Original Article

Comparison of radial endobronchial ultrasound-guided transbronchial lung biopsy with distance measurement versus with guide sheath in diagnosing peripheral pulmonary lesions with a diameter ≥3 cm by thin bronchoscope

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Abstract:

OBJECTIVE: This study aims to explore the diagnostic values of radial endobronchial ultrasound-guided transbronchial lung biopsy with distance (rEBUS-D-TBLB) measurement and with guide sheath (rEBUS-GS-TBLB) for peripheral pulmonary lesions (PPLs) with a diameter ≥3 cm by thin bronchoscope.

PATIENTS AND METHODS: Six hundred and three patients with PPL (diameter ≥3 cm) were enrolled in this study. The subjects were divided into the rEBUS-D-TBLB and rEBUS-GS-TBLB groups by the random number table method. Patients were assigned to undergo rEBUS-D-TBLB or rEBUS-GS-TBLB, respectively. The histopathology, positive diagnosis rates, duration of the procedure, and postoperative adverse effects between the two groups were examined.

RESULTS: A total of 569 patients were included in this study according to the inclusion and exclusion criteria, with 282 cases in the rEBUS-D-TBLB group and 287 cases in the rEBUS-GS-TBLB group. For malignant diseases, the positive diagnosis rates of PPL in the outer/inner-middle lung bands and the right-upper/-lower lung lobes by rEBUS-D-TBLB were noninferior to those of rEBUS-GS-TBLB. The duration of the procedure of rEBUS-D-TBLB was longer than that of rEBUS-GS-TBLB. There were 14 cases of hemorrhage >50 mL, 1 case of postoperative chest pain in the rEBUS-D-TBLB group, and 3 cases of hemorrhage >50 mL in the rEBUS-GS-TBLB group.

CONCLUSION: REBUS-D-TBLB by thin bronchoscope has a high diagnostic value for PPL with a diameter ≥3 cm, which may be considered a useful alternative for rEBUS-GS-TBLB in the clinic.

Keywords:

Bronchoscopy, distance, guide sheath, peripheral pulmonary lesion, radial endobronchial ultrasound

The peripheral pulmonary lesions (PPLs) are very common lung lesions that are rarely observed before transbronchial biopsy and without pleural contact.[1-3] The diagnosis of PPL has long been a great clinical challenge compared with that of the central lesions,[4] and many efforts have been made to overcome this challenge. In 2002, the radial endobronchial ultrasound (rEBUS) technology emerged with a reported diagnostic yield of 80% for PPL.[5-7] The core of this technology is that the small ultrasound probe can reach the lesions through the bronchoscope working channel, and the ultrasonic radial scan produces a 360° image within a range of

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4 cm perpendicular to the airway. The probe can be inserted within the lesions, adjacent to the lesions, or outside the lesions to guide the biopsy.[8-10] However, the probe must be removed after reaching the lesions, and then the biopsy forceps can be inserted to perform the biopsy. Therefore, rEBUS is a nonreal-time guidance technology.

In 2004, Kurimoto *et al*.[11] first reported that rEBUS-guided transbronchial lung biopsy (rEBUS-TBLB) with guide sheath (rEBUS-GS-TBLB) can further improve the diagnostic accuracy of PPL. The detection process of rEBUS-GS-TBLB is as follows. The ultrasound probe is inserted into the guide sheath and then extended into the bronchoscopy working channel. After reaching the lesions, the ultrasound probe is removed and the guide sheath is kept *in situ*. The biopsy forceps are then inserted into the working channel through the guide sheath to obtain the appropriate tissues for biopsy. This method largely avoids the deviation of the biopsy forceps from the lesion when re-entering. It has been reported that rEBUS-D-TBLB measurement can be employed as an alternative method to rEBUS-GS-TBLB.[12] Briefly, when the lesions are revealed on an ultrasound scan, the distance between the lesions and the target bronchus is measured to determine the advanced length of biopsy forceps. Although rEBUS-D-TBLB is a nonreal-time guidance technology, its safety and validity have been proven by many researchers including our respiratory intervention team.[9,13,14] Besides, the application of this method by thin bronchoscope can further improve the diagnosis rate for PPL (53% vs. 73%).[9,15,16]

Since the guide sheath is expensive and fewer prospective studies have focused on rEBUS-TBLB with or without a guide sheath,[14] we designed this prospective randomized controlled study to investigate the diagnostic values of rEBUS-D-TBLB and rEBUS-GS-TBLB for PPL with a diameter ≥3 cm by thin bronchoscope.

