Diagnosing a solitary pulmonary nodule using multiple bronchoscopic guided technologies: A prospective randomized study

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ABSTRACT

Background: The rate of detection of pulmonary nodules on computed radiography (CR) is approximately 0.09–0.2%, so rapid identification of the nature of solitary pulmonary nodules (SPNs) with a likelihood of malignancy is a critical challenge in the early diagnosis of lung cancer.

Objective: We conducted this study to compare the diagnostic yield and safety of endobronchial ultrasonography with a guide sheath (EBUS-GS), and the combination of EBUS-GS and virtual bronchoscopic navigation (VBN).

Methods: This was a prospective, multicenter, multi-arm, randomized controlled trial involving a total of 1010 subjects. All the patients recruited underwent a chest CT scan which found SPNs that needed to be diagnosed. The subjects were randomly divided into one of three groups: a traditional, non-guided, bronchoscopy biopsy group (NGB group), an EBUS-GS guided bronchoscopy biopsy group (EBUS group), and a guided bronchoscopy biopsy group that combined EBUS-GS with VBN (combined group). The primary endpoint was to investigate the differences between the diagnostic yields of the three groups.

Results: There was no significant difference in the diagnostic yield between the EBUS group (72.3%) and the combined group (74.3%), but the diagnostic yield for the NGB group was 41.2%. The time required to reach biopsy position was significantly less in the combined group (7.96 ± 1.18 min in the combined group versus 11.92 ± 5.37 min in the EBUS group, p < 0.05). However, the bronchoscope operation time was the same in the EBUS-GS and combined groups. The diagnostic yield for peripheral pulmonary lesions (PPLs) > 20 mm in diameter was significantly higher than for those < 20 mm in diameter.

Conclusion: The results of our study suggest that guided bronchoscopy could increase the diagnostic yield in the context of peripheral lesions. There was no significant difference in the diagnostic yield between the EBUS and combined groups, but use of EBUS-GS with VBN could significantly shorten the bronchoscope arrival time.

1. Introduction

Rapid identification of the nature of solitary pulmonary nodules (SPNs) with a likelihood of malignancy is a critical task in the early diagnosis of lung cancer and is worthy of all efforts. Our goal is to be able to detect and treat SPNs before these lesions become incurable, and

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at the same time to avoid futile invasive diagnostic procedures—particularly open-chest surgery—for benign SPNs. SPNs found by computed tomography (CT) examination are usually evaluated by intensive follow-up, percutaneous needle biopsy, bronchoscopy, or surgical resection [1,2]. Thus, selecting an appropriate diagnostic method based on the character and location of the nodule is critical for the safe and, most important of all, early diagnosis of lung cancer.

For nodules with a high risk of malignancy, percutaneous needle biopsy and transbronchial lung biopsies might be the best choices. In particular, percutaneous needle biopsy has a high diagnostic yield in peripheral pulmonary lesions (PPLs), ranging from 68% to 99% [1,3,4]. However, it is not the best choice for the detection of nodules far from the chest wall because of a relatively high complication rate [3,5]. Transbronchial biopsy has a significantly lower complication rate (approximately 3%) when compared with percutaneous needle biopsy [4]. However, the diagnostic yield of PPLs with traditional bronchoscopy is very low, ranging from 14% to 62% [4,6,7,8], especially for lesions located beyond the segmental bronchus that are not detectable. Therefore, many guided methods have been developed to improve the diagnostic yield of transbronchial biopsy, including fluoroscopy-guided transbronchial biopsy, CT-guided transbronchial biopsy, endobronchial ultrasonography with a guide sheath (EBUS-GS), virtual bronchoscopic navigation (VBN), and electromagnetic navigation bronchoscopy (ENB) [9]. According to a meta-analysis based on more than 3000 patients [4], the diagnostic yield of guided bronchoscopy is much better than that of traditional transbronchial biopsy, ranging from 67.1% to 72.9%. However, until now, percutaneous needle biopsy and transbronchial lung biopsies cannot fully replace one another but do complement each other.

