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Usefulness of virtual bronchoscopic navigation combined with endobronchial ultrasound guided transbronchial lung biopsy for solitary pulmonary nodules

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Abstract

Background: The aim of this study was to evaluate the diagnostic utility of virtual bronchoscopic navigation (VBN) combined with endobronchial ultrasound (EBUS) guided transbronchial lung biopsy for solitary pulmonary nodules (SPN).

Methods: A total of 115 patients with suspected SPN who underwent transbronchial lung biopsy were evaluated. The patients were randomly divided into an EBUS (EBUS) group and a virtual bronchoscopic navigation combined with endobronchial ultrasound (VBN+EBUS) group. The diagnostic yield and examination time were compared.

Results: There was no significant difference in the diagnostic yield between the VBN+EBUS group and the EBUS group (83.6% vs 66.7%, $P = .419$). When the lesions less than 20 mm in diameter of the lesions were analyzed, the diagnostic yield was higher in the VBN+EBUS group than in the EBUS group (80.0% vs 53.6%, $P = .041$). The time for positioning lesions in VBN+EBUS group was less than that in EBUS group (5.67 ± 2.48 min vs 8.65 ± 2.23 min, $P = .015$). But the total examination time was not significantly different between the 2 groups (20.59 ± 2.12 min vs 21.53 ± 1.62 min, $P = .236$). The incidence of complications did not differ between the 2 groups.

Conclusions: In conclusion, VBN can shorten the positioning time and it is a safe and effective technique for pulmonary nodules.

Abbreviations: EBUS = endobronchial ultrasound, SPN = solitary pulmonary nodules, VBN = virtual bronchoscopic navigation.

Keywords: endobronchial ultrasound, solitary pulmonary nodules, transbronchial lung biopsy, virtual bronchoscopic navigation

1. Introduction

Lung cancer leads to the highest incidence and mortality in the world.[1] Most patients with lung cancer have developed in the middle and advanced stage, with the 5-year survival rate only 15.6%. Meanwhile, the 5-year survival rate of early lung cancer patients can be reached as high as 80%, therefore, early diagnosis of lung cancer is particularly important.[2] In recent years, with the extensive application of chest computed tomography (CT), especially high-resolution CT (HRCT), solitary pulmonary nodules (SPN) have been detected in early time. The diagnosis of SPN depends on sufficient tissue or cell material to obtain pathological diagnosis.[3] Surgical biopsy is the most accurate diagnostic method, but small lesions are usually benign and do not require surgical resection. CT-guided percutaneous transthoracic needle biopsy shows high diagnostic accuracy, is recommended for definite diagnosis of the SPN in diameter of 20 mm or less, but also often associated with complications such as pneumothorax, hemoptysis.[4,5] There were fewer complications of transbronchial lung biopsy (TBLB), but lower yield for the small lesions in diameter of 20 mm or less.[6] In recent years, virtual bronchoscopic navigation (VBN) has been gradually applied in clinical, a number of research confirmed that EBUS combined with VBN guide could obviously improve the diagnostic accuracy of pulmonary peripheral lesions.[7–11] Meanwhile, the study of diagnostic accuracy of EBUS combined with in SPN was less. In this study, the diagnostic rate of TBLB in SPN guided by EBUS combined with VBN was discussed. The purpose of this study was to explore the clinical application value of EBUS combined with VBN guiding TBLB for SPN.

2. Materials and methods

2.1. Patients

Total of 115 patients with SPN was recruited, who underwent TBLB guided by EBUS alone or VBN+EBUS in the Endoscopy Center of Nanjing Chest Hospital from January 2015 to December

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2017. Inclusion criteria: chest CT showed pulmonary nodules in diameter from 8 mm to 30 mm and were wrapped around by parenchyma, no lesion was detected under endotracheal. Exclusion criteria: anaphylaxis, risk of bleeding, poor cardiopulmonary function, or nonconformity to the standard. The enrolled patients were randomly divided into VBN+EBUS group and EBUS group, with 55 cases of VBN+EBUS group and 60 EBUS group.

