) was used for the 1.4-mm probe. After the probe was inserted and the radial endobronchial ultrasound (R-EBUS) image was confirmed, it was withdrawn and transbronchial forceps biopsy (FB-233D; Olympus) was performed at least nine times under fluoroscopic guidance, according to the Kurimoto method (10). Samples for pathological evaluation were only collected by the guide sheath using forceps. We classified the EBUS probe positions into three as follows: (I) within, when the probe was located inside the PPL; (II) adjacent to, when the probe was located at the periphery of the PPL; and (III) outside, when the probe was located away from the PPL. Furthermore, if an EBUS image could not be visualized, as in the case of a solid lesion, the probe was manipulated under X-ray fluoroscopic guidance until a whitish acoustic shadow (e.g., a blizzard sign or mixed blizzard sign) could be visualized (21-23). The virtual bronchoscopic navigation (VBN) was created on the workstation (Ziostation2, Ziosoft Ltd., Tokyo, Japan, or SYNAPSE VINCENT version 4.0, Fuji Medical Systems, Tokyo, Japan) by an experienced chest radiologist (S.I.) in 81.3% of the total cases.

Variables

The following clinical information were collected from all patients who underwent the procedure: age, sex, pulmonary function test results, lesion size, lesion lobe, lesion location from the hilum, lesion structure, bronchus sign, visibility on chest X-ray, background lung, EBUS image, bronchoscopic diagnosis, and final diagnosis. The lesion location from the hilum was classified into two: "inner" for lesions within the inner and middle third ellipses and "outer" for lesions within the outer third ellipse (24). The lesion structure was classified into two groups as follows: solid and others (25). Based on the background lung, patients were classified into having ILD (ILD group) and not having ILD (without ILD). ILD was identified based on radiological findings according to the official ATS/ERS/JRS/ALAT Clinical Practice Guidelines for diagnosis of IPF and classified into the two groups of UIP and non-UIP patterns (probable UIP, indeterminate for UIP, and alternative diagnosis) (26). The final diagnosis was confirmed based on the pathological findings of biopsy specimens from bronchoscopy, TTNB, and SLB. When the collected specimens showed malignancy (i.e., specific findings on histology or cytology positive) and this was consistent with the final diagnosis, bronchoscopy was considered diagnostic. When the collected specimens showed specific benign findings (e.g., granuloma and organizing pneumonia) and the subsequent clinical course was assessed to have decreased radiologically and stabilised in size during follow-up of more than 2 years after the procedure, bronchoscopy was considered diagnostic. Moreover, when the samples were not adequate (e.g., peripheral lung tissue and peribronchial tissue), bronchoscopy was regarded as non-diagnostic. If the lesions of part-solid or pure ground-glass structures were undiagnosed by bronchoscopy, follow-up was performed using CT at the physician's discretion, and a definite diagnosis and appropriate therapy were obtained by surgery.

Statistical analysis

The data are presented as median and range. Mann-Whitney U and Pearson chi-square tests were used in analysing continuous and categorical variables, respectively. Multivariable logistic regression analyses were performed to investigate the significant predictors of the positive results of EBUS-GS TBB for all patients and those with ILD. Statistical significance was set at $P<0.05$, and all reported P values were two-sided. All analyses were performed using SPSS Statistics version 28 (IBM, Armonk, NY, USA).

Results

Patient characteristics

During the study, 691 patients underwent diagnostic bronchoscopy with R-EBUS for one PPL. A total of 431 lesions in 431 patients were included in the analyses after excluding 87 endobronchial lesions, 27 lesions that had an uncertain final diagnosis, and 146 lesions presenting solely with pulmonary emphysema without ILD. Finally, we identified 69 lesions associated with ILD and 362 lesions without ILD (*Figure 1*). The characteristics of the patients in the two groups are shown in *Table 1*. In addition to lesion lobe, there were significant differences in proportion of males, outer lesions, and solid nodules between patients with ILD and those without ILD. Furthermore, the histological findings between the two groups are shown in *Table 2*. The most frequent histological finding was adenocarcinoma in both groups.