EBUS-GS is a technology that combines bronchoscopy with radial endobronchial ultrasound (R-EBUS); once the lesion is reached and verified, a biopsy is performed through a guided sheath to maintain the position. VBN is a technology that can create a virtual bronchoscopic image and guide a pathway to the nodule. Although several studies have investigated and reported the diagnostic yield of these methods [1,10–12], there are few prospective randomized studies that compare these guided methods and clarify which is most appropriate. Therefore, we conducted this study to compare the diagnostic yield and safety of EBUS-GS and the combination of EBUS-GS and VBN.

2. Methods

2.1. Subjects

This was a prospective, multicenter, multi-arm, randomized controlled trial involving a total of 1095 subjects. There were eight participating centers (Tangdu Hospital, Changhai Hospital, The Second Hospital of Fujian Medical University, The Second Hospital of Gansu Province, The First Affiliated Hospital of Guangzhou Medical University, Hunan People's Hospital, Shanghai Pulmonary Hospital and The Second Xiangya Hospital), and all of them had access to EBUS-GS and VBN. The enrolment criteria were as follows: (a) patients having SPNs with a high likelihood of malignancy [2,13], being non-calcified lung nodules with pleural retraction, lobular sign, spiculation, or other indications that need biopsy as recommended by the guidelines, and (b) the diameter of the nodule ≤30 mm and ≥8 mm. The exclusion criteria were as follows: (a) age ≤18 years or ≥75 years; (b) patients with contraindications for bronchoscopy, such as severe coagulopathy or cardiac infarction; (c) patients with other potentially fatal diseases; (d) gravitas; and (e) SPNs with an endobronchial component observed using a traditional bronchoscope. This study was approved by the Regional Ethics Committee of our hospital (Tangdu Hospital). Informed consent was obtained from all subjects.

2.2. Procedures

First, all potential subjects underwent a chest CT scan, and the size of the SPN was measured on the axial lung window setting; the largest diameter and the location of the nodule were recorded. If the inclusion criteria were met, the subjects were randomly divided into one of three groups by the computer according to the ratio 1:1:1. The three groups comprised the traditional non-guided bronchoscopy biopsy group (NGB group), the EBUS-GS-guided bronchoscopy biopsy group (EBUS-GS group), and the guided bronchoscopy biopsy group that combined EBUS-GS with VBN (combined group). After randomization, the virtual bronchoscopic images from the patients in the combined group were reconstructed (the reconstruction interval was ≤1 mm), and the bronchial routes to the target nodules were selected.

Following preparation, the bronchoscopies were conducted using local anesthesia with inhalation of 1% tetracaine and intratracheal instillation of 2% lidocaine. All the endoscopists had more than 5 years' experience of relevant operations, and they were trained before conducting this study to familiarize themselves with the process and standardized operation. All the subjects first underwent a regular bronchoscopic inspection of the central airways to exclude the SPNs with an endobronchial component. The patients then underwent a transbronchial biopsy based on group assignment. The examination procedures for the different groups were as follows. (a) For the NGB group: after local anesthesia and preliminary inspection the bronchoscopist advanced the bronchoscope as far as possible into the suspected bronchi based on the CT scan results. Then, five pieces of tissue were collected though transbronchial lung biopsies using biopsy forceps. (b) For the EBUS-GS group: the process was the same as for the NGB group, but after advancing the bronchoscope to the suspected bronchi, the EBUS probe and guide sheath were inserted into the endoscopic channel together to detect the SPNs. Once the nodule was localized, we fixed the guide sheath and collected five pieces of tissue from the nodule using biopsy forceps. (c) For the combined group: after local anesthesia and preliminary inspection, the bronchoscopist first watched the virtual bronchoscopic image and carefully directed a pathway to the nodule. They were then able to accurately insert the bronchoscope into the affected bronchus with the help of VBN every step of the way. When the bronchoscope reached the nodule marked by the VBN, the EBUS probe and guide sheath were inserted into the endoscopic channel to confirm the location of the SPN. Then, five pieces of tissue were collected though the fixed guide sheath using biopsy forceps.