Methods

Subjects

This prospective randomized controlled study was approved by the Ethics Committee of Changzhou No. 1 Hospital (Changzhou, China). All patients have signed the written informed consent. Data were collected from 603 patients who underwent rEBUS-TBLB at the Department of Respiratory and Critical Care Medicine of Changzhou No. 1 Hospital from August 2015 to April 2019. Based on the sample size of the rate indicator in the noninferiority trial, at least 198 patients were required for each group. Excluding 34 patients (9 patients with intracavity lesions, 7 patients lost to follow-up, and 18 patients whose follow-up was in progress), 569 patients (sex, 380 males and 189 females; age, 15–89 years old) who met the criteria were included in this study and were divided into rEBUS-D-TBLB group (282 patients) and rEBUS-GS-TBLB group (287 patients) by the random number table method. There were no significant differences in the number of cases, gender, size of PPL, lung bands of PPL distribution, lung lobes of PPL distribution, bronchial sign, disease spectrum, and the number of operations between patients of the two groups [Table 1], suggesting no significant impact on the outcome. The trial flow diagram is shown in Figure 1.

The inclusion criteria were as follows: (i) patients with PPL of cross-sectional diameter ≥3 cm as revealed by chest computed tomography (CT), except pure ground-glass nodules; (ii) patients without bronchial lesions on routine bronchoscopy (outer diameter of 4.0 cm); (iii) patients underwent EBUS at least once; and (iv) patients with a definitive diagnosis. The exclusion criteria were as follows: (i) patients who were unsuitable for bronchoscopy examination due to serious organic diseases; (ii) patients who were allergic to local anesthetics such as tetracaine and lidocaine; (iii) patients who were pregnant or planning to become pregnant; (iv) patients who were unable to provide informed consent and with enhanced CT value ≥100 HU; (v) patients with hemorrhagic tendency; and (vi) patients who did not want to join this study.

Methods

Preoperative preparation

Before rEBUS-D-TBLB or rEBUS-GS-TBLB, the results of the chest CT scan were thoroughly read to determine the location of the target bronchus. The size, lung bands, and lung lobes of the lesions were recorded. The lung bands were divided as reported by Baaklini *et al*.[17] The routine preoperative preparation and anesthesia bronchoscopy was performed as previously described.[18]

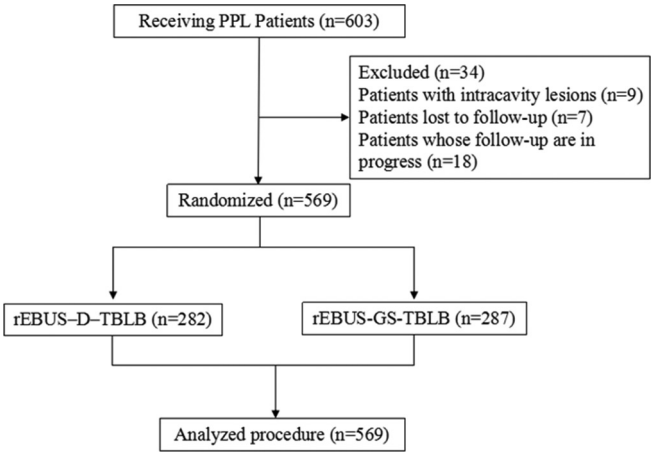

Figure 1: The trial flow diagram of this study. PPL: Peripheral lung lesion; rEBUS-D-TBLB: Radial endobronchial ultrasound-guided transbronchial lung biopsy with distance; rEBUS-GS-TBLB: Radial endobronchial ultrasound-guided transbronchial lung biopsy with guide sheath