The diagnostic yield according to lesion characteristics and EBUS images

The EBUS-GS TBB in patients with ILD had a

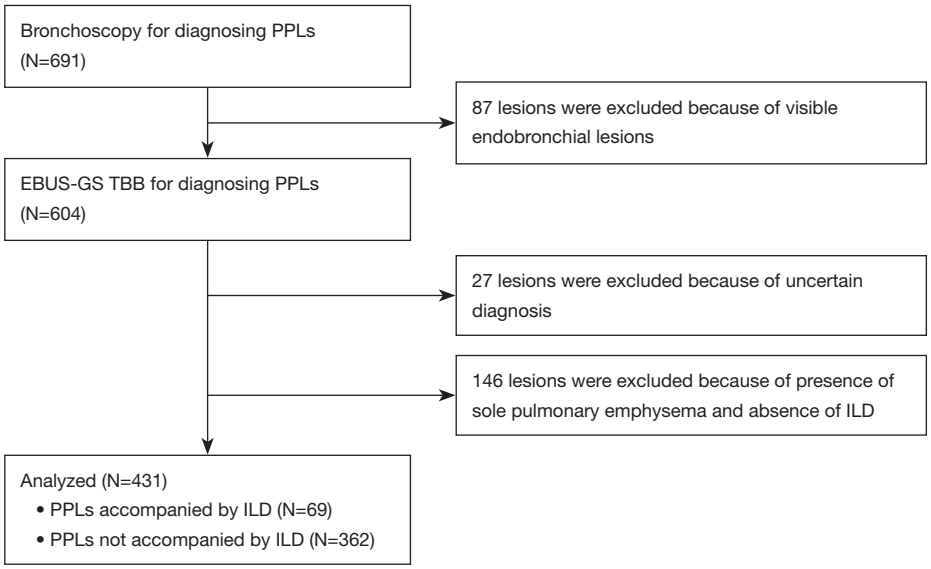

Figure 1 Flow diagram of 431 lesions diagnosed based on bronchoscopy with radial endobronchial ultrasound. PPLs, peripheral pulmonary lesions; EBUS-GS TBB, radial endobronchial ultrasonography with a guide sheath transbronchial biopsy; ILD, interstitial lung disease.

Table 1 Clinical and demographic characteristics of patients

Variables	ILD (n=69)	Without ILD (n=362)	P value
Age, median [range], years	73 [53–86]	71 [43–88]	0.097
Sex, male, n (%)	60 (87.0)	178 (49.2)	<0.001
FEV_1/FVC, %, median [range]	78 [42–131]	76 [43–164]	0.654
FEV_1, percent predicted, %, median [range]	90 [57–117]	92 [48–152]	0.688
FVC, percent predicted, %, median [range]	99 [40–131]	104 [58–157]	0.069
Size, median [range], mm	26.5 [11–120]	27 [10.8–150]	0.983
Lobe, n (%)			0.036
Right upper/left upper	22 (31.9)	171 (47.2)	
Right middle/lingula	8 (11.6)	45 (12.4)	
Right lower/left lower	39 (56.5)	146 (40.3)	
Location: outer, n (%)	40 (58.0)	161 (44.5)	0.039
Structure: solid nodule, n (%)	62 (89.9)	276 (76.2)	0.012
Bronchus sign: positive, n (%)	66 (95.7)	344 (95.0)	0.559
Chest X-ray: visible, n (%)	61 (88.4)	340 (93.9)	0.087

ILD, interstitial lung disease; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity.

significantly lower diagnostic yield than in patients without ILD (62.3% *vs.* 75.4%, P=0.024). The diagnostic yields of PPLs with larger lesions (>20 mm), upper lesions, solid lesions, positive bronchus sign, and malignant lesions were significantly lower in patients with ILD than in those without ILD. When the probe was located within, adjacent to, or outside the lesion, the diagnostic yields for the patients with ILD were 80%, 53.8%, and 0%, respectively,

