Utility of Radial Endobronchial Ultrasound with a Guide Sheath for Peripheral Pulmonary Lesions in Patients with Pulmonary Emphysema: A Retrospective Study

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Abstract

Background: Radial endobronchial ultrasound with a guide sheath for transbronchial biopsy (EBUS-GS-TBB) can be considered for diagnosing peripheral pulmonary lesions (PPLs) with fewer complications in patients with emphysema. However, the utility and safety of bronchoscopy for PPLs in the proximity of emphysema-area lesions remain unclear. The aim of this study was to assess the efficacy and complications of the initial diagnostic procedure of bronchoscopy with EBUS-GS-TBB according to the proximity of PPLs to emphysema areas, along with factors affecting the successful diagnostic yield for PPLs, and to identify the feasibility of molecular and genetic testing using EBUS-GS-TBB-obtained tumor samples.

Methods: The medical records of 278 consecutive patients with PPLs who underwent EBUS-GS-TBB without X-ray fluoroscopy guidance were screened. We compared PPLs with emphysema in such lesions. PPLs with emphysema were divided into two groups: PPLs located in non-emphysema areas and those inside or near emphysema areas.

Results: This study included 84 patients with emphysema (non-emphysema area group=46; inside or near emphysema area group=38). The diagnostic yield was significantly higher for PPLs located in non-emphysema areas than for PPLs inside or near emphysema areas (82.6% vs. 52.6%, p=0.013). Multivariate analysis revealed that PPLs located in non-emphysema areas (odds ratio=5.614) and EBUS images within lesions were significant factors affecting diagnostic yield. Further, 91.7%–100% of EBUS-GS-TBB-obtained tissue samples were sufficient for molecular testing of PD-L1, EGFR, ALK, and ROS1.

Conclusions: In patients with emphysema, the positional relation of PPLs to emphysema lesions and EBUS images within lesions were important factors affecting successful diagnosis using EBUS-GS-TBB.

Background

Lung cancer is a major health problem and a leading cause of cancer-related mortality worldwide [1], often occurring in patients with pulmonary emphysema [2]. The most frequent locations of lung cancer in patients with emphysema are inside or near the emphysema area [2, 3]. However, lesions occurring in patients with emphysema are not always malignant. Therefore, it is important to obtain a correct histological diagnosis by sampling the lesions. Choosing an appropriate therapy mainly depends on the definitive diagnosis and obtaining a sufficient biopsy sample for advanced molecular and genetic analyses, especially for patients diagnosed with non-small cell lung cancer (NSCLC), which highlights the importance of a correct histological diagnosis for patients with emphysema.

In patients with emphysema, known risk factors for pneumothorax are computed tomography (CT)-guided needle biopsy (CTNB) and surgical lung biopsy (SLB) [4]. Recently, novel therapeutic bronchoscopy procedures [5, 6] and stereotactic radiotherapy have been used for early-stage lung cancer [7, 8]. Endobronchial ultrasound (EBUS) transbronchial biopsy with a guide sheath (EBUS-GS-TBB) is a safe and minimally invasive technique for the investigation of peripheral pulmonary lesions (PPLs) with

significantly lower complication rates than CTNB and SLB [4]. Moreover, it is important to determine the possibility of minimally invasive treatment. However, the utility and safety of EBUS-GS-TBB for PPLs based on the proximity of PPLs to emphysema-area lesions in patients with emphysema remain unknown.

We retrospectively analyzed the data of patients with emphysema who underwent EBUS-GS-TBB and compared the diagnostic yield and complications for PPLs located in non-emphysema areas with those of PPLs located inside or near emphysema areas. Additionally, we analyzed the factors affecting successful diagnostic yield for PPLs. We also identified the feasibility of molecular and genetic testing using the EBUS-GS-TBB-obtained tumor samples, which is often critical for patient management, as it informs on the potential usefulness of molecularly targeted treatment [9].

Methods

Patients

We performed a retrospective study of consecutive patients who underwent EBUS-GS-TBB for PPLs at the Beijing Chao-yang Hospital, Capital Medical University, between January 1, 2020, and May 1, 2021. A total of 278 patients were screened for this study. PPLs were defined as lesions that were surrounded by normal lung parenchyma or emphysema lung areas and were not visible on bronchoscopy. Patients with an unknown final diagnosis, those who did not receive the procedure with a guide sheath owing to availability, and those who underwent procedures assisted by electromagnetic navigation bronchoscopy (ENB), virtual bronchoscopy (VB), or X-ray fluoroscopy were excluded (Fig. 1).