The protocol was approved by the Ethics Committee of the Nanjing Chest Hospital, and written informed consent was obtained from all patients before the study. Doctors recorded the obtainment of the written consent in patients' clinical files. The informed consent was signed before undergoing bronchoscopy, the patients also noted in the check agreement that she/he was informed about and agreed to participate in this study. The Ethics Committee approved this written consent procedure and had unscheduled inspection of documents and records to assure the study was compliant.

2.2. Procedure

All patients underwent multilayer spiral chest CT scan (64-slice, 0.5 mm-1.0 mm) before bronchoscopy. The scanned DICOM data was imported to computer via VBN software (DirectPath V1.02, Cybernet Systems), creating the target virtual bronchoscope bronchial images automatically, and the guidance pathway to lesions was established (Fig. 1A and B). Patients of both groups underwent local anesthesia with 2% lidocaine aerosol inhalation, and 2% lidocaine nasal and endotracheal drip, fasting for solids and liquids 6 hours before operation.

VBN+EBUS group: bronchoscope (Olympus BF-P260F, outer diameter in 4.0 mm, working aperture in 2.0 mm) was navigated to the target of the bronchi by the VBN system, pushing into the ultrasonic probe (UM-S20-20R, Olympus) to the corresponding segment and then explored to low echo ultrasound images (Fig. 1C). Afterward withdrew the ultrasonic probe slowly and measured the distance from the opening of segmental bronchus to area of the lesion indicated by ultrasound. Then, according to the measured distance, repeated observing whether the operation path was correct by the ultrasonic probe twice. The biopsy forceps was inserted to the positioning of the bronchial subsegment after ultrasonic probe was withdrawn, for sampling at the same position where the lesion located by the ultrasound.

EBUS group: according to the location of the lesion determined by the preoperative chest CT, the ultrasonic probe was pushed to the corresponding subsegment, remaining operation steps were same with the VBN+EBUS group.

All locations were biopsied for 3 times, and the samples were fixed in 4% formaldehyde solution, with the smear sent for pathological examination (Fig. 1D). Time required for EBUS to location: from the bronchoscope reaching the carina to ultrasonogram of the lesions attained. Total operating time: from the bronchoscope reaching the carina to exiting the glottis.