Table 1: Baseline characteristics of patients

Baseline characteristics	rEBUS-D-TBLB group	rEBUS-GS-TBLB group	*P*
Number (cases)	282	287	
Sex (cases, male/female)	194/88	186/101	0.313
Size of PPL (cm)	4.33±1.36	4.29±1.33	0.734
Lung bands of PPL distribution (cases, outer band/inner-middle band)	185/97	201/86	0.258
Lung lobes of PPL distribution (cases, right-upper/right-middle/ right-lower/left-upper/left-lower)	92/28/50/68/44	97/23/57/70/40	0.869
Bronchial sign (positive/negative)	198/84	191/96	0.348
Disease spectrum (cases)	52/122/43/65	54/108/53/72	0.523
Numbers of operations (cases, operator A/B/C)	89/97/96	91/102/94	0.939

rEBUS-D-TBLB=Radial endobronchial ultrasound-guided transbronchial lung biopsy with distance, rEBUS-GS-TBLB=Radial endobronchial ultrasound with guide sheath transbronchial lung biopsy, PPL=Peripheral pulmonary lesion

Procedures of radial endobronchial ultrasound-guided transbronchial lung biopsy with distance

Patients in the rEBUS-D-TBLB group received routine bronchoscopes for observation of the central airway. If no intraluminal lesions were found, the bronchoscope was wedged into the subsegmental or sub-subsegmental bronchus, and the ultrasound probe was inserted through the bronchoscope working channel. The ultrasonic scan was turned on when meeting resistance and the ultrasound probe was then slowly withdrawn while the ultrasonic scanning image was observed. The probe was advanced and pulled back several times after the images of representative lesions were observed to confirm the touching of the probe to lesions and to obtain the optimum location and record the relations between probes and lesions. The assistant marked the insertion site of the ultrasonic probe at the opening of the bronchoscopy biopsy channel, and then the probe was pulled back slowly and stayed at the target bronchial opening. After the distance between the marker and the opening location of the working channel was measured,[14,19] the probe was withdrawn. The biopsy forceps were inserted into the opening location of the target bronchus and the required advanced length of biopsy forceps was the same as the measured distance above. Once reaching the required length, the biopsy forceps were opened and then advanced 1–2 mm to clip the tissues. Four to six specimens were obtained for the pathological examination.

Procedures of radial endobronchial ultrasound-guided transbronchial lung biopsy with guide sheath

Patients in the rEBUS-GS-TBLB group received routine bronchoscopes to inspect the central airway. If no intraluminal lesions were found, the bronchoscope was wedged into the subsegmental or sub-subsegmental bronchus. The small ultrasound probe was then inserted into the guide sheath and kept in a fixed position. The guide sheath-covered probe was advanced through the bronchoscope working channel. On meeting resistance, the ultrasonic scan was turned on and the ultrasound probe was then slowly withdrawn while the ultrasonic scanning image was observed. When the image of the representative lesion was observed, the probe was advanced and pulled back several times to confirm the touching of the probe to lesions and to obtain the optimum location. The guide sheath was then fixed and the probe was withdrawn from the guide sheath. The biopsy forceps were inserted into the guide sheath to perform the biopsy.[20] Eight to ten specimens were obtained for the pathological examination.

Evaluation indicators

The diagnostic yield, duration of the procedure, and safety of rEBUS-D-TBLB and rEBUS-GS-TBLB for PPL with a diameter ≥3 cm were assessed.

Statistical analysis

All data were analyzed using Statistical Product and Service Solutions (SPSS, IBM, Chicago, USA) 19.0 software. The enumeration data were expressed as number/percentage (n/%). The u-test for the noninferiority trial was used for inter-group comparisons. The Chi-square test was employed for comparisons within groups. The measurement data were expressed as mean ± standard deviation. The mean was compared by one-way analysis of variance. $P \leq 0.05$ indicated statistically significant differences.

