



# Efficacy and safety of radial probe endobronchial ultrasound-guided biopsy for peripheral lung lesions in chronic obstructive pulmonary disease patients

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**Background:** Chronic obstructive pulmonary disease (COPD) is associated with frequent complications after transthoracic biopsy. Radial probe endobronchial ultrasound-guided transbronchial lung biopsy (RP-EBUS-TBLB) is widely used to diagnose peripheral pulmonary lesions (PPLs). However, the efficacy and safety of this procedure for the diagnosis of PPLs in patients with COPD remain poorly understood. We investigated the usefulness of RP-EBUS-TBLB for diagnosing PPLs in patients with COPD.

**Methods:** This retrospective observational study aimed to identify clinical outcomes of RP-EBUS-TBLB in patients with COPD. A total of 175 patients with COPD and 439 patients without COPD were included in this study. RP-EBUS-TBLB was performed without fluoroscopy using a guide sheath.

**Results:** The overall diagnostic accuracies in patients with COPD and without COPD were 80.6% (141/175) and 78.8% (346/439), respectively. There was no significant difference in the diagnostic yield based on the severity of airflow limitation (80.0%, 81.4%, and 79.2% for mild, moderate, and severe to very airflow limitations, respectively;  $P=0.97$ ). In patients with COPD, diagnostic yields for malignant and benign lesions were 85.6% (95/111) and 71.9% (46/64). In multivariable analyses, larger lesion size [ $\geq 30$  mm; odds ratio (OR), 2.86; 95% confidence interval (CI): 1.10–7.45;  $P=0.03$ ] and within the lesion on EBUS image (OR 9.29; 95% CI: 3.79–22.79;  $P<0.001$ ) were associated with diagnostic success in patients with COPD, whereas lesion location of upper lobe (OR, 0.36; 95% CI: 0.14–0.92;  $P=0.03$ ) were associated with diagnostic failure. The overall complication rate in our study was 7.4% (13/175) in patients with COPD. Pneumothorax occurred in 4.6% (8/175), and chest tube insertion was needed in 1.7% (3/175) of the patients.

**Conclusions:** RP-EBUS-TBLB can be used as an appropriate method to diagnose PPLs in patients with COPD. The size of the lesion ( $\geq 30$  mm) and having the probe within the lesion were important for successful diagnosis. The location of the lesion in the upper lobe is associated with diagnostic failure. No difference was observed in the diagnostic yield based on the severity of airflow limitation. The complication rates were acceptable.

**Keywords:** Biopsy; bronchoscopy; chronic obstructive pulmonary disease (COPD); lung neoplasms; ultrasonography

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## Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic lung disease characterized by airflow limitation and is the leading cause of mortality worldwide (1,2). Lung cancer, which is a major comorbidity of COPD, is a major cause of death. COPD is associated with an increased risk of lung cancer (3). While airflow obstruction, emphysema, older age, and a lower body mass index are risk factors for lung cancer in patients with COPD (4), smoking history is the strongest risk factor. Therefore, routine chest computed tomography (CT) scans are recommended for lung cancer screening in patients with smoking-related COPD (2), and the need for lung nodule biopsy is increasing as the number of CT cases increases.

In patients with COPD, lung nodule biopsy is challenging. Transthoracic needle biopsy (TTNB) is the most frequently used nonsurgical biopsy technique for

the diagnosis of peripheral pulmonary lesions (PPL) and has high diagnostic accuracy. However, a major problem with TTNB is the high incidence of complications after the procedure, including pneumothorax and pulmonary hemorrhage, which are more common in patients with COPD (5-7). In contrast, radial probe endobronchial ultrasound-guided transbronchial lung biopsy (RP-EBUS-TBLB) has a low risk of pneumothorax development and acceptable diagnostic accuracy for PPL (8). Although some studies have evaluated the safety and diagnostic yield of RP-EBUS-TBLB in patients with COPD (9,10), one study included patients with emphysema rather than all patients with COPD and another study included a small number of patients with COPD. Therefore, the efficacy and safety of RP-EBUS-TBLB in patients with COPD have not been fully established.

This study aimed to investigate the diagnostic accuracy and safety of RP-EBUS-TBLB in patients with COPD. We present this article in accordance with the STROBE reporting checklist (available at <https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-484/rc>).