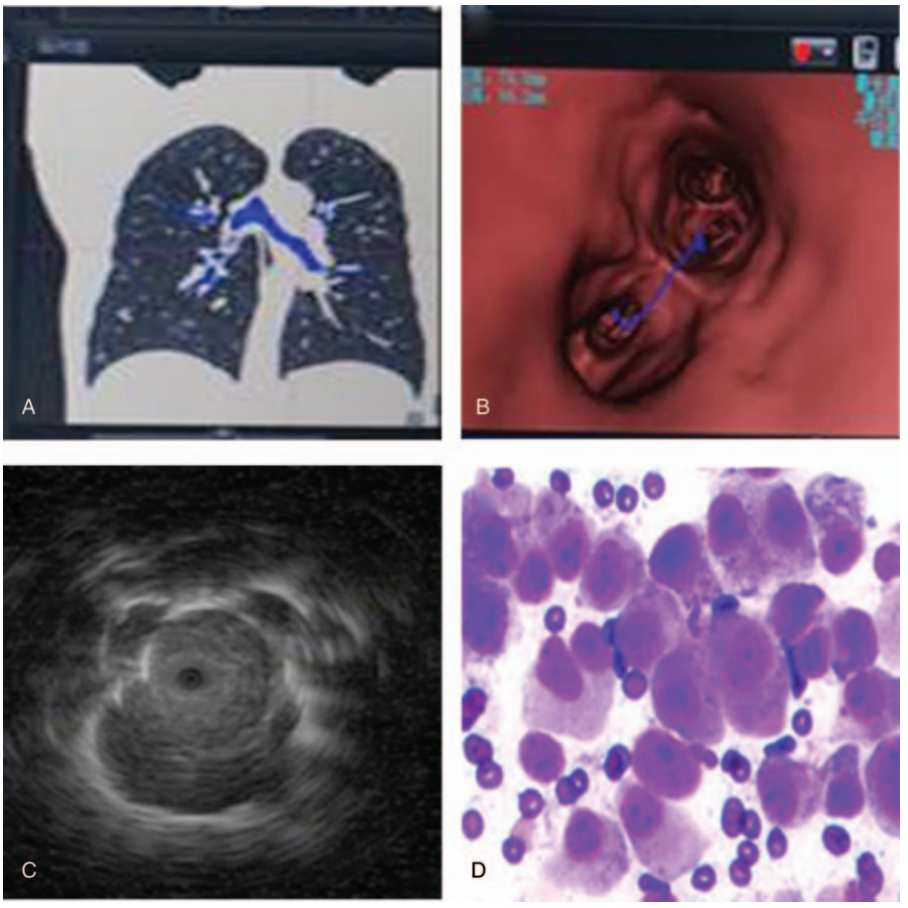

Figure 1. (A) The coronal position setting navigation path. (B) VBN demonstrated a precise route to the peripheral nodule. (C) EBUS showed a low-echoic nodule surrounded by a highly reflective interface produced between the aerated lung and the lesion. (D) Adenocarcinoma of the lung was diagnosed from EBUS-guided TBLB. EBUS = endobronchial ultrasound, TBLB = transbronchial lung biopsy, VBN = virtual bronchoscopic navigation.

2.3. Follow-up and intervention

If pulmonary lesions are not diagnosed by the bronchoscopy, we recommend that patients consider other further diagnostic methods, including CT-guided percutaneous puncture or surgical intervention. Patients were followed up for 6 months if they refused further examination.

2.4. Statistical analysis

SPSS software version 19.0 (SPSS, Chicago, IL) was used for data analysis. Measurement data expressed by mean ± standard deviation, enumeration data expressed as a percentage. Direct comparisons between groups were accomplished with a Student *t* test. The characteristics were compared using χ^2 tests. Value of $P < .05$ was considered statistically significant.

3. Result

3.1. Clinical characteristics

Among 115 patients with SPN, 55 were in the VBN+EBUS group, of which 34 were male, 21 were female, the oldest was 70 years old, and the youngest was 35 years old, with an average of 56.7 ± 11.8 years old, and the lesion diameter was (27 ± 2) mm. Among the 60 patients in EBUS group, 35 were male, 25 were female, the oldest was 72 years old, and the youngest was 36 years old, with an average age of 57.8 ± 12.3 years, and the diameter of the lesion was (28 ± 1) mm. Lesions of VBEBUS group located in the upper lobe is 15 cases (27.3%), right middle lobe in 7 cases (12.7%), 16 cases (29.1%), upper left upper lobe 6 cases (10.9%), and 11 in left lower lobe (20.0%). Lesions of group EBUS located in the upper lobe in 15 cases (25.0%), 8 cases (13.3%) in right middle lobe, 17 cases (28.3%) in right lower lobe, left upper lobe 7 cases (11.7%), left lower lobe in 13 (21.7%). There was no statistically significant difference between the 2 groups (Table 1).

3.2. Diagnostic yield

The diagnostic yield of EBUS group and VBN+EBUS group was 66.7% and 83.6% respectively, and the difference between the 2 groups was not statistically significant ($P = .419$). In the SPN with diameter <20 mm, the diagnostic yield of the VBN+EBUS group was 80.0%, higher than the diagnostic yield of the EBUS group of 53.6%, and the difference was statistically significant ($P = .041$). The diagnosis yield of benign lesions in EBUS group and VBN +EBUS group was 65% and 82% respectively, and the difference was not statistically significant ($P = .240$). The diagnosis yield of malignant lesions in EBUS group and VBN+EBUS group was 67.5% and 85.7% respectively, and the difference was not statistically significant ($P = .057$). However, there was no significant difference in diagnosis rate between EBUS group and VBN+EBUS group in different location lesions (Table 2).

Table 1

Baseline characteristics and final diagnoses.