Table 2 Case diagnoses

Diagnosis	ILD (n=69)	Without ILD (n=362)	P value
Malignant lesions	66	339	0.042
Diagnostic case	41	252	
Adenocarcinoma	19	184	
Squamous cell carcinoma	11	32	
Small cell carcinoma	4	4	
Non-small cell carcinoma	6	19	
Malignant lymphoma	1	2	
Metastatic lung cancer	0	10	
Spindle cell carcinoma	0	1	
Non-diagnostic case	25	87	
Benign lesions	3	23	0.319
Diagnostic case	2	21	
Inflammatory lesions	2	9	
Aspergillosis	0	2	
Cryptococcus	0	1	
NTM	0	4	
Organizing pneumonitis	0	1	
Sarcoidosis	0	1	
Actinomycosis	0	1	
Tuberculosis	0	1	
Abscess	0	1	
Non-diagnostic case	1	2	

ILD, interstitial lung disease; NTM, non-tuberculous mycobacteria.

while the yields for the patients without ILD were 85.2%, 66.7%, and 10.7%, respectively. There was no significant difference in the diagnostic yields of the two groups based on the EBUS images (*Table 3*).

Factors possibly affecting the successful diagnosis based on EBUS-GS TBB

Multivariate analysis showed that the presence of ILD as the background lung [odds ratio (OR) =0.517, 95% confidence interval (CI): 0.270–0.988, P=0.046], solid lesion (OR =1.946, 95% CI: 1.116–3.393, P=0.019), and probe position within the lesion (OR =4.654, 95% CI: 2.771–7.816, P<0.001) were significant factors that affected the diagnostic yield of EBUS-GS TBB (*Table 4*).

Table 3 The diagnostic yield according to lesion characteristics and EBUS images

Variables	ILD (n=69)	Without ILD (n=362)	P value
Size			
≤20 mm	7/14 (50.0)	52/89 (58.4)	0.554
>20 mm	36/55 (65.5)	221/273 (81.0)	0.011
Location			
Upper	11/22 (50.0)	126/171 (73.7)	0.021
Others	32/47 (68.1)	147/191 (77.0)	0.207
Location			
Inner	17/29 (58.6)	152/201 (75.6)	0.053
Outer	26/40 (65.0)	121/161 (75.2)	0.195
Structure			
Solid	40/62 (64.5)	221/276 (80.1)	0.008
Others	3/7 (42.9)	52/86 (60.5)	0.300
Bronchus sign			
Positive	42/66 (63.6)	262/344 (76.2)	0.033
Negative	1/3 (33.3)	11/18 (61.1)	0.388
Visibility on chest X-ray			
Visible	40/61 (65.6)	262/340 (77.1)	0.055
Invisible	3/8 (37.5)	11/22 (50.0)	0.426
EBUS image			
Within	36/45 (80.0)	218/256 (85.2)	0.380
Adjacent to	7/13 (53.8)	52/78 (66.7)	0.531
Outside	0/11 (0)	3/28 (10.7)	0.545
Final diagnosis			
Malignant	41/66 (62.1)	252/339 (74.3)	0.042
Benign	2/3 (66.7)	21/23 (91.3)	0.319
Total	43/69 (62.3)	273/362 (75.4)	0.024

Data are shown as numbers of lesions/total lesions (%). EBUS, endobronchial ultrasound; ILD, interstitial lung disease.

The diagnostic yield according to the pattern of ILD and factors associated with the diagnostic yield of EBUS-GS TBB in patients with ILD

The diagnostic yield of EBUS-GS TBB was not

Table 4 Multivariate logistic regression analysis of factors affecting diagnostic yield

Variables	Reference	Multivariate	
		OR (95% CI)	P value
Age ≥70 (n=262)	<70 (n=169)	1.139 (0.700–1.854)	0.599
Sex, male (n=238)	Female (n=193)	0.769 (0.461–1.283)	0.315
ILD (n=69)	Without ILD (n=362)	0.517 (0.270–0.988)	0.046
Size >20 mm (n=328)	≤20 mm (n=103)	1.413 (0.798–2.503)	0.235
Lobe upper lobe (n=193)	Others (n=238)	0.815 (0.502–1.324)	0.410
Location, outer (n=201)	Inner (n=230)	0.928 (0.572–1.507)	0.763
Structure, solid nodule (n=338)	Others (n=93)	1.946 (1.116–3.393)	0.019
Bronchus sign positive (n=410)	Negative (n=21)	0.959 (0.318–2.897)	0.941
Chest X-ray visible (n=401)	Invisible (n=30)	1.995 (0.827–4.812)	0.124
EBUS image within (n=301)	Others (n=130)	4.654 (2.771–7.816)	<0.001

OR, odds ratio; CI, confidence interval; ILD, interstitial lung disease; EBUS, endobronchial ultrasound.