### Highlight box

#### Key findings

- The diagnostic yield of radial probe endobronchial ultrasound-guided transbronchial lung biopsy (RP-EBUS-TBLB) was not significantly different between patients with and without chronic obstructive pulmonary disease (COPD) (80.6% and 78.8%, respectively).
- The diagnostic yield did not differ according to airflow obstruction in patients with COPD.
- The overall complication rate was 7.4% in patients with COPD. Pneumothorax occurred in 4.6% (8/175) and chest tube insertion was required in 1.7% (3/175) of the patients.
- Larger lesion size, within the lesion on EBUS image, and lesion location were associated with diagnostic yield.

#### What is known and what is new?

- RP-EBUS-TBLB is widely used to diagnose peripheral pulmonary lesions and has a low risk of complications and acceptable diagnostic accuracy.
- The efficacy and safety of RP-EBUS-TBLB in patients with COPD have not been fully established.

#### What is the implication, and what should change now?

- RP-EBUS-TBLB had an acceptable diagnostic yield and complication rate for diagnosing peripheral pulmonary lesions in patients with COPD.

## Methods

### Study design and participants

This was a single-center, retrospective, observational study. We analyzed the RP-RUBS dataset collected at Yeungnam University Hospital (a 930-bed, university-affiliated, tertiary referral hospital in Daegu, South Korea) from January 2019 to July 2020. Inclusion criteria were as follows: (I) patients who underwent RP-EBUS to evaluate PPLs; (II) patients with pulmonary function test results and records confirming the presence of COPD from electronic medical records. COPD was diagnosed by a physician based on respiratory symptoms (cough, sputum, and dyspnea) and a post-bronchodilator ratio of forced expiratory volume in one second to forced vital capacity ( $FEV_1/FVC$ )  $<0.7$ .

This study was conducted in accordance with the tenets of the Declaration of Helsinki (as revised in 2013) and the protocol was reviewed and approved by the Institutional Review Board of Yeungnam University Hospital (YUH IRB 2020-09-025). The requirement for informed consent was

waived because of the retrospective study design.

### **Outcome measures**

Clinical information was collected on demographics (age and sex), pulmonary function test results (FVC, FEV<sub>1</sub>, FEV<sub>1</sub>/FVC), chest CT findings (lesion location, lesion size, distance from pleura, lesion type, and bronchus sign), EBUS procedure findings (EUBS image, number of samples taken per lesion, and procedure time), the final diagnosis of PPLs, and complications. On pulmonary function test, airflow limitation was defined as FEV<sub>1</sub>/FVC <0.7. Severity of airflow limitation was classified on the basis of FEV<sub>1</sub> (mild airflow limitation, >80%; moderate, 50–80%; severe to very severe, <50%). Bronchus sign on CT was defined as the presence of a bronchus leading to the target lesion. The shortest distance from the lesion to the pleura was measured on an axial-plane CT scan. The lesion type was classified as solid, part-solid, ground-glass opacity, cavity, and consolidation. The EBUS image of the target lesion was classified as within the lesion, adjacent to the lesion, and invisible.

The primary outcome was the diagnostic accuracy of RP-EBUS in patients with COPD. The diagnostic accuracy was calculated by dividing the number of diagnostic successes by the total number of cases. Secondary outcomes were the rate of complications after RP-EBUS-TBLB and factors associated with diagnostic success.

### **Chest CT scan and bronchoscopy procedure**

All patients underwent thin-section chest CT (0.75 mm slice thickness at intervals of 0.75 mm; SOMATOM Definition AS 64-slice CT system; Siemens Healthcare, Erlangen, Germany) before performing bronchoscopy. Three expert pulmonologists reviewed the chest CT images before the procedure. Emphysema was assessed visually and was defined as a low-attenuation lung area without a clear wall. The degree of emphysema was categorized into three groups: mild, moderate and severe. Mild emphysema included mild centrilobular emphysema (scattered lucencies affecting an estimated 0.5–5% of a lung zone) and mild paraseptal emphysema (less than 1 cm, well-demarcated rounded juxtaleural lucencies). Moderate emphysema was defined as many centrilobular emphysema occupying more than 5% of any lung zone. Severe emphysema included confluent emphysema, advanced destructive emphysema, panlobular emphysema, and substantial paraseptal

emphysema (11).