The bronchoscope operation time and the time of arrival at the nodule were recorded separately. The bronchoscope operation time was defined as the time from the insertion of the bronchoscope into the trachea until the time of completion of the operation. The time of arrival at the nodule was defined as the time from the insertion of the bronchoscope into the trachea until the time of confirmation of the location of the SPNs. The duration of EBUS-GS detection was limited to 30 min, and the subjects whose detection time was more than 30 min were recorded as SPNs not detected. The ultrasonic probe locations were recorded as outside, and five pieces of tissue were collected based on the bronchoscopist's preference.

The histological diagnosis was recorded to calculate the diagnostic yield. A definite histological diagnosis means either malignancy or defined benign pathology (such as granuloma or pneumonia). If the histological diagnosis was unclear, fibrosis, normal, or inflammation, the patients underwent further examination, such as by repeat transbronchial biopsy, transthoracic needle biopsy, positron emission computed tomography (PET/CT), surgery, or follow-up for 2 years to clarify and confirm the diagnosis. The selections were based on the patients' condition and willingness. The follow-up usually lasted for 2 years, and we called patients every 6 months to obtain their status and record changes in the nodules. If we got a confirmed diagnosis, the follow-up would terminate.

2.3. Study endpoints

The primary endpoint was the difference between the diagnostic yields of the three groups. A secondary endpoint was calculation of the mean bronchoscope operation time and the time of arrival at the nodule in the three groups.

2.4. Statistical analysis

The data were analyzed using SPSS (IBM Corporation, New York, USA). The data were reported as the mean values ± standard deviations. Continuous datasets were analyzed by one-way ANOVA. Count data were analyzed using chi-square tests or Fisher's exact tests. All p values were double-sided, and $p < 0.05$ meant that differences in the mean values were significant.

3. Results

3.1. Participants

A total of 1095 patients met the inclusion criteria and were recruited into this trial between January 2014 and December 2016; they were then randomly assigned into one of the three groups. There were 365 subjects enrolled in each group. As shown in Fig. 1, after the traditional bronchoscopic inspection, 52 subjects were excluded because of the discovery of an endobronchial component. Another 33 subjects were withdrawn because of failure to collect their tissue specimens or losing them to follow-up after the predesigned bronchoscopic inspection and transbronchial lung biopsies. In the end, there were 340 subjects in the NGB group, 336 subjects in the EBUS-GS group, and 334 subjects in the combined group. The age, sex, lobar distribution of nodules, nodule size, and spectrum of disease at baseline were similar among the groups (Table 1).

3.2. Diagnostic yield

Among the 1010 eligible cases, 631 cases were diagnosed using the histological results from the tissue collected by transbronchial biopsy under bronchoscopic guidance. In all, in 379 cases there was a failure to obtain a clear diagnosis during the predesigned bronchoscopic inspection and transbronchial lung biopsies; however, 295 of those cases were diagnosed though other methods of inspection, and the remaining 84 cases were diagnosed by close follow-up. As shown in Table 2, among the 1010 eligible cases, approximately half were diagnosed as malignant disease, with adenocarcinoma making up the largest percentage (28.3%, 286/1010). In addition, among the non-malignant cases, normal lung tissue/bronchial epithelium made up the largest percentage (10.3%, 104/1010).