Results

The positive diagnosis rates of radial endobronchial ultrasound-guided transbronchial lung biopsy with distance and radial endobronchial ultrasound-guided transbronchial lung biopsy with guide sheath

The positive diagnosis rates of benign and malignant diseases

The final diagnosis of patients in the rEBUS-D-TBLB and rEBUS-GS-TBLB groups is shown in Table 2, and partial pathological results are shown in Figure 2. As shown in Table 3, the numbers of positive diagnosis of benign diseases by rEBUS-D-TBLB or rEBUS-GS-TBLB were 52 cases (64.2%) and 54 cases (65.06%). Furthermore, the numbers of positive diagnosis of malignant

Table 2: The final diagnosis of patients

Final diagnosis	Diagnosed by rEBUS-D-TBLB (cases)	Diagnosed by rEBUS-GS-TBLB (cases)
Positive diagnosis of malignant diseases		
Adenocarcinoma	123	107
Squamous cell carcinoma	30	32
Small cell carcinoma	3	4
Poorly differentiated neuroendocrine carcinoma	4	13
Mucosa-associated lymphoid tissue lymphoma	4	2
Large cell carcinoma	1	0
Adenosquamous carcinoma	0	1
Sarcomatoid carcinoma	0	1
Metastatic carcinoma	0	1
Positive diagnosis of benign diseases		
Pneumonia	39	31
Tuberculosis	5	12
Pulmonary cryptococcosis	3	1
Pulmonary mycosis	1	3
Cryptogenic organizing pneumonia	1	3
Inflammatory pseudotumor	2	2
Podoconiosis	1	0
Pulmonary nodule	0	2
Negative diagnosis of malignant diseases		
Adenocarcinoma	24	31
Squamous cell carcinoma	4	4
Small cell carcinoma	1	2
Poorly differentiated neuroendocrine carcinoma	7	2
Adenosquamous carcinoma	0	3
Sarcomatoid carcinoma	0	1
Negative diagnosis of benign diseases		
Pneumonia	13	17
Tuberculosis	8	7
Pulmonary cryptococcosis	1	3
Cryptogenic organizing pneumonia	4	2
Pulmonary nodule	3	0
Total	282	287

rEBUS-D-TBLB=Radial endobronchial ultrasound-guided transbronchial lung biopsy with distance, rEBUS-GS-TBLB=Radial endobronchial ultrasound with guide sheath transbronchial lung biopsy

diseases by rEBUS-D-TBLB or rEBUS-GS-TBLB were 165 cases (82.09%) and 161 cases (78.92%). The positive diagnosis rate of total diseases by rEBUS-D-TBLB or rEBUS-GS-TBLB was 76.95% and 74.91% and the positive diagnosis rate by rEBUS-D-TBLB of malignant diseases was noninferior to that of rEBUS-GS-TBLB ($P \leq 0.05$).

The positive diagnosis rates of the lesions in different lung bands

As shown in Table 4, the numbers of positive diagnosis of lesions in outer bands by rEBUS-D-TBLB or rEBUS-GS-TBLB were 138 cases (74.59%) and 161 cases (76.3%) and the numbers of positive diagnosis of lesions in inner-middle bands by rEBUS-D-TBLB or rEBUS-GS-TBLB were 79 cases (81.44%) and 55 cases (72.37%). The positive diagnosis rates of lesions in different lung bands by rEBUS-D-TBLB were noninferior to those of rEBUS-GS-TBLB ($P \leq 0.05$).