All bronchoscopic procedures were performed on by expert pulmonologists using a thin bronchoscope (BF P260F; Olympus, Tokyo, Japan). Briefly, a thin bronchoscope was inserted to reach the bronchus nearest to the target lesion, and RP-EBUS (UM S20-17S; Olympus) inside a guide sheath (GS) was inserted through the bronchoscope working channel. After the target lung lesion was identified, the RP was withdrawn, leaving the GS in place. Subsequently, a bronchial brush and biopsy forceps were introduced through the GS, and brushings and biopsy specimens were obtained. Transbronchial needle aspiration was not performed. If the target lung lesion was not detected, the examination was performed without a bronchial brush or biopsy. No X-ray fluoroscopy and was performed. Chest CT scan and bronchoscopy procedures have been previously described (12,13).

All bronchoscopy procedures were performed on an inpatient basis to monitor for procedure-related complications. Vital signs and the development of any complications were monitored for at least 24 hours after the procedure. Chest radiographs were obtained immediately after the bronchoscopy procedure and on the next day to investigate the development of pneumothorax. Physicians closely monitored patients for signs of hemoptysis immediately after the bronchoscopy procedure and during the 24-hour observation period. Infectious complications were defined as new respiratory symptoms (fever >37.8 °C body temperature, cough, sputum, or chest pain) or new lung infiltrates on chest radiograph after bronchoscopy.

### **Statistical analyses**

Continuous data are expressed as means ± standard deviation and were compared with Student's *t*-test. Categorical variables are described as numbers (percentages) and were compared with the  $\chi^2$  test or Fisher's exact test. Participants with missing data were excluded from the analysis. Multivariate logistic regression analysis was performed to assess the factors affecting successful RP-EBUS-TBLB and adjusted for age, sex, lesion size (<30, ≥30 mm), lesion location (middle and lower lobe, upper lobe), bronchus sign on CT (negative, positive), and EBUS findings (adjacent to the lesion or invisible, within the lesion). In all analyses, a two-sided *P*<0.05 was considered statistically significant. All statistical analyses were performed using SPSS software (version 24.0; IBM, Chicago, IL, USA).

## Results

### Baseline characteristics of study participants

The baseline characteristics of the participants are summarized in *Table 1*. There were 627 participants who underwent RP-EBUS between January 2019 and July 2020. Participants with no pulmonary function result ( $n=3$ ) and no record of confirming the presence of COPD ( $n=10$ ) were excluded (*Figure 1*). A total of 614 patients were included in the analysis, patients with COPD were 175 patients (28.5%). Older age, male sex, and lower FEV<sub>1</sub> were associated with COPD ( $P<0.001$  for all variables). Regarding lesion characteristics, patients with COPD had a longer distance from the pleura and fewer bronchial signs on CT than those without COPD.

### Results of RP-EBUS

The diagnostic yield of RP-EBUS was not significantly different between patients with and without COPD (80.6% and 78.8%, respectively) (*Table 2*). Of the malignant lesions, 85.6% (95/111) were successfully diagnosed in patients with COPD and 80.1% (220/272) in patients without COPD (*Table 3*). Of the benign lesions, 71.9% (46/64) were successfully diagnosed, and 90.6% (126/139) in patients without COPD. In patients with COPD, there was no significant difference in diagnostic yield based on airflow limitation (mild, 80.0%; moderate, 81.4%; severe to very severe, 79.2%;  $P=0.97$ ) (*Figure 2*). There were no significant differences in EBUS visualization, biopsy sampling, or procedure time between the patients with and without COPD. There were no differences in diagnostic yield according to lesion location in patients without COPD. However, in patients with COPD, the diagnostic yield differed according to the lesion location, with the right upper lobe and left upper lobe having lower diagnostic yields (78% and 67%, respectively) (*Figure 3*).

Regarding complication rate, there were no early terminations, deaths or life-threatening complications during or after bronchoscopy. The incidence of pneumothorax was higher in patients with COPD compared to those without COPD (4.6% *vs.* 1.1%, respectively,  $P=0.008$ ). The complication rate did not differ according to the severity of airflow limitation in patients with COPD (mild, 3.1%; moderate, 10.5%; severe to very severe, 8.3%;  $P=0.27$ ) (*Figure 2*). Hemoptysis occurred after RP-EBUS in 5 (2.9%) patients with COPD and 11 (2.5%) patients without COPD ( $P=0.50$ ). None of the patients with COPD

and 6 (1.4%) of the patients without COPD developed infectious complications ( $P=0.13$ ).