Table 5 The diagnostic yield of EBUS-GS TBB according to the pattern of ILD

	UIP pattern (n=25)	Probable UIP pattern (n=21)	Indeterminate for UIP (n=15)	Alternative Diagnosis (n=8)	P value
Diagnostic yield	14/25 (56.0)	12/21 (57.1)	12/15 (80.0)	5/8 (62.5)	0.447

Data are shown as numbers of lesions/total lesions (%). EBUS-GS TBB, radial endobronchial ultrasonography with a guide sheath transbronchial biopsy; ILD, interstitial lung disease; UIP, usual interstitial pneumonia.

Table 6 Multivariate logistic regression analysis of factors affecting diagnostic yield in patients with ILD

Variables	Reference	Multivariate	
		OR (95% CI)	P value
Size, >20 mm (n=55)	≤20 mm (n=14)	1.348 (0.289–6.298)	0.704
UIP pattern (n=25)	Non-UIP pattern (n=44)	0.453 (0.131–1.564)	0.210
Structure, solid nodule (n=62)	Others (n=7)	3.359 (0.537–21.025)	0.195
The lesion location from the hilum, inner (n=29)	Outer (n=40)	1.697 (0.499–5.775)	0.397
EBUS image, within (n=61)	Others (n=8)	12.074 (3.304–44.128)	<0.001

ILD, interstitial lung disease; OR, odds ratio; CI, confidence interval; UIP, usual interstitial pneumonia; EBUS, endobronchial ultrasound.

significantly different according to the pattern of ILD (P=0.447) (*Table 5*). In patients with ILD, the positional relationship of PPLs on EBUS images was the only significant predictor of the successful diagnosis based on EBUS-GS TBB (OR =12.074, 95% CI: 3.304–44.128, P<0.001) (*Table 6*).

Complications

The complications rate in patients with ILD were significantly higher than in those without ILD (8.7% *vs.* 1.1%, P=0.002). There was a significant difference in the prevalence of pneumothorax among the patients with ILD

Table 7 Complications of the two groups

Variables	ILD (n=69)	Without ILD (n=362)	P value
Complications, n (%)	6 (8.7)	4 (1.1)	0.002
Pneumothorax	3 (4.3)	2 (0.6)	0.031
Pneumonia	2 (2.9)	2 (0.6)	0.122
Mediastinal emphysema	1 (1.4)	0 (0)	0.160

ILD, interstitial lung disease.

and those without ILD (4.3% *vs.* 0.6%, P=0.031) (*Table* 7). Pneumothorax occurred in three patients with ILD (4.3%). Of these, two required thoracic drainage. Conversely, two patients without ILD did not require thoracic drainage (0.6%).

Discussion

Our results revealed that the diagnostic yield of EBUS-GS TBB in patients with ILD was significantly lower than that in those without ILD. Multivariate logistic analysis revealed that the presence of ILD as the background lung, lesion structure, and EBUS image significantly affected the diagnostic yield of EBUS-GS TBB. Furthermore, the probe position was considerably associated with the diagnostic yield of EBUS-GS TBB in patients with ILD. As for the complications, pneumothorax occurred more frequently in patients with ILD than in those without ILD.

Previous studies have reported that intra-procedural imaging facilitated accurate diagnoses based on EBUS-GS TBB (14,15). Similarly, the probe position relative to the lesion significantly affected the diagnostic yield. Furthermore, Yoshikawa *et al.* reported that solid lesions had a significantly higher diagnostic yield than ground-glass lesions (27). The reasons for the lower yields for ground-glass lesions include the difficulties in obtaining EBUS images for ground-glass lesions and ensuring an accurate position for ground-glass lesion fluoroscopy. Consistent with a previous report, lesion structure significantly affected the diagnostic yield of EBUS-GS TBB. Regarding the background lung in patients who underwent EBUS-GS TBB, the diagnostic yield and safety profile of EBUS-GS TBB in patients with IPF were reported. Lee *et al.* revealed that in patients with IPF, the presence of UIP pattern significantly influenced the lower diagnostic yield of PPLs with R-EBUS compared to the probable UIP/non ILD group (17). Our study indicated that the presence of ILD not limited to UIP pattern in patients with IPF had a significant influence on the lower diagnostic yield based on EBUS-GS TBB.