The EBUS-GS and combined groups had a significantly higher diagnostic yield (72.3% and 74.3%) than the NGB group (41.2%, $p < 0.01$). No matter the mode of analysis—whether by lobar distribution, by pathology, or by nodule size—the EBUS-GS and the combined groups always had a heightened yield (Table 3). However, the diagnostic yield of the combined (EBUS-GS + VBN) group was not significantly different from that of the EBUS-only group. Of note, there was a higher diagnostic yield for malignancy in all three groups; this might be because of the degree of difficulty in distinguishing between nodules from benign diseases and malignant nodules. In addition, the ultrasonic probe location significantly affected the diagnostic yields in the EBUS-GS and combined groups; the diagnostic yield was approximately 86.8% if the probe was internal to the nodule before the biopsy. However, when the probe was near or outside the nodule, the diagnostic yields were only 64.5% and 37%, respectively. As in many former trials, the diagnostic yield for PPLs > 20 mm in diameter in our trial was significantly higher than that for those < 20 mm in diameter (Table 4).

As shown in Table 5, although EBUS-GS + VBN did not increase the diagnostic yield when compared with EBUS-GS alone, the required time to reach the biopsy position was significantly less than in the combined group (7.96 ± 1.18 min in the combined group versus 11.92 ± 5.37 min in the EBUS-GS group, $p < 0.01$). However, the bronchoscope operation time was the same in the EBUS-GS and combined groups, and that in NGB group was one third shorter compared with the other groups. This was because that the biopsy procedure took up the greatest part of the operation time.
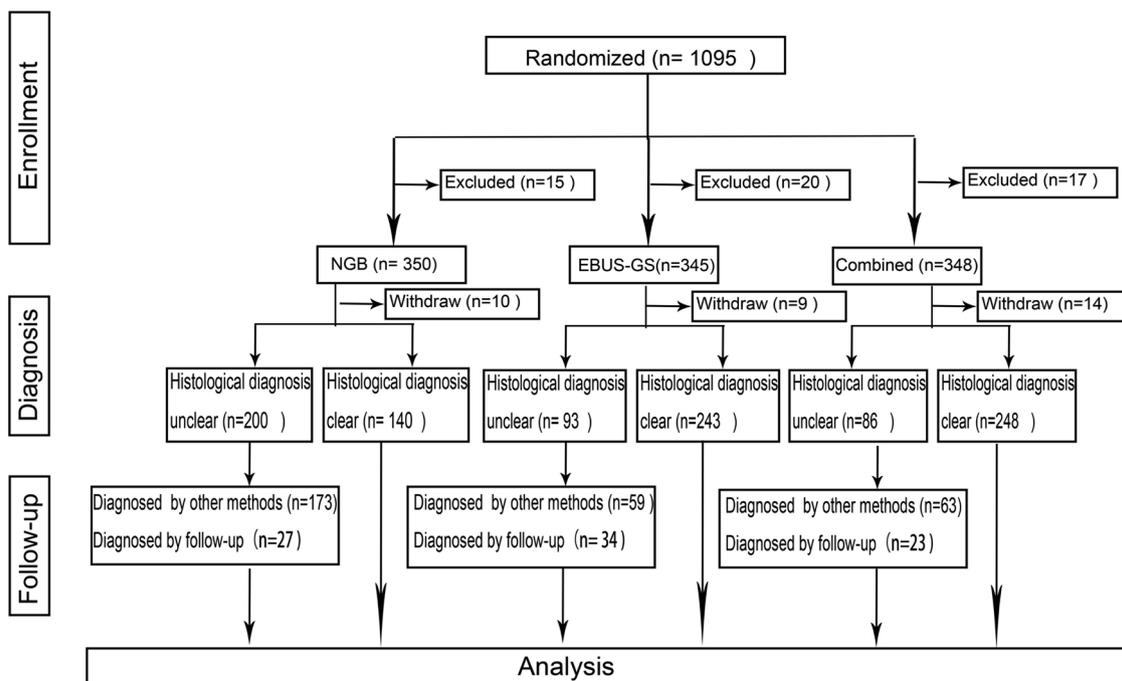

Fig. 1. Flow diagram of the study. NGB, non-guided bronchoscopy; EBUS-GS, endobronchial ultrasonography with a guide sheath.