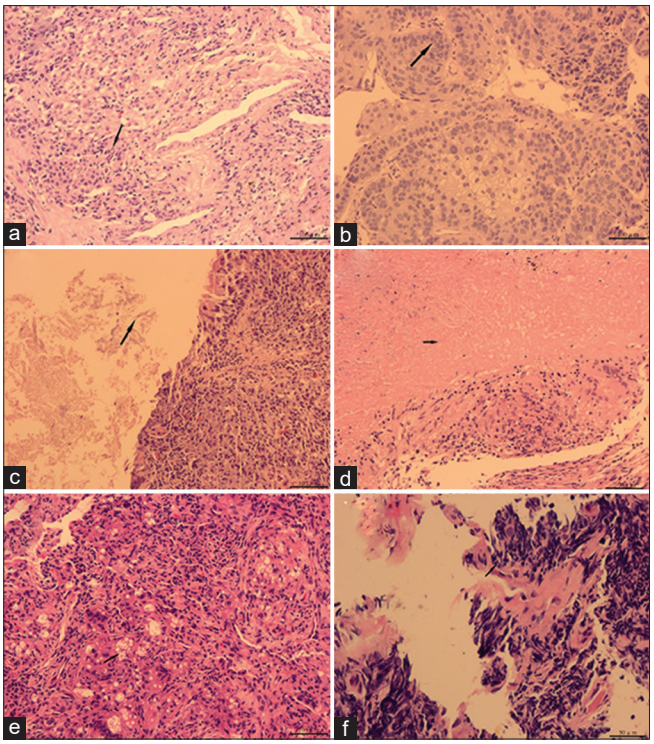

Figure 2: The representative pathological images of patients who underwent rEBUS-TBLB. (a) A representative pathological image of patients with pulmonary adenocarcinoma diagnosed by rEBUS-D-TBLB. Arrow points to lung adenocarcinoma cells; magnification ×200. (b) A representative pathological image of patients with pulmonary squamous carcinoma diagnosed by rEBUS-GS-TBLB. Arrow points to lung squamous cancer cells; magnification ×200. (c) A representative pathological image of patients with pulmonary aspergillosis diagnosed by rEBUS-GS-TBLB. Arrow points to *Aspergillus* hyphae; magnification ×200. (d) A representative pathological image of patients with pulmonary tuberculosis rEBUS-D-TBLB. Arrow points to typical caseous necrosis of pulmonary tuberculosis; magnification ×200. (e) A representative pathological image of patients with pulmonary cryptococcosis diagnosed by rEBUS-D-TBLB. Arrow points to *Cryptococcus*; magnification ×200. (f) A representative pathological image of patients with small cell lung cancer (SCLC) diagnosed by rEBUS-GS-TBLB. Arrow points to SCLC cells; magnification ×400. rEBUS-D-TBLB: Radial endobronchial ultrasound-guided transbronchial lung biopsy with distance; rEBUS-GS-TBLB: Radial endobronchial ultrasound-guided transbronchial lung biopsy with guide sheath

The positive diagnosis rates of the lesions in different lung lobes

The numbers of positive diagnosis of lesions in the right-upper lobe by rEBUS-D-TBLB or rEBUS-GS-TBLB were 73 cases (79.35%) and 72 cases (74.23%) and the numbers of positive diagnosis of lesions in the right-lower lobe by rEBUS-D-TBLB or rEBUS-GS-TBLB were 40 cases (80%) and 41 cases (71.93%). The test for

noninferiority demonstrated that the positive diagnosis rates of lesions in the right-upper and right-lower lung lobe by rEBUS-D-TBLB were noninferior to those of rEBUS-GS-TBLB ($P \leq 0.05$). Furthermore, the numbers of positive diagnosis of lesions in the left-upper lobe by rEBUS-D-TBLB or rEBUS-GS-TBLB were 48 cases (70.59%) and 58 cases (82.26%) and the numbers of positive diagnosis of lesions in the left-lower lobe by rEBUS-D-TBLB or rEBUS-GS-TBLB were 33 cases (75%) and 29 cases (72.5%). Noninferiority was not shown in the positive diagnosis rates of lesions in the left-upper and left-lower lobe by rEBUS-D-TBLB ($P > 0.05$) [Table 5].

The duration of the procedure of radial endobronchial ultrasound-guided transbronchial lung biopsy with distance and radial endobronchial ultrasound-guided transbronchial lung biopsy with guide sheath

As shown in Figure 3, the procedure duration of

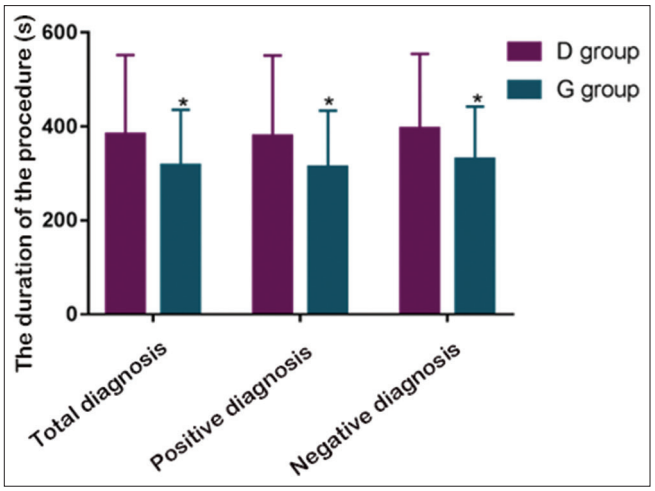

Figure 3: The duration of the procedure of the rEBUS-D-TBLB group and rEBUS-GS-TBLB group. D group: REBUS-D-TBLB group. G group: REBUS-GS-TBLB. $P \leq 0.05$