According to the lesion size (size ≤20 or >20 mm), lesion lobe (upper or others), lesion texture (solid or others), bronchus sign (positive or negative), underlying disease (malignant or benign), the diagnostic yield of EBUS-GS TBB with larger lesions (>20 mm), upper lesions, solid lesions, positive bronchus sign, and malignant lesions were significantly lower in patients with ILD than in those without ILD. In patients with ILD, there might be technical problems related to the difficulty of detecting the lesions because reticular shadows around PPLs preclude their detection and make it difficult to perform biopsies from the lesions appropriately during EBUS-GS TBB.

Moreover, in patients with ILD, the insertion of the device to target bronchus was reported to be difficult because of bronchial narrowing and torsion associated with traction bronchiectasis as anatomical changes (17). Conversely, Herth *et al.* reported that the diagnostic yield for lesions located within the right upper lobe was lower than that for other lesions because the right upper lesions were particularly difficult to reach due to affected manoeuvrability in the tortuous airways and sharp bends, resulting in a lower diagnostic yield (28). Furthermore, Kurimoto *et al.* reported that the lower diagnostic yield of PPLs located in the left upper lobe apical posterior segment is thought to be due to the difficulty in inserting the probe into B1+2 (10). In addition to anatomical changes associated with ILD, the difficulty of inserting the device into upper lesions might be linked to lower diagnostic yield in patients with ILD compared to those without ILD.

A previous report demonstrated that in patients with ILD, inflammatory cell infiltration and fibrotic changes increased in the PPL lung compared to the other one (29). Furthermore, in patients with ILD, the diagnostic yield of EBUS-GS TBB within or near fibrotic lesions was reported to be lower than that of PPLs distant from fibrotic lesions because small biopsy forceps may be associated with