The most common of the established diagnoses using RP-EBUS-TBLB in patients with COPD and without COPD were lung cancer (66.7% and 60.7%, respectively), followed by infectious diseases (23.4% and 28.0%, respectively) (*Table 3*).

### Factors associated with successful RP-EBUS-TBLB in patients with COPD

Factors associated with successful RP-EBUS-TBLB are shown in *Table 4*. In univariable analysis, older age ( $\geq 70$  years), larger lesion size ( $\geq 30$  mm), positive bronchus sign on CT scan, and within the lesion on EBUS image were positively associated with diagnostic success, whereas upper lobe location of the lesion was negatively associated with diagnostic success. In multivariable analysis, large lesion size [odds ratio (OR), 2.86; 95% confidence interval (CI): 1.10–7.45] and within the lesion on EBUS image (OR, 9.29; 95% CI: 3.79–22.79) were associated with increased diagnostic success, whereas upper lobe location of the lesion had a 0.36-fold OR (95% CI: 0.14–0.92) for diagnostic success in patients with COPD.

## Discussion

In this study, RP-EBUS-TBLB was found to be an accurate and relatively safe diagnostic method for patients with COPD and PPLs. The diagnostic yield of 175 COPD patients was 80.6%, which was not different from the patients without COPD. Procedural complications were more common in patients with COPD (7.4%) than those without COPD (5.1%). In patients with COPD, the size of the lesion  $\geq 30$  mm, and within the lesion in EBUS image were associated with diagnostic success. However, the upper lobe location of the lesion was associated with diagnostic failure. The diagnostic yield and complication rates were not significantly different according to the severity of airflow limitation. To our knowledge, this is the largest study to analyze the utility of RP-EBUS-TBLB in patients with COPD.

COPD is a well-known risk factor for lung cancer. Both diseases share the same underlying predispositions, such as oxidative stress, cellular aging, telomere shortening, genetic predisposition, and altered epigenetic regulation of gene expression (14). A pooled meta-analysis demonstrated that the prevalence of lung cancer in COPD patients was

**Table 1** Baseline characteristics of the study participants

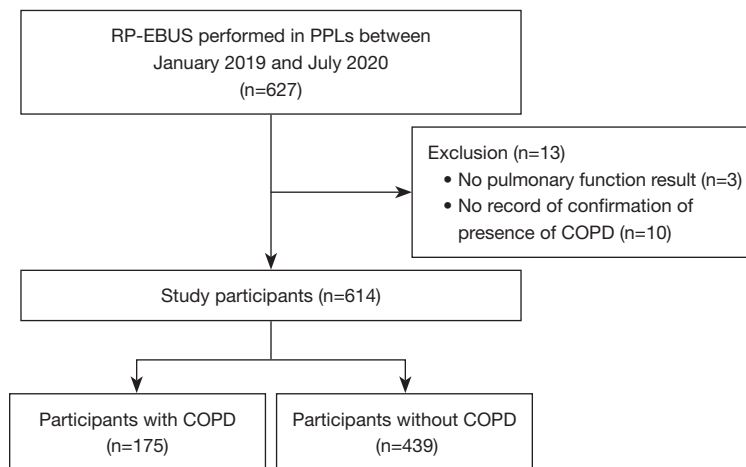
Variables	Patients with COPD (n=175)	Patients without COPD (n=439)	P value
Patients characteristics			
Age, years	72.72±8.44	65.63±12.61	<0.001
Male	141 (80.6)	262 (59.7)	<0.001
Pulmonary function test (%)			
FEV <sub>1</sub> %pred	71.95±19.49	87.90±17.15	<0.001
FVC %pred	82.07±16.54	83.95±46.66	0.60
FEV <sub>1</sub> /FVC	59.99±8.84	79.19±6.55	<0.001
Lesion characteristics			
Location			0.90
RUL	51 (29.1)	128 (29.2)	
RML	7 (4.0)	22 (5.0)	
RLL	47 (26.9)	107 (24.4)	
LUL	43 (24.6)	120 (27.3)	
LLL	27 (15.4)	62 (14.1)	
Size (mm)	31.96±16.15	30.62±16.00	0.35
Distance from pleura (mm)	14.69±13.632	12.23±12.59	0.04
Lesion type			0.36
Solid	93 (53.1)	261 (59.5)	
Part-solid	15 (8.6)	37 (8.4)	
Ground-glass opacity	4 (2.3)	18 (4.1)	
Cavity	32 (18.3)	54 (12.3)	
Consolidation	31 (17.7)	69 (15.7)	
Bronchus sign in CT			0.003
Positive	127 (72.6)	364 (82.9)	
Negative	48 (27.4)	75 (17.1)	

Data are presented as mean ± standard deviation and n (%). COPD, chronic obstructive pulmonary disease; FEV<sub>1</sub>, forced expiratory volume in one second; FVC, forced vital capacity; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; CT, computed tomography.