We selected patients with emphysema who underwent EBUS-GS-TBB for PPLs. Emphysema was defined as a low-attenuation lung area lacking a distinct wall by visual estimation according to previous guidelines [10, 11]. Patient history data included data obtained from physical examination, CT, and pulmonary function tests. PPLs in patients with emphysema were divided into two groups: 1) PPLs located in non-emphysema areas, wherein the PPLs and the emphysema area did not overlap; and 2) PPLs located inside/near emphysema areas, wherein the PPLs and the emphysema area overlapped (Fig. 2).

All patients provided written informed consent before undergoing bronchoscopy. This study was reviewed and approved by the ethics committee of the Capital Medical University and was conducted in accordance with the World Medical Association Declaration of Helsinki.

Ct Signs

CT signs of PPLs were defined as intrapulmonary lesions beyond the segmental bronchus visible on axial CT scans. The thin-section CT scans were reviewed by two experienced pulmonologists. The mean diameter of the PPLs was defined as the mean of the maximum transverse diameter and its

perpendicular diameter on axial images with a lung window setting. PPLs were classified as solid, part-solid, or pure ground-glass opacity using a visual assessment method based on CT attenuation modified from a previous study [12]. The location of the lesion relative to the hilum was classified into inner (lesions in the inner and in the middle third of ellipses) and outer (lesions in the outer third of ellipses) groups. Bronchus on CT was defined as the presence of a bronchus leading directly to the PPLs. Pulmonary hypertension was identified on CT using the ratio of the diameters of the pulmonary artery and the aorta.

Radial EBUS-GS-TBB

CT images were thoroughly examined before the procedure to confirm the location of the lesion in the lobe. EBUS was performed using an endoscopic ultrasound system (BF-P-260F; Olympus, Tokyo, Japan) equipped with a guide sheath (GS; K-201; Olympus; external diameter, 1.95 mm) for a 20-MHz mechanical radial-type probe (UM-S20-17R; Olympus) with an external diameter of 1.7 mm. All procedures were performed without assistance from navigation modalities such as ENB, X-ray fluoroscopy, and VB. All patients were administered an intravenous bolus of midazolam and remifentanil and were locally anesthetized with a 2% lidocaine spray. A bronchoscope was inserted as deeply as possible into the target bronchus under direct vision. Subsequently, a radial EBUS probe was introduced through the working channel of the bronchoscope to precisely locate the target lung lesions, which were classified as within or adjacent to the lesion. After identifying the target lesion using the radial EBUS probe, the probe was withdrawn and the suit bag was opened, including a guided sheath, forceps biopsy, and brush cytology. A radial EBUS probe covered with a GS was inserted into the target lesion. When the EBUS image confirmed the lesion, the probe was withdrawn, and transbronchial forceps biopsy was repeated according to the coaxial principle until an adequate number of specimens had been sampled.

Samples Obtained With Ebus-gs-tbb Used For Molecular And Genetic Evaluation Of Malignancy

The samples obtained with EBUS-GS-TBB were diagnosed as NSCLC, and molecular target tests for gene mutations were performed using the obtained tumor tissue samples. Companion diagnostic tests for each gene mutation were performed, including programmed death-ligand 1 (PD-L1), immunohistochemistry (IHC), epidermal growth factor receptor gene (EGFR) mutation, anaplastic lymphoma kinase (ALK) IHC, and recombinant C-Ros oncogene 1 (ROS1) IHC.

Diagnosis

Each histological and cytological specimen was interpreted by two experienced pathologists. We confirmed the final pathological diagnosis and microbiological analysis obtained with biopsy via bronchoscopy, CTNB, or SLB, and clinical follow up. A successful diagnosis obtained using bronchoscopy was defined as the presence of malignant lesions based on histopathology. A failed

diagnosis was defined as a case in which the sample was inadequate. When the collected specimens showed specific benign findings and during the subsequent clinical course, the specimens radiologically decreased in size or became stable in the follow-up period of more than 1 year after the procedure, bronchoscopy was considered diagnostic. Conversely, for PPLs that had increased in size within 1 year after the procedure, a definite diagnosis was obtained using additional diagnostic modalities. In these cases, if the initial diagnosis via bronchoscopy was inconsistent with the final diagnosis at re-examination, bronchoscopy was considered nondiagnostic. Benign lesions that could not be pathologically or microbiologically diagnosed were evaluated by confirming radiologic size stability during the follow-up period for at least 1 year after bronchoscopy. If lesions of part-solid or pure ground-glass structures were undiagnosed with bronchoscopy, follow up was performed using CT according to the Fleischner Society guidelines [13], and surgery was performed for definite diagnosis and appropriate therapy.