Table 3: Analysis of positive diagnosis rates of benign and malignant diseases using noninferiority *U*-test

Groups		Total diagnosis (cases)	Positive diagnosis (cases)	Negative diagnosis (cases)	Positive diagnosis rate (%)	Noninferiority *U*-test	
						U	*P*
rEBUS-D-TBLB	Total diseases	282	217	65	76.95	3.36	≤0.05
rEBUS-GS-TBLB		287	215	72	74.91		
rEBUS-D-TBLB	Benign diseases	81	52	29	64.20	1.22	>0.05
rEBUS-GS-TBLB		83	54	29	65.06		
rEBUS-D-TBLB	Malignant diseases	201	165	36	82.09	3.35	≤0.05
rEBUS-GS-TBLB		204	161	43	78.92		

rEBUS-D-TBLB=Radial endobronchial ultrasound-guided transbronchial lung biopsy with distance, rEBUS-GS-TBLB=Radial endobronchial ultrasound with guide sheath transbronchial lung biopsy

Table 4: Analysis of positive diagnosis rates of lesions in different lung bands using noninferiority *U*-test

Lung bands	Group	Total diagnosis (cases)	Positive diagnosis (cases)	Negative diagnosis (cases)	Positive diagnosis rate (%)	Noninferiority *U*-test	
						U	*P*
Outer band	rEBUS-D-TBLB	185	138	47	74.59	1.91	≤0.05
	rEBUS-GS-TBLB	211	161	50	76.30		
Inner-middle band	rEBUS-D-TBLB	97	79	18	81.44	2.95	≤0.05
	rEBUS-GS-TBLB	76	55	21	72.37		

rEBUS-D-TBLB=Radial endobronchial ultrasound-guided transbronchial lung biopsy with distance, rEBUS-GS-TBLB=Radial endobronchial ultrasound with guide sheath transbronchial lung biopsy

Table 5: Analysis of positive diagnosis rates of lesions in different lung lobes using noninferiority *U*-test

Lung lobes	Group	Total diagnosis (cases)	Positive diagnosis (cases)	Negative diagnosis (cases)	Positive diagnosis rate (%)	Noninferiority *U*-test	
						U	*P*
Right-upper lobe	rEBUS-D-TBLB	92	73	19	79.35	2.47	≤0.05
	rEBUS-GS-TBLB	97	72	25	74.23		
Right-middle lobe	rEBUS-D-TBLB	28	24	4	85.71		
	rEBUS-GS-TBLB	23	20	3	86.96		
Right-lower lobe	rEBUS-D-TBLB	50	40	10	80.00	2.2	≤0.05
	rEBUS-GS-TBLB	57	41	16	71.93		
Left-upper lobe	rEBUS-D-TBLB	68	48	20	70.59	–0.23	>0.05
	rEBUS-GS-TBLB	70	58	12	82.26		
Left-lower lobe	rEBUS-D-TBLB	44	33	11	75.00	1.3	>0.05
	rEBUS-GS-TBLB	40	29	11	72.50		

rEBUS-D-TBLB = Radial endobronchial ultrasound-guided transbronchial lung biopsy with distance, rEBUS-GS-TBLB = Radial endobronchial ultrasound with guide sheath transbronchial lung biopsy

rEBUS-D-TBLB for positive diagnosis and the negative diagnosis was significantly longer than those of rEBUS-GS-TBLB ($P \leq 0.05$).