5.08%, and it is even higher in current and former smokers (8.98%) (15). However, diagnosing PPLs in patients with COPD is challenging because the presence of COPD is a risk factor for pneumothorax during percutaneous needle biopsies. A population-based cohort study reported that patients with COPD had a 1.36-fold increased risk of pneumothorax after TTNB compared with patients without COPD (5). Advanced bronchoscopic techniques such as radial EBUS and electromagnetic navigational

bronchoscopy (ENB) approach PPLs without directly punctuating the lung parenchyma, as in percutaneous needle biopsy, and complication rates are significantly lower (16). Thus, advanced bronchoscopic procedures have recently been increasingly used as alternatives to percutaneous needle biopsy to diagnose high-risk patients (9,17,18).

No significant differences in the diagnostic yield between patients with and without COPD were observed. No significant differences in the diagnostic yield according to



**Figure 1** Flow chart of the study participants. RP-EBUS, radial probe endobronchial ultrasound; PPLs, peripheral pulmonary lesions; COPD, chronic obstructive pulmonary disease.

**Table 2** Results and complications of RP-EBUS-TBLB

Variables	Patients with COPD (n=175)	Patients without COPD (n=439)	P value
Diagnostic yield	141 (80.6)	346 (78.8)	0.63
Complication	13 (7.4)	22 (5.0)	0.02
Pneumothorax	8 (4.6)	5 (1.1)	0.008
Chest tube insertion	3 (1.7)	0 (0.0)	0.02
Hemoptysis	5 (2.9)	11 (2.5)	0.50
Infection	0 (0.0)	6 (1.4)	0.13
EBUS image			0.72
Within	127 (72.6)	309 (70.4)	
Adjacent	32 (18.3)	80 (18.2)	
Invisible	16 (9.1)	50 (11.4)	
No. of samples taken per lesion	5.37±1.59	5.36±1.60	0.95
Procedure time (min)	17.65±7.94	18.44±8.01	0.27

Data were presented as n (%) and mean ± standard deviation. RP-EBUS-TBLB, radial probe endobronchial ultrasound-guided transbronchial lung biopsy; COPD, chronic obstructive pulmonary disease; EBUS, endobronchial ultrasound.

the severity of airflow limitation were observed. Lee *et al.* reported clinical outcomes of RP-EBUS in patients with emphysema. In that study, the diagnostic yield was not different between patients with or without emphysema, as in our study. In addition, the overall diagnostic yields in patients with mild, moderate, or severe pulmonary emphysema were not significantly different (9). Although the number of studies is small and insufficient to draw a definitive conclusion, these two studies suggest that RP-

EBUS-TBLB can be considered for the diagnosis of PPLs in patients with COPD, regardless of the severity of airflow limitation and emphysema.

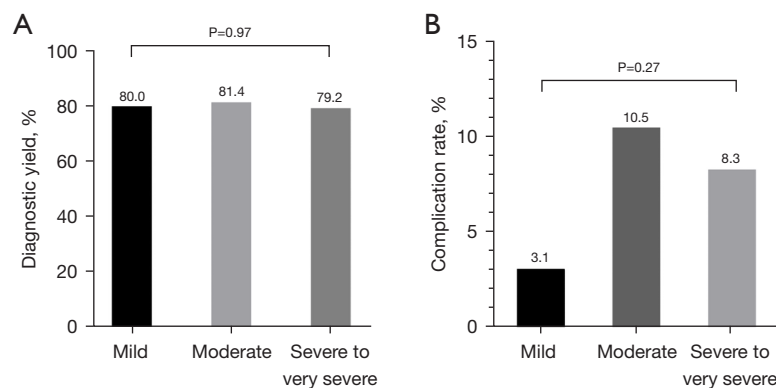
Similar to other RP-EBUS-TBLB-related studies (9,19,20), in this study, we found that the size of the lesion ( $\geq 30$  mm) and having the probe within the lesion were associated with diagnostic success.