Statistical analysis

Data are presented as median and range. Mann–Whitney U and Pearson chi-squared tests were used to analyze continuous variables. Multivariate logistic regression analyses were performed to investigate the significant predictors of positive EBUS-GS-TBB results as follows: 1. mean diameter (≤ 20 mm or > 20 mm); 2. bronchus sign (positive or negative); 3. EBUS image (within or adjacent); 4. location (outer or inner); and 5. positional relation of PPLs to emphysema lesions (PPLs in non-emphysema areas or PPLs inside or near emphysema areas). Variables that attained a significance level of 5% in the univariate analysis were tested using logistic regression analysis. The statistical software SPSS Statistics (version 20; IBM Corp., Armonk, NY, USA) was used for statistical analysis.

Results

Patient characteristics

The medical records of 278 patients with PPLs who underwent radial EBUS-GS-TBB revealed 123 (44.2%) lesions in patients with emphysema. A total of 39 (31.7%) lesions were excluded because ENB, VB, or X-ray fluoroscopy was used for diagnosis, a GS was not available, or the diagnosis was uncertain. Among the remaining 84 patients, 46 lesions were located in non-emphysema areas and 38 were located inside or near emphysema areas (Fig. 1). Table 1 shows the baseline characteristics of the patients and targeted lesions in the two groups. There was a significant difference in age between the two groups.

Table 1
Characteristics of the two patient groups and their targeted lesions

Variables	PPLs in non-emphysema-area lesions (n = 46)	PPLs inside or near emphysema-area lesions (n = 38)	p-value
Age, years	67 (61–72)	57 (38–72)	0.021
Sex, male, n (%)	35 (76)	27 (71)	0.232
Lesion diameter, mm	26 (18–35)	24 (17–32)	0.743
PFT	-	-	-
FEV1%	89 (47–132)	93 (58–136)	0.132
FVC%	87 (50–125)	97 (42–134)	0.471
FEV1/FVC%	76 (41–112)	85 (45–117)	0.883
RV%	83 (43–118)	93 (52–132)	0.625
TLC%	93 (59–124)	98 (56–135)	0.467
RV/TLC%	45 (21–75)	35 (17–56)	0.293
DLco%	72 (37–118)	87 (47–117)	0.411
Pulmonary hypertension, n (%)	14 (30.4)	12 (31.5)	0.852
Lesion lobe, n (%)	-	-	0.829
Upper	27 (58.7)	22 (57.9)	-
Middle or lingual	6 (13)	7 (18.4)	-
Lower	13 (28.3)	9 (23.7)	-
Location, n (%)	-	-	0.476
Outer	28 (60.8)	23 (60.5)	-
Inner	18 (39.2)	15 (39.5)	-
CT lesion character, n (%)	-	-	0.177
Solid	21 (45.7)	19 (50)	-
Part-solid	16 (34.7)	13 (34.2)	-
Pure ground-glass	7 (19.6)	6 (15.8)	-
CT bronchus sign, n (%) positive	29 (63)	23 (60.5)	0.340

Variables	PPLs in non-emphysema-area lesions (n = 46)	PPLs inside or near emphysema-area lesions (n = 38)	p-value
Number of biopsies	7.8 (3–15)	7.6 (3–14)	0.921

Values are presented as median (range) unless specified otherwise

CT: computed tomography; DLco%: percentage of diffusing capacity of the lung for carbon monoxide; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; PFT: pulmonary function test; PPLs: peripheral pulmonary lesions; RV: residual volume; TLC: total lung capacity

Diagnostic yield based on the EBUS image and final disease type between PPLs located in non-emphysema areas and those inside or near emphysema areas

The diagnostic yield of EBUS-GS in patients with emphysema for PPLs located in non-emphysema areas was significantly higher than that for PPLs inside or near emphysema areas (82.6% vs. 52.6%, p = 0.010). When the probe was located within the PPLs, reflected in the EBUS images, the diagnostic yield for PPLs in non-emphysema areas was significantly higher than that for those inside or near emphysema areas (96.2% vs. 63.3%, p = 0.011). However, the frequency of the probe being located within the PPL did not differ between the two groups (54.3% vs. 50%, respectively). Furthermore, the diagnostic yield for malignant lesions was significantly higher for PPLs in non-emphysema areas than for PPLs inside or near emphysema areas (92.3% vs. 50%, p = 0.002) (Table 2).