The adverse effects of radial endobronchial ultrasound-guided transbronchial lung biopsy with distance and radial endobronchial ultrasound-guided transbronchial lung biopsy with guide sheath

There were 14 patients with hemorrhage >50 mL (4.96%, 14/282) and 1 patient with chest pain (0.35%, 1/282) after rEBUS-D-TBLB, while 3 patients had hemorrhage >50 mL (1.05%, 3/287) after rEBUS-GS-TBLB. No pneumothorax and infection were found in the two groups [Table 6].

Discussion

The application of EBUS guidance has improved the accuracy of bronchoscopy in diagnosing PPL to a great extent.[19] rEBUS-TBLB has been considered the only alternative method to bronchoscopy for the early screening of PPL in patients with a high risk of lung cancer.[21] Currently, the limitation is that rEBUS-TBLB belongs to "nonreal-time" guided biopsy, but rEBUS-TBLB and the guide sheath/distance measurement methods in combination can break through this limitation and elevate the positive diagnosis rates. rEBUS-GS can be used for molecular diagnosis of patients with peripheral NSCLC, including ALK translocations and EGFR mutations.[19] However, the application of small forceps through GS in small specimens may hamper diagnosis and molecular analysis.[22] It has been reported that rEBUS-D-TBLB has high specificity and sensitivity, excellent safety, and low cost in the diagnosis of malignant PPLs.[9] Nevertheless, the diagnostic efficacy, duration of the procedure, and safety of rEBUS-D-TBLB and rEBUS-GB-TBLB have not been prospectively investigated.

In a previous prospective randomized controlled study, we compared the diagnostic values of rEBUS-D-TBLB and rEBUS-GS-TBLB for PPL with a diameter ≥3 cm by thin bronchoscope from August 2015 to April 2019. Results showed that rEBUS-D-TBLB was not inferior to rEBUS-GS-TBLB in the diagnosis of malignant PPL. The diagnostic rate of rEBUS-D-TBLB was not inferior to that of rEBUS-GS-TBLB regardless of PPL distribution in the outer or middle lung bands. For right lobe PPL, the diagnostic rate of rEBUS-D-TBLB was not inferior to that of rEBUS-GS-TBLB, and the diagnostic rate of right middle lobe PPL needs to be further clarified by accumulating sample size. However, the operation time of rEBUS-D-TBLB was longer than that of rEBUS-GS-TBLB, and there were more adverse events, such as hemorrhage and chest pain. Our study confirmed that rEBUS-D-TBLB has excellent diagnostic performance and is slightly inferior to rEBUS-GS-TBLB in terms of operation time and safety.

Table 6: The adverse effects of the radial endobronchial ultrasound-guided transbronchial lung biopsy with distance and radial endobronchial ultrasound with guide sheath transbronchial lung biopsy group

Adverse effects	rEBUS-D-TBLB (cases/%)	rEBUS-GS-TBLB (cases/%)
Hemorrhage >50 mL	14/4.96	3/1.05
Postoperative chest pain	1/0.35	0/0.00
Pneumothorax	0/0.00	0/0.00
Infection	0/0.00	0/0.00

rEBUS-D-TBLB=Radial endobronchial ultrasound-guided transbronchial lung biopsy with distance, rEBUS-GS-TBLB=Radial endobronchial ultrasound with guide sheath transbronchial lung biopsy

Although rEBUS-D-TBLB has noninferior diagnosis efficacy to rEBUS-GS-TBLB, many experts have adopted rEBUS-GS-TBLB because it is easy to achieve repeated biopsy.[11,23-25] However, rEBUS-GS-TBLB has the following 4 drawbacks: (1) the bending part of the bronchoscope becomes rigid after the guide sheath is inserted into the bronchoscope, which makes the bronchoscope difficult to enter the bronchus that requires a larger bending angle of bronchus, such as the bronchus at the tips of both lungs; (2) the guide sheath is easy to be bent and folded, which hinders the smooth insertion of biopsy forceps or cell brushes; (3) the specimens obtained by guide sheath biopsy are relatively small, leading to some limitations in diagnosing lymphoma, mixed tumors, benign diseases, and complex diseases; and (4) the guide sheath is expensive, which will cause a high economic cost on patients. Due to these inherent drawbacks of rEBUS-GS-TBLB, especially the high economic cost, it is difficult to popularize this technology.