Regarding the location of the PPLs, the diagnostic yield of the upper lobe was significantly lower than that of the

**Table 3** Established diagnoses in patients with and without COPD

Variables	Patients with COPD		Patients without COPD	
	Diagnosis (+) (n=141)	Diagnosis (-) (n=34)	Diagnosis (+) (n=346)	Diagnosis (-) (n=93)
<b>Malignant</b>				
Lung cancer	94 (66.7)	14 (41.2)	210 (60.7)	46 (49.5)
Metastatic carcinoma	1 (0.7)	2 (5.9)	7 (2.0)	6 (6.5)
Lymphoma	0	0	3 (0.9)	0
<b>Benign</b>				
Pneumonia or lung abscess	17 (12.1)	1 (2.9)	41 (11.8)	2 (2.2)
Pulmonary tuberculosis	10 (7.1)	1 (2.9)	33 (9.5)	3 (3.2)
Nontuberculous mycobacteria	3 (2.1)	2 (5.9)	18 (5.2)	1 (1.1)
Fungal infection	3 (2.1)	1 (2.9)	5 (1.4)	0
Chondroid hamartoma	0	0	1 (0.3)	2 (2.2)
COP	5 (3.5)	1 (2.9)	10 (2.9)	2 (2.2)
Sarcoidosis	1 (0.7)	0	4 (1.2)	1 (1.1)
Chronic inflammation	7 (5.0)	2 (5.9)	14 (4.0)	2 (2.2)
No definitive diagnosis	0	10 (29.4)	0	28 (30.1)

Data were presented as n (%). COPD, chronic obstructive pulmonary disease; Diagnosis (+), diagnostic success; Diagnosis (-), diagnostic failure; COP, cryptogenic organizing pneumonia.

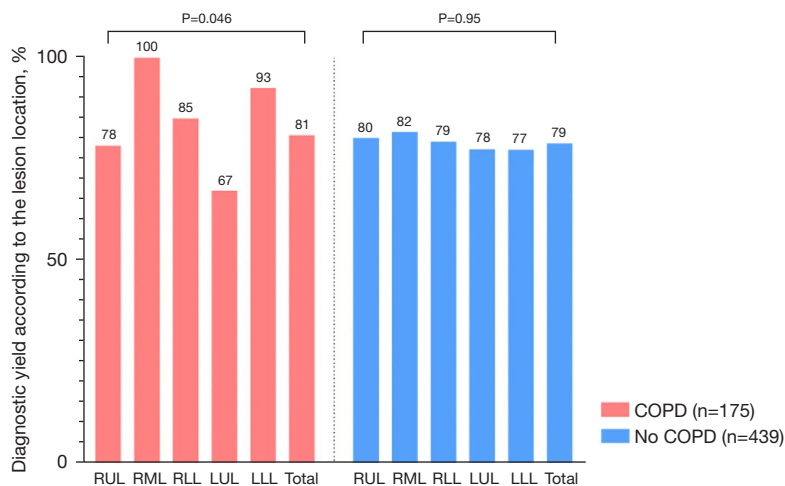


**Figure 2** Diagnostic yield (A) and complication rate (B) according to airflow limitation in patients with COPD. COPD, chronic obstructive pulmonary disease.

middle and lower lobes, particularly in patients with COPD. The diagnostic yield of the left upper lobe (67%) was the lowest among the five lobes of the COPD lung in this study. However, in patients without COPD, the diagnostic yield did not differ between the bronchi. The bronchus of the upper lobe is often difficult to access because of the stiff angle, and even if the GS is accessible, it is difficult to re-access it if it

falls out during the examination; therefore, the diagnosis rate is likely to be low. A meta-analysis of 31 studies reported lower diagnostic rates in the upper lobes (21).

There is one factor that makes this study unique compared with studies conducted in the general patient population. A positive bronchus sign on CT is associated with diagnostic success in most studies; however, our study,



**Figure 3** Diagnostic yield according to the lesion location in patients with and without COPD. COPD, chronic obstructive pulmonary disease; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe.