Table 2
Comparison of diagnostic yield with EBUS imaging and final disease type

	PPLs in non-emphysema-area lesions (n = 46)	PPLs inside or near emphysema-area lesions (n = 38)	p-value
EBUS image, n (%)	-	-	-
Within	25/26 (96.2)	19/30 (63.3)	0.011
Adjacent to	3/20 (15)	1/8 (12.5)	0.398
Final diagnosis, n (%)	-	-	-
Benign lesions	14/20 (70)	7/12 (58.3)	0.057
Malignant lesions	24/26 (92.3)	13/26 (50)	0.002
Total	38/46 (82.6)	20/38 (52.6)	0.010

EBUS: endobronchial ultrasound; PPLs: peripheral pulmonary lesions

In the 26 patients undiagnosed using EBUS-GS, CTNB or SLB was performed as an additional procedure, which provided a final diagnosis. Among the patients who underwent CTNB, 13 lesions were identified, consisting of four adenocarcinomas, three squamous cell carcinomas, two small cell lung carcinomas, two lymphomas, and two unknown diagnoses requiring SLB, meaning that both CTNB and SLB were performed. Among the patients who underwent SLB, four lesions were identified consisting of one small cell lung carcinoma, one adenocarcinoma, one poorly differentiated neuroendocrine carcinoma, and one sarcomatoid carcinoma. The remaining nine lesions undiagnosed using EBUS-GS were evaluated using radiologic surveillance and underwent resolution, as followed up using serial CT images; they were finally diagnosed as benign lesions. For these additional diagnostic procedures, the diagnostic accuracies of CTNB and SLB were 84.6% (11/13) and 100% (4/4), respectively.

Factors Related To Successful Diagnosis Of Ppls With Ebus-gs-tbb In Patients With Emphysema

Multivariate analysis revealed that PPLs located in non-emphysema areas (odds ratio [OR] = 5.614) and EBUS images within the lesion (OR = 3.394) were significant factors affecting diagnostic yield. The position on the EBUS image and the positional relation of PPLs with emphysema areas were significant predictors of successful diagnosis using EBUS-GS-TBB (Table 3).

Table 3
Analysis of factors affecting the diagnostic yield of EBUS-GS-TBB in patients with emphysema

Variables	Reference	OR (95% CI)	p-value
Size > 20 mm (39)	≤ 20 mm (45)	1.516 (0.054–5.023)	0.859
Bronchus sign positive (52)	Negative (32)	0.877 (0.095–3.683)	0.497
Location inner (33)	Outer (51)	1.409 (0.433–4.824)	0.637
EBUS image within (44)	Adjacent (40)	3.394 (1.015–15.277)	0.020
PPLs in non-emphysema-area lesions (n = 46)	PPLs inside or near emphysema-area lesions (n = 38)	5.614 (0.736–28.536)	0.008

CI: confidence interval; EBUS: endobronchial ultrasound; EBUS-GS-TBB: endobronchial ultrasound with a guide sheath transbronchial biopsy; OR: odds ratio; PPLs: peripheral pulmonary lesions

Molecular And Genetic Investigation Of Malignancy In Ebus-gs-tbb Specimens

Of the specimens from the 37 patients with malignancies, molecular and genetic mutation testing for PD-L1, EGFR, ALK, and ROS1 was performed in 26 specimens diagnosed as adenocarcinoma. Specimens were sufficient for testing in 91.7% (11/12), 100% (17/17), 94.1% (16/17), and 100% (17/17) of cases, respectively (Table 4).

Table 4
Molecular and genetic IHC tests for detecting malignancy in the EBUS-GS-TBB samples

Molecular/genetic IHC testing	PD-L1 IHC in ADC (n = 26)	EGFR IHC in ADC (n = 26)	ALK IHC in ADC (n = 26)	ROS1 IHC in ADC (n = 26)
Attempted	12	17	17	17
Successful	11	17	16	17
Inadequate	1	0	1	0
Not attempted	14	9	9	9

ADC: adenocarcinoma; ALK: anaplastic lymphoma kinase; EBUS-GS-TBB: endobronchial ultrasound with a guide sheath transbronchial biopsy; EGFR: epidermal growth factor receptor; IHC: immunohistochemistry; PD-L1: programmed death-ligand 1; ROS1: recombinant C-Ros oncogene 1

Complications

No mortality or life-threatening complications were associated with any of the procedures during the study period. Among the 84 patients with emphysema, two cases of pneumothorax occurred; one patient whose PPLs were located in the non-emphysema area after the EBUS-GS procedure recovered after oxygen therapy and close observation; another patient with PPLs inside or near the emphysema area underwent CTNB requiring intercostal catheter insertion. Severe hemorrhage, air embolism, or pulmonary infection was not detected in the post-procedure follow up.