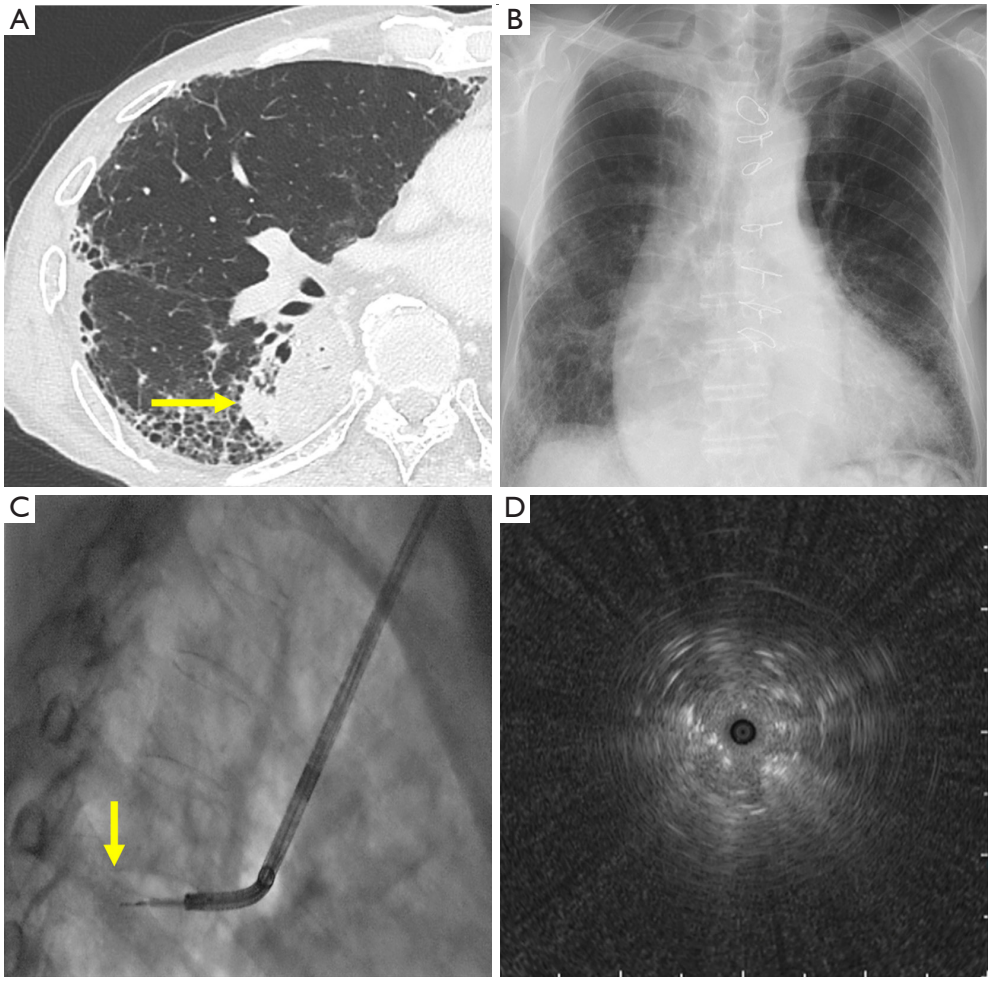

Figure 2 A representative case of a 73-year-old male with interstitial lung disease who was diagnosed based on endobronchial ultrasonography with a guide sheath. (A) High-resolution computed tomography showed a 15-mm solid nodule (arrow) with positive bronchus sign in his right lower lobe. Interstitial lung disease was present as the background lung. (B) The nodule was invisible on the posterior-anterior position of his chest X-ray. (C) The nodule (arrow) was visible at a 45° angle on the right side. Additionally, on fluoroscopy, the probe position was consistent with the lesion. (D) The radial endobronchial ultrasound probe was located within the lesion, and he was diagnosed with squamous cell carcinoma.

sampling only inflammatory cells or fibrotic changes around lung cancer co-existing with ILD (30).

In patients with ILD, EBUS image rather than the presence of UIP pattern was significantly associated with a successful bronchoscopic diagnosis with EBUS-GS TBB. We considered that the diagnostic yield of EBUS-GS TBB in patients with ILD was lower than in those without ILD, because of the difficulty in correctly reaching the lesions around reticular shadows and distinguishing lesions as background lung on EBUS image. However, when the probe was located within the lesions, the diagnostic yield of EBUS-GS TBB was not significantly different between the two groups. In patients with ILD, the detection of subsolid lesions on EBUS images might be difficult. However, when physicians performed EBUS-GS TBB for diagnosing solid lesions in these patients, they should perform biopsies in the position in which the probe was located within the lesion as much as possible (*Figure 2*). This result was similar to most previous studies which reported that the probe position relative to the lesion was a predictor of successful bronchoscopic diagnosis using R-EBUS (14,15,31).

Previous reports showed that the rate of pneumothorax

with EBUS-GS TBB was approximately 3% (32,33). In our patients with ILD, the rate of pneumothorax was 4.3%, which was significantly higher than that in patients without ILD. In our study, outer lesions were more prevalent in patients with ILD than in those without ILD. We considered that the damage to alveolar tissue accompanied by biopsy and the location of the lesion near the visceral pleura might be related to pneumothorax.

Our study has some limitations. First, it used a small cohort and was a retrospective study in a single centre. Second, the severity of ILD has not been fully investigated. Finally, before comparing the diagnostic outcomes and complications between ILD and without ILD patients, there was a bias in baseline characteristics between the two groups. A larger sample and a prospective randomized design will be needed to overcome these limitations.

Conclusions

In conclusion, the presence of ILD significantly affected the diagnostic yield of EBUS-GS TBB for PPLs. Moreover, in patients with ILD, the probe position relative to the lesion was a significant predictor of the diagnostic yield of EBUS-GS TBB. Regarding complications, the rate of pneumothorax during EBUS-GS TBB in patients with ILD was significantly higher than in those without ILD.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-809/coif). TFCY serves as an unpaid editorial board member of *Journal of Thoracic Disease* from April 2022 to March 2024. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was performed in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Nagoya University Hospital Institutional Review Board (No. 2021-0272). The requirement for informed consent was waived due to the retrospective design of the study.

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