Table 1
Subject demographics.

Items	NGB group (n = 340)	EBUS-GS group (n = 336)	Combined (EBUS-GS + VBN) group (n = 334)	Analytic result	p value
Age (years)	57.14 ± 11.46 (18–75)	58.42 ± 11.26 (18–75)	58.03 ± 11.92 (18–75)	F = 1.10	0.33
Female/male	147/193	134/202	118/216	χ^2 = 4.44	0.11
Nodules location				χ^2 = 2.55	0.96
Right upper lung	110 (32.4%)	105 (31.3%)	104 (31.1%)		
Right middle lung	24 (7.0%)	27 (8.0%)	29 (8.7%)		
Right lower lung	84 (24.7%)	78 (23.2%)	80 (24.0%)		
Left upper lung	71 (20.9%)	83 (24.7%)	74 (22.1%)		
Left lower lung	51 (15.0%)	43 (12.8%)	47 (14.1%)		
Nodule size (diameter, mm)	21.01 ± 5.08 (8–30)	21.29 ± 5.29 (9–30)	21.81 ± 4.79 (10–30)	F = 2.13	0.12
8–20mm	148 (43.5%)	136 (40.5%)	127(38.0%)		
21–30mm	192 (56.5%)	200 (59.5%)	207 (62.0%)		
Ultrasonic probe location				χ^2 = 0.70	0.70
Internal	NA	189 (56.3%)	198 (59.3%)		
Near	NA	94 (28.0%)	89 (26.6%)		
Outside	NA	53 (15.7%)	47 (14.1%)		
Final diagnosis				χ^2 = 4.85	0.31
Malignancy	155 (45.6%)	181 (53.9%)	163 (48.8%)		
Non-malignancy	147 (44.0%)	125 (37.2%)	135 (40.4%)		
Normal tissue	38 (11.2%)	30 (8.9%)	36 (10.8%)		
Withdrawn	25	29	31	χ^2 = 0.71	0.70

Data are presented as n/N (%) or mean ± standard deviation (n) (range).
NGB, non-guided bronchoscopy; EBUS-GS, endobronchial ultrasonography with a guide sheath; VBN, virtual bronchoscopic navigation; NA, not applicable.

Table 2
Pathological diagnosis.

Pathology result	NGB group (n = 340)	EBUS-GS group (n = 336)	Combined (EBUS-GS + VBN) group (n = 334)	Total (n = 1010)
Malignant	45.6% (155/340)	53.9% (181/336)	48.8% (163/334)	49.4% (499/1010)
Lung cancer				
Non-small-cell lung cancer (NSCLC)				
Adenocarcinoma	25.3% (86/340)	32.4% (109/336)	27.2% (91/334)	28.3% (286/1010)
Squamous carcinoma	7.1% (24/340)	6.8% (23/336)	6.0% (20/334)	6.6% (67/1010)
Other NSCLC	2.4% (8/340)	3.0% (10/336)	2.4% (8/334)	2.6% (26/1010)
Small-cell carcinoma	3.5% (12/340)	3.6% (12/336)	3.6% (12/334)	3.6% (36/1010)
Metastatic carcinoma of extrathoracic origin	1.8% (6/340)	1.8% (6/336)	1.2% (4/334)	1.6% (16/1010)
Malignant cells (unable to characterize)	5.6% (19/340)	6.3% (21/336)	8.4% (28/334)	6.7% (68/1010)
Other	0% (0/340)	0% (0/336)	0% (0/334)	0% (0/1010)
Non-malignant				
Normal lung tissue/bronchial epithelium	11.2% (38/340)	8.9% (30/336)	10.8% (36/334)	10.3% (104/1010)
Benign inflammation	10.6% (36/340)	7.7% (26/336)	6.0% (20/334)	8.1% (82/1010)
Infection				
Bacterial	10.9% (37/340)	7.1% (24/336)	9.3% (31/334)	9.1% (92/1010)
Fungal	0% (1/340)	2.1% (7/336)	1.5% (5/334)	1.3% (13/1010)
Granuloma	15.9% (54/340)	10.4% (35/336)	13.2% (44/334)	13.2% (133/1010)
Organizing pneumonia	0.3% (0/340)	0.9% (3/336)	0.9% (3/334)	0.6% (6/1010)
Interstitial lung disease	3.8% (13/340)	7.1% (24/336)	6.6% (22/334)	5.8% (59/1010)
Benign tumor	0.6% (2/340)	0% (0/336)	0.9% (3/334)	0.5% (5/1010)
Other	1.2% (4/340)	1.8% (6/336)	2.1% (7/334)	1.7% (17/1010)
Total	340	336	334	1010