Discussion

Lung cancers in patients with emphysema often present as PPLs inside or near the emphysema area. A report demonstrated that pulmonary infiltrates, such as those resulting from inflammatory cells and emphysematous changes, were increased on the side with lung cancer development compared to the other side [3]. De Torres et al. suggested that the presence of emphysema is an independent risk factor for lung cancer; the incidence of lung cancer in patients with emphysema is higher than that in patients without emphysema (relative risk: 3.33; 95% CI, 1.41–7.85), even in patients without airflow restriction. It has also been shown that the presence of emphysema increases the risk of lung cancer (relative risk, 2.51; 95% CI, 1.01–6.23)) [14]. Similarly, we discovered that malignant lesions were more frequent in

patients with emphysema (44% [37/84]), but the diagnostic yield for PPLs located in non-emphysema-area lesions was significantly higher than for PPLs located inside or near emphysema-area lesions (92.3% vs 50%, p = 0.002). The reason for this may be that PPLs located in non-emphysema areas could be more easily reached by the probe than PPLs inside or near emphysema areas, which are characterized by the destruction of the lung parenchyma and alveolar attachment [15]. A systematic review and meta-analysis reported that, assisted by ENB, VB, and X-ray fluoroscopy, the overall weighted diagnostic yield of EBUS-GS-TBB was 70.6% (95% CI, 68–73%) [16]. Similarly, the present study found a mean diagnostic yield of 69% (58/84), higher than that reported by Georgiou et al. who showed a diagnostic yield of 63% in patients with advanced chronic obstructive pulmonary disease (COPD) (mean forced expiratory volume in 1 s (FEV1)/ forced vital capacity ratio of 1.33 and mean predicted FEV1 of 54.2%) utilizing electromagnetic navigation [17]. Lee et al. reported that the diagnostic yield of EBUS-GS under X-ray fluoroscopic guidance in patients with no or mild emphysema was significantly higher than that in those with moderate or severe emphysema (78% vs. 61%, p = 0.007) [18]. In the present study, according to the proximity of PPLs to emphysema lesions, the diagnostic yield for PPLs in non-emphysema areas was higher than that for PPLs in or near emphysema areas (82.6% vs. 52.6%, p = 0.010), although no X-ray fluoroscopic guidance was used for assistance. The EBUS-GS technique can improve the biopsy accuracy rate [19]. In addition, a previous study reported a fairly good diagnostic yield using EBUS-GS-TBB, where X-fluoroscopy alone was incapable of detecting solitary nodules [20].

The results of the present study may be supported by the following. First, EBUS with a GS can ensure that TBBs are performed at the correct location as identified using EBUS. Second, we selected two groups of patients with light emphysema (mean FEV1 of 89–93%). We categorized the patients according to the proximity of PPLs to emphysema lesions and not according to the severity of emphysema. This finding may also support the idea that PPLs in non-emphysema areas were more frequently diagnosed than PPLs located inside or near emphysema areas. Third, we discovered that the diagnostic yield of EBUS images was higher within the lesion than outside the lesion (96.2% vs 63.3%, p = 0.11); this also demonstrates the fact that the probe reached the PPLs appropriately in both groups with nearly the same frequency (54.3% [25/46] vs. 50% [19/30]). If target lesions could be confirmed on EBUS, even with the probe located within the lesion, the diagnostic yield for PPLs located inside or near emphysema areas would be lower than that for PPLs in non-emphysema area lesions. All of the above may reflect the fact that only the surfaces of PPLs inside or near emphysema areas were sampled owing to the destruction of the lung parenchyma, which obliterates the small airways [21]. To improve the diagnostic yield for PPLs inside or near emphysema areas, additional conventional transbronchial lung biopsy (TBLB) after EBUS-GS-TBB may be effective if a larger tissue sample is obtained [22]. Furthermore, transbronchial needle aspiration through a GS using the PeriView FLEX needle may improve the diagnostic yield by penetrating the lesions and collecting samples [23, 24]; the diagnostic yield may also be improved using EBUS-GS transbronchial lung cryobiopsy to obtain adequate samples [25].