**Table 4** Univariable and multivariable analyses for factors associated with the diagnostic yield in patients with COPD

Variables	Univariable analysis		Multivariable analysis	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Age, years				
<70	Ref.			
≥70	2.81 (1.30–6.07)	0.009		
Sex				
Male	Ref.			
Female	0.91 (0.36–2.32)	0.85		
Size of lesion, mm				
<30	Ref.			
≥30	4.26 (1.80–10.07)	0.001	2.86 (1.10–7.45)	0.03
Lesion location				
Middle and lower lobe	Ref.			
Upper lobe	0.35 (0.15–0.79)	0.01	0.36 (0.14–0.92)	0.03
Bronchus sign				
Negative	Ref.			
Positive	3.55 (1.62–7.75)	0.001		
EBUS image				
Adjacent to or invisible	Ref.			
Within	11.70 (4.96–27.61)	<0.001	9.29 (3.79–22.79)	<0.001
Emphysema		0.30		
No	Ref.			
Mild	1.12 (0.39–3.60)			
Moderate	0.57 (0.19–1.70)			
Severe	1.48 (0.41–5.39)			

For multivariable analysis, all variables with P<0.1 in the univariable analysis were adjusted. COPD, chronic obstructive pulmonary disease; CI, confidence interval; EBUS, endobronchial ultrasound.



which analyzed only patients with COPD, did not show statistical significance in the multivariable analysis. The bronchial characteristics of COPD include inflammation, fibrosis, narrowing, and obliteration of bronchioles, which make it difficult to detect bronchial signs on chest CT (22). However, it can be assumed that diagnostic success is higher for PPLs that are directly connected to the bronchus, as the EBUS image within the lesion is more likely to be associated with a higher success rate.

Regarding complications, complications in patients with COPD (7.4%) were statistically higher than those in patients without COPD (5.1%). As expected, there was a high rate of pneumothorax requiring chest tube insertion. Lee *et al.* reported no procedure-related EBUS complications in 129 patients (9). However, their study used fluoroscopy for precise localization, which differs from our study. In addition, the predicted FEV<sub>1</sub> of emphysema patients was 79% in their study compared to 71.95% in our study, indicating that the study enrolled relatively milder patients. Given that RP-EBUS-TBLB complications in patients with COPD were identified in 7.4% of cases in this study, but the actual TTNB complication rate was reported to be 20–40% during meta-analysis (23), thus RP-EBUS-TBLB can be considered safe in patients with COPD.

This study had several limitations. First, because this was a retrospective study conducted at a single center with PPLs, the results cannot be generalized. Different hospitals may have different approaches for PPL biopsy in patients with COPD. Thus, a potential selection bias may have influenced the results. Second, although our patients were followed up for at least 12 months, 38 patients (10 with COPD and 28 without COPD) still had nodules without a definite diagnosis. Third, the diagnostic yield and complications of RP-EBUS-TBLB may be affected by the use of additional modalities, such as GS, fluoroscopic guidance, virtual bronchoscopic navigation, and transbronchial needle aspiration. At our center, we only used the GS to perform RP-EBUS-TBLB. Combining different modalities may improve diagnostic yield and reduce complications. Further studies are needed to clarify the benefits of these modalities in RP-EBUS-TBLB in patients with COPD. Finally, within the lesion on the EBUS image was the strongest factor associated with diagnostic yield in this study. However, this factor is not available before EBUS is performed. Although bronchus sign on CT no longer has a significant association with diagnostic yield after adjusting for EBUS image, physicians may consider the bronchus sign on CT as a clinical factor

before performing EBUS in patients with COPD.

## Conclusions

RP-EBUS-TBLB can be used as an acceptable method to diagnose PPLs in patients with COPD, regardless of the severity of airflow limitation. Lesion size ( $\geq 30$  mm) and size within the lesion on EBUS were factors associated with a successful diagnosis, whereas lesion location in the upper lobe was associated with diagnostic failure.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at <https://tldr.amegroups.com/article/view/10.21037/tldr-24-484/rc>

*Data Sharing Statement:* Available at <https://tldr.amegroups.com/article/view/10.21037/tldr-24-484/dss>

*Peer Review File:* Available at <https://tldr.amegroups.com/article/view/10.21037/tldr-24-484/prf>

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://tldr.amegroups.com/article/view/10.21037/tldr-24-484/coif>). The 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 conducted in accordance with the tenets of the Declaration of Helsinki (as revised in 2013) and the protocol was reviewed and approved by the Institutional Review Board of Yeungnam University Hospital (YUH IRB 2020-09-025). The requirement for informed consent was waived because of the retrospective study design.

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