Data are presented as n/N (%) or mean ± standard deviation (n) (range).
NGB, non-guided bronchoscopy; EBUS-GS, endobronchial ultrasonography with a guide sheath; VBN, virtual bronchoscopic navigation.

3.3. Safety

There were two major complications: pneumothorax and hemorrhage. The incidence of complications did not vary among the groups, and no severe adverse events occurred (Table 6). Every case that developed a pneumothorax after surgery was admitted for inpatient observation, and all recovered following treatment. Regarding hemorrhage, the bleeding stopped following treatment, and none of the patients with bleeding required therapeutic intervention.

4. Discussion

According to former studies, the rate of detection of pulmonary nodules on computed radiography (CR) is approximately 0.09–0.2% [14,15]. A systematic review of CT-screening lung cancer trials noted that a lung nodule was detected in up to 51% of study participants [16].

The probability of malignancy is < 5% [16], and in nodules 4–7 mm, 8–20 mm and 20–30 mm it is approximately 0.9%, 18% and 50%, respectively [17–20]. In patients with resected malignant nodules, survival may be as high as 80% at 5 years; in contrast, survival rates at 5 years among those with advanced malignant disease remain below 18% [13,21,22]. Therefore, once identified, a lung nodule must be evaluated to determine the likelihood of malignancy using several diagnostic criteria [2], and it is crucial to be able to distinguish lung cancer from benign lesions by using a safer and more accurate diagnostic method in order to avoid unnecessary surgical procedures.

Percutaneous needle biopsy has a high diagnostic yield and is recommended for the definitive diagnosis of peripheral lesions < 20 mm [10,23]. However, it is not suitable for the detection of nodules far from the chest wall because of a relatively high complication rate. Transbronchial biopsies (TBBs) have a low complication rate, so a transbronchial lung biopsy is an indispensable method for the diagnosis of

Table 3
Diagnosis yield.

Items	NGB group (n = 340)	EBUS-GS group (n = 336)	Combined (EBUS-GS + VBN) group (n = 334)	Analytic result	p value
Lobar distribution					
Right upper lung	35.5% (39/110)	72.4% (76/105)	71.2% (74/104)	$\chi^2 = 39.40$	< 0.01
Right middle lung	37.5% (9/24)	92.6% (25/27)	93.1% (27/29)	$\chi^2 = 28.43$	< 0.01
Right lower lung	45.2% (38/84)	66.7% (52/78)	72.5% (58/80)	$\chi^2 = 14.29$	< 0.01
Left upper lung	42.3% (30/71)	71.1% (59/83)	71.6% (53/74)	$\chi^2 = 17.61$	< 0.01
Left lower lung	47.1% (24/51)	72.1% (31/43)	76.6% (36/47)	$\chi^2 = 10.87$	< 0.01
Ultrasonic probe location					
Internal	NA	85.2% (161/189)	88.4% (175/198)	$\chi^2 = 0.86$	0.35
Near	NA	68.1% (64/94)	60.7% (54/89)	$\chi^2 = 1.10$	0.30
Outside	NA	34.0% (18/53)	40.4% (19/47)	$\chi^2 = 0.34$	0.56
Pathology					
Malignancy	43.9% (68/155)	81.8% (148/181)	85.9% (140/163)	$\chi^2 = 83.71$	< 0.01
Benign	23.1% (34/147)	52.0% (65/125)	56.3% (76/135)	$\chi^2 = 37.55$	< 0.01
Size					
8–20mm	20.9% (31/148)	47.1% (64/136)	50.4% (64/127)	$\chi^2 = 30.99$	< 0.01
21–30mm	56.8% (109/192)	89.5% (179/200)	88.9% (184/207)	$\chi^2 = 82.09$	< 0.01
Total	41.2% (140/340)	72.3% (243/336)	74.3% (248/334)	$\chi^2 = 99.4$	< 0.01