Previous studies have reported that malignancy status, lesion size, bronchus signs on CT, and probe position on EBUS images were significant factors affecting diagnostic yield for PPLs using EBUS-GS-TBB [18, 19, 26, 27, 28]. Previous reports have indicated the probe position to be the only significant diagnostic

factor [26, 29], and the present multivariate analysis found that probe location within the PPLs was significantly associated with a successful diagnosis using radio EBUS (OR, 2.542; p = 0.007) [29]. Similarly, the present study demonstrated that, in patients with emphysema, the probe position on EBUS images was a significant factor affecting the diagnostic yield of PPLs using EBUS-GS-TBB (OR, 3.394; p = 0.020). Moreover, the positional relationship of PPLs with emphysema lesions or the lesion status was a significant factor in the successful diagnosis of PPLs in patients with emphysema (OR, 5.614; p = 0.008) (Table 3). This factor affecting the diagnosis of PPLs in patients with emphysema has not been previously reported; in this situation, if the probe is located inside or near emphysema areas, CT bronchus signs may not be clearly evident, and the probe may not touch the center of the lesions because of the emphysematous destruction of the lung parenchyma. This may be important to physicians who use EBUS-GS-TBB in patients with emphysema. We also found that the positional relationship of PPLs to emphysema areas, rather than the bronchus sign, was a significant factor affecting the successful diagnostic yield of EBUS-GS-TBB.

Regarding the feasibility of molecular and genetic testing, a previous report showed that EBUS-TBB without GS and fluoroscopy could obtain sufficient tissue samples in almost all cases (94–100%) for testing of EGFR, ALK IHC, and PD-L1 IHC [30]. Similarly, the present study showed that the EBUS-GS-TBB-obtained samples from patients with emphysema and malignancies were sufficient for molecular and genetic tests, including for PD-L1, EGFR, ALK, and ROS1. However, molecular testing of samples from EBUS-guided transbronchial needle aspiration has also shown high efficacy [31]. Another report using 1.5-mm biopsy forceps to obtain samples for genotype analysis showed a 67–89% success rate in NSCLC [32]. Using a coaxial GS, EBUS-TBB can be repeatedly performed in a minimally invasive manner, with local anesthesia, reducing the chance of inserting the biopsy forceps into the wrong bronchioles, and multiple tissue specimens can be obtained. Thus, it is expected that this method will enable physicians to avoid unnecessary surgery and more easily select appropriate therapy.

In the present study, the rate of pneumothorax in the two groups was not significantly different; the total rate was 1/84 (< 1%) in patients with emphysema who underwent EBUS-GS-TBB without intercostal catheter insertion. Similarly, previous studies have reported that the rate of pneumothorax was less than 1% [21, 33]. In a study of 965 PPLs using EBUS-GS, there were eight patients with pneumothorax, three of whom required intercostal catheter insertion [33]. However, in the present study, we performed EBUS-GS and did not use assistance from navigation modalities, such as ENB, X-ray fluoroscopy, or VB. The incidence of pneumothorax was 2.1% for EBUS using electromagnetic navigation without GS [17] in patients with COPD undergoing TBLB [34], even lower than that in patients with advanced COPD.

The present study has certain limitations. First, the age of patients with PPLs in non-emphysema areas was significantly higher than that of patients with PPLs within or near emphysema areas. Second, this was a retrospective and small cohort study conducted at a single facility, and selection bias could have influenced our results; therefore, it is difficult to generalize the findings. In particular, the EBUS-GS-TBB complication rate may have been underestimated in this study. Third, all EBUS-GS-TBB procedures were performed without the assistance of a navigation system, such as ENB, X-ray fluoroscopy, or VB [35, 36].

The method utilized may be more suitable for medical centers without navigation devices. Prospective trials that consider these limitations are recommended.

Conclusions

In conclusion, the diagnostic yield for PPLs located in non-emphysema areas was significantly higher than that for PPLs within or near emphysema areas. Moreover, the positional relationship of PPLs to emphysema areas and the probe position on the EBUS images were significant factors affecting diagnostic yield. Additionally, EBUS-GS-TBB samples were sufficient for further molecular and genetic testing.