Therefore, our respiratory intervention team conducted some meaningful explorative studies on rEBUS-D-TBLB, an alternative approach of rEBUS-GS-TBLB. For example, we diagnosed 117 PPL patients using rEBUS-D-TBLB by thin bronchoscope, and the total diagnosis rate was 65.0% (76/117), including 66 patients with malignant diseases and 10 patients with benign diseases.[26] From October 2013 to November 2016, we retrospectively analyzed the data of 193 malignant PPL patients who underwent rEBUS-D-TBLB by thin bronchoscopy and found that the diagnosis sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 63.73%, 100%, 100%, 65.85%, and 78.40%, respectively.[9] Besides, a prospective randomized cross-control study of rEBUS-D-TBLB and rEBUS-GS-TBLB was conducted in 47 patients with PPL under thin bronchoscopy, which preliminarily confirmed that there was no significant difference in the diagnostic values between rEBUS-D-TBLB and

rEBUS-GS-TBLB for lesions in different lung lobes or with different sizes.[14] In like manner, in this study, we also found that rEBUS-D-TBLB and rEBUS-GS-TBLB had similar diagnosis values for PPL with a diameter ≥ 3 cm. The possible reasons might be as follows: (1) the outer diameter of the thin bronchoscope is 4–4.2 mm, allowing it to advance further and partly replace the function of guide sheath; (2) since the absence of guide sheath during diagnosis, the bending part of the bronchoscope is soft and not easy to be folded, making the bronchoscope more flexibly to reach the bronchus with a larger bending angle and the biopsy forceps to access more smoothly; and (3) the pathological diagnosis has more clinical value because it can obtain larger specimens without a guide sheath.

In the current study, we found that the duration of the procedure of rEBUS-D-TBLB was about 1 min longer than that of rEBUS-GS-TBLB. 4.96% of patients who underwent rEBUS-D-TBLB suffered from intraoperative hemorrhage, as did David W Hsia *et al*.[27] The rEBUS-D-TBLB resulted in slightly more adverse effects than rEBUS-GS-TBLB, while these adverse effects were improved by routine treatments, such as local hemostasis. Furthermore, compared with a previous study,[13] rEBUS-D-TBLB did not result in massive hemorrhage, life danger, and complications such as hemopneumothorax and infection. The findings of this study are in accordance with the previous study.[14] Furthermore, rEBUS-D-TBLB can reduce the economic cost since the expensive guide sheath is not necessary. Hence, rEBUS-D-TBLB is especially suitable for the global population not only for China.

Conclusion

rEBUS-D-TBLB has a high positive diagnosis rate for PPL with a diameter ≥3 cm. The positive rates were not inferior to rEBUS-GS-TBLB in the diagnosis of malignant diseases and right lobe lesions. In addition, the diagnosis rates of rEBUS-D-TBLB were not affected by the distribution of lesions in lung bands. The duration of the procedure of rEBUS-D-TBLB was slightly longer than that of rEBUS-GS-TBLB, but the economic cost of rEBUS-D-TBLB is relatively lower. Therefore, rEBUS-D-TBLB is suitable for patients who are financially constrained.

However, there are several limitations. Firstly, due to fewer adverse effects in the rEBUS-GS-TBLB group to meet the data requirements for statistical analysis, we have not carried out statistical analysis between the adverse effects of the rEBUS-D-TBLB and rEBUS-GS-TBLB groups. Secondly, patients with obvious CT lesions and hemorrhagic tendencies were excluded, which may underestimate the hemorrhage risk of rEBUS-D-TBLB. For patients with high hemorrhage risk, the rEBUS-GS-TBLB is preferable over rEBUS-D-TBLB. We believe that rEBUS-D-TBLB will be practiced better with the shortened duration of the procedure, reduced adverse effects, increased safety, and improved tolerance and comfort of patients caused by the combination of painless and rapid on-site examination technology and the optimization of operator skills. Furthermore, we will enroll more subjects to perform the comparison of the adverse effects of the two methods in future.

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Conflicts of interest

There are no conflicts of interest.

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