NGB, non-guided bronchoscopy; EBUS-GS, endobronchial ultrasonography with a guide sheath; VBN, virtual bronchoscopic navigation.

Table 4
Detection proportion of nodules of different sizes.

Group	8–20 mm	21–30 mm	Analytic result	p value
NGB group (n = 340)	20.9% (31/148)	56.8% (109/192)	$\chi^2 = 43.09$	< 0.01
EBUS-GS group (n = 336)	47.1% (64/136)	89.5% (179/200)	$\chi^2 = 72.84$	< 0.01
Combined (EBUS-GS + VBN) group (n = 334)	50.4% (64/127)	88.9% (184/207)	$\chi^2 = 61.01$	< 0.01

NGB, non-guided bronchoscopy; EBUS-GS, endobronchial ultrasonography with a guide sheath; VBN, virtual bronchoscopic navigation.

Table 5
Operation time.

Items	NGB group (n = 340)	EBUS-GS group (n = 336)	Combined (EBUS-GS + VBN) group (n = 334)	Analytic result	p value
Bronchoscope operation time	18.40 ± 5.19	29.06 ± 6.40	28.34 ± 5.65	F = 361.00	< 0.01
Bronchoscope arrival time	NA	11.92 ± 5.37	7.96 ± 1.18	t = 13.17	< 0.01

NGB, non-guided bronchoscopy; EBUS-GS, endobronchial ultrasonography with a guide sheath; VBN, virtual bronchoscopic navigation.

Table 6
Complications.

Complication	NGB group (n = 340)	EBUS-GS group (n = 336)	Combined (EBUS-GS + VBN) group (n = 334)	Analytic result	p value
Pneumothorax	6	7	5	$\chi^2 = 0.32$	0.85
Pneumothorax requiring intervention	2	1	3	$\chi^2 = 1.01$	0.60
Hemorrhage	4	4	3	$\chi^2 = 0.17$	0.92
Hemorrhage requiring interventional therapy	0	0	0	NA	NA
Death	0	0	0	NA	NA

NGB, non-guided bronchoscopy; EBUS-GS, endobronchial ultrasonography with a guide sheath; VBN, virtual bronchoscopic navigation; NA, not applicable.

peripheral lung lesions, even though the diagnostic yield remains unsatisfactory. Percutaneous needle biopsy and transbronchial lung biopsies cannot fully replace one another but do complement each other. VBN is a method used to guide a bronchoscope using virtual bronchoscopic (VB) images along the bronchial route to a peripheral lesion, and EBUS-GS is used to confirm the arrival of the biopsy instrument at the lesion.