Abbreviations

endobronchial ultrasound with a guide sheath for transbronchial biopsy (EBUS-GS-TBB)

peripheral pulmonary lesions (PPLs)

non-small lung cancer (NSCLC)

computed tomography (CT)

computed tomography-guided needle biopsy (CTNB)

surgical lung biopsy (SLB)

electromagnetic navigation bronchoscopy (ENB)

virtual bronchoscopy (VB)

endobronchial ultrasound (EBUS)

programmed death-ligand 1 (PD-L1)

immunohistochemistry (IHC)

epidermal growth factor receptor gene (EGFR),

anaplastic lymphoma kinase (ALK)

recombinant C-Ros oncogene 1 (ROS1)

odds ratio (OR)

chronic obstructive pulmonary disease (COPD)

Declarations

Ethics approval and consent to participate

This study was reviewed and approved by the ethics committee of Capital Medical University. All patients provided written informed consent before undergoing bronchoscopy.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors have contributed significantly to the content of the article. LZ: Substantial contributions to the conception and design of the work and drafting the work. FW, ZW, and LX: Substantial contributions to the acquisition and analysis of the data for the work. LZ and FW contributed equally to this manuscript. ZT: Substantial contributions to the conception or design of the work. The authors agree to be accountable for authors' contributions in the work and would ensure that questions related to the accuracy or integrity of the work are appropriately investigated and resolved.

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Figures

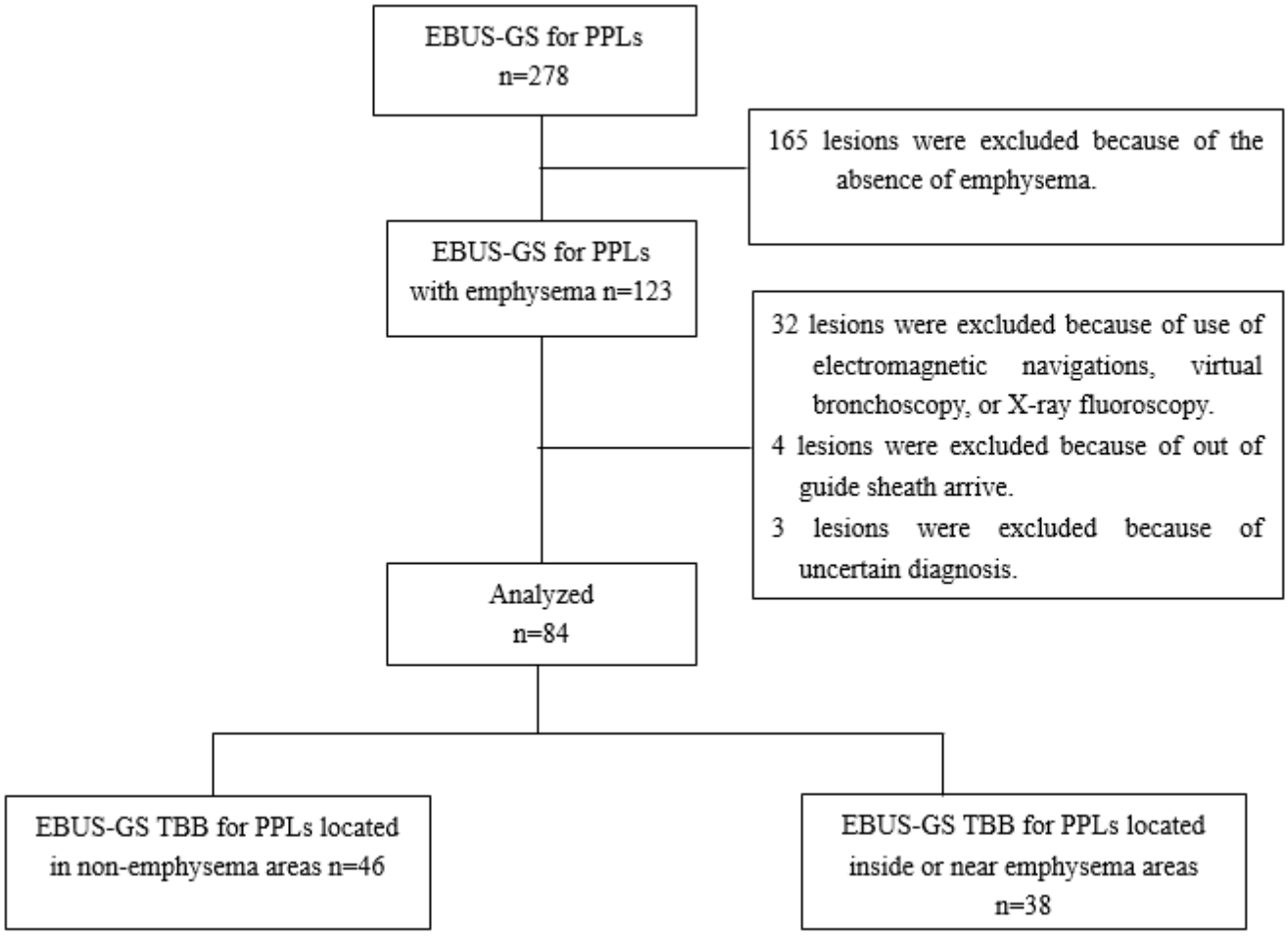

Figure 1

Patient selection and classification flowchart; EBUS-GS-TBB, endobronchial ultrasound with a guide sheath for transbronchial biopsy; PPLs, peripheral pulmonary lesions