To date, several reports [24,25] have proved the utility of EBUS for visualizing the parabronchial structures and confirming the precise location of PPLs as well as diagnosing them. According to one report [26], transbronchial biopsies performed using endobronchial ultrasonography with a guide sheath (TBLB-EBUS-GS) had a diagnosis rate of 77% for peripheral lung lesions and 74% in particular for those with a diameter ≤ 3 cm. Yamada et al. [27] reported that TBLB-EBUS-GS had a diagnosis rate of 67% for peripheral lung nodules and proposed that, to maximize the diagnostic accuracy, at least five biopsies should be performed. Similarly, the diagnostic yield of the EBUS group in our study was 72.3%, while the diagnostic yield of the control group was 41.2%. Apparently, EBUS has significantly improved the level of diagnosis for peripheral lung nodules. However, since EBUS is a method used for confirming arrival at the target lesion and is not a navigation device, it was reported [28,29] that there was an unsuccessful visualization rate of 11–24% due to failure to reach the lesions.

EBUS enables direct visualization of the target lesion before biopsy is attempted. However, EBUS lacks a navigation system and requires the operator to maneuver the bronchoscope blindly to the lesion based on their knowledge of prior radiological investigations similar to CT scans. VBN is a promising navigational bronchoscopy method in that it requires no specific training, has a low overall complication rate of 1.0% (95%CI 0.2–1.8%), and does not directly induce or cause severe complications [30]. In several trials [31,32] the combination of VBN with EBUS-GS improved the diagnostic yield and shortened the

examination time. A previous study [33] found that the approach to the lesion is the most significant factor influencing the diagnostic accuracy in identifying small PPLs, and the introduction of navigable technology such as an EBUS-GS or a VBN system may improve such accuracy. In our study, the combined group had an increased diagnostic yield compared with the NGB group. However, the diagnostic yields between the EBUS group and the combined group were similar, and this might suggest that the application of VBN cannot improve the diagnostic accuracy for SPNs when EBUS-GS has already used.

We evaluated the performance of a new diagnostic technique combining EBUS-GS and a VBN system for the diagnosis of small (≤ 30 mm) PPLs. Existing studies are limited by the uncertain representativeness of the study populations and by the lack of conventional bronchoscopic controls. According to our results, there was no significant difference in the diagnostic yield between the EBUS group (72.3%) and the combined group (74.3%). The required time to determine the biopsy position was significantly less in the VBN/EBUS-GS group (7.96 ± 1.18 min in the combined group versus 11.92 ± 5.37 min in the EBUS group, $p < 0.05$). However, the bronchoscope operation time was similar in the EBUS-GS and combined groups, and that in the NGB group was one third shorter than in the other groups. This was because the biopsy procedure took up most of the operation time. The diagnostic yield for PPLs > 20 mm in diameter was significantly higher than that for those < 20 mm in diameter. Thus, a radial endobronchial ultrasonography device can increase the diagnostic yield of bronchoscopy when dealing with peripheral lesions. Its use might be considered prior to diagnosis of a patient with SPNs.

4.1. Limitations

There are several limitations in our study. First, our sample size was insufficient, especially in terms of lesions with a diameter < 20 mm. Second, according to some research, four to five block specimens may not be sufficient for the diagnosis of peripheral pulmonary benign lesions with REBUS-GS using thin bronchoscopy. Third, owing to the difficulties in keeping in contact with the patients, some patients were withdrawn.

5. Conclusions

The results of our study suggest that a guided bronchoscope can increase the diagnostic yield of bronchoscopy when dealing with peripheral lesions. In addition, there was no significant difference in the diagnostic yield between the VBN-assisted group and the EBUS-GS-assisted group. With the help of VBN, the required time to determine the biopsy position was significantly less in the combined group, but the bronchoscope operation time was the same in the EBUS-GS and combined groups. Further studies are needed to compare these guided technologies with other more advanced technologies such as EBN.

Availability of data and materials

The dataset will be made publicly available on ClinicalTrials.gov (NCT02268162) after the completion of study follow-up.

Competing interests

On behalf of all authors, the corresponding author states that there are no conflicts of interest.

Ethics approval and consent to participate

This study was approved by the Regional Ethics Committee of our hospital (Tangdu Hospital). Informed consent was obtained from all subjects.

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