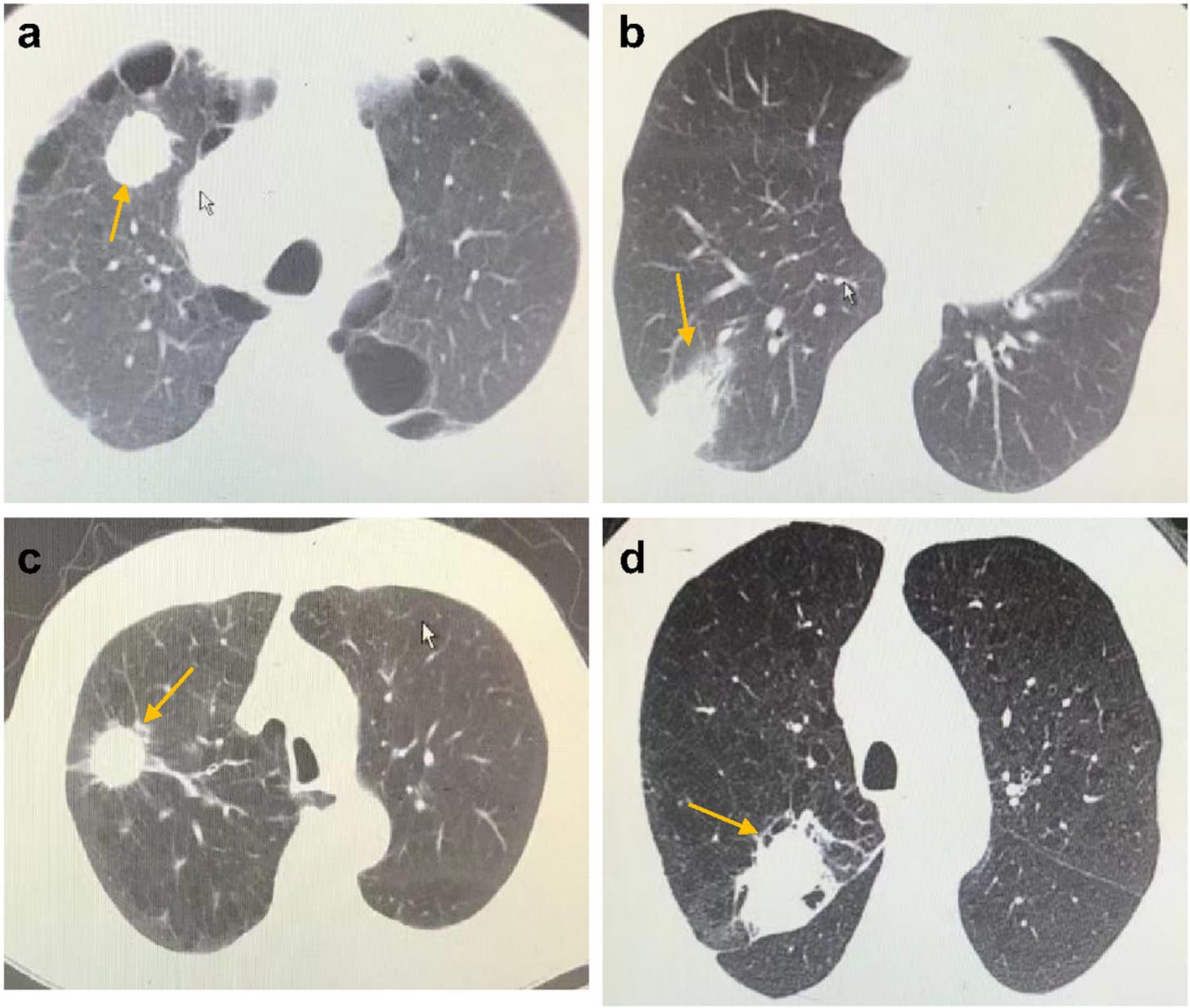

Figure 2

Chest computed tomography findings; **(a, b)** Chest computed tomography images showing peripheral pulmonary lesions in non-emphysema areas (yellow arrow) and **(c, d)** those inside or near emphysema areas (yellow arrow)