Variables	EBUS group (n = 60)	VBN+EBUS group (n = 55)	*P* values
Age (yr, median; range)	56.7 ± 11.8	57.8 ± 12.3	.005
Male, n, %	35/60 (58.3%)	34/55 (61.8%)	.425
Lesion size (mm, median; range)			
<20 mm, n, %	28/60 (46.7%)	25/55 (45.5%)	.535
20–30 mm, n, %	32/60 (53.3%)	30/55 (54.5%)	.534
Lesion location			
Right upper lobe, n, %	15 (25.0%)	15 (27.3%)	.497
Right middle lobe, n, %	8 (13.3%)	7 (12.7%)	.576
Right lower lobe, n, %	17 (28.3%)	16 (29.1%)	.551
Left upper lobe, n, %	7 (11.7%)	6 (10.9%)	.572
Left lower lobe, n, %	13 (21.7%)	11 (20.0%)	.520
Final diagnosis			
Malignant disease			
Primary lung cancer n, %	35 (58.3%)	30 (54.5%)	.544
Metastatic lung cancer n, %	5 (8.3%)	5 (9.1%)	.553
Non-malignant disease			
Infectious disease n, %	14 (23.3%)	12 (21.8%)	.479
Other benign condition n, %	6 (10.0%)	8 (14.5%)	.442

EBUS = endobronchial ultrasound, VBN = virtual bronchoscopic navigation.

Table 2

Clinical factors associated with diagnostic yield.

Factors	EBUS group (n = 60)	VBN+EBUS group (n = 55)	*P* values
Diagnostic yields	40 /60 (66.7%)	46/55 (83.6%)	.029
Gender			
Male	24/35 (68.6%)	28/34 (82.4%)	.147
Female	16/25 (64.0%)	18/21 (85.7%)	.190
Lesion size (mm, median; range)			
<20 mm, n, %	15/28 (53.6%)	20/25 (80.0%)	.041
20–30 mm, n, %	25/32 (78.1%)	26 /30 (86.7%)	.294
Lesion location			
Right upper lobe, n, %	12/15 (80.0%)	14/15 (93.3%)	.299
Right middle lobe, n, %	5/8 (62.5%)	5/7 (71.4%)	.573
Right lower lobe, n, %	11/17 (64.7%)	14/16 (87.5%)	.131
Left upper lobe, n, %	4/7 (57.1%)	5/6 (83.3%)	.343
Left lower lobe, n, %	8/13 (61.5%)	8/11 (72.7%)	.444
Final diagnosis			
Malignant disease n, %	27/40 (67.5%)	30/35 (85.7%)	.057
Non-malignant disease n, %	13/20 (65.0%)	16/20 (80.0%)	.240

EBUS = endobronchial ultrasound, VBN = virtual bronchoscopic navigation.

3.3. Procedure times

In regard to the time for localization of the lesion, the VBN+EBUS group was 5.67 ± 2.48 minutes, the EBUS group was 8.65 ± 2.23 minutes, and the VBN+EBUS group was significantly shorter than the EBUS group ($P = .015$). The total examination time of VBN+EBUS group was shorter than EBUS group, but the difference was not statistically significant ($P = .236$) (Table 3).

3.4. Complications

One case of VBN+EBUS group was complicated with pneumothorax (compressed 15%), and the pneumothorax was healed after 5 days of oxygen inhalation. In the EBUS group, there was hemorrhage in 1 case, with the bleeding amount about 20 mL, and stopped after local injection of thrombin and epinephrine. There was no significant difference between the 2 groups.

Table 3

Procedure times in the EBUS and VBN+EBUS group.

Procedure time	EBUS group (n = 60)	VBN+EBUS group (n = 55)	*P* values
Time for positioning lesions, min	8.65 ± 2.23 min	5.67 ± 2.48 min	.015
Total examination time, min	21.53 ± 1.62 min	20.59 ± 2.12 min	.236

EBUS = endobronchial ultrasound, VBN = virtual bronchoscopic navigation.

4. Discussion

Histopathology is the "gold standard" for diagnosis of SPN, and the biopsy methods include TBLB. Conventional bronchoscopy can attain to the 4th to 5th bronchial tube. By virtue of ultrafine bronchoscope, endobronchial ultrasound (EBUS) and virtual navigation technology, the operating field can be extended to 6th to 7th bronchial tube and even further, which contribute to more accurate positioning of SPN, and multiple combined techniques guided TBLB may improve the diagnosis rate.

Diagnostic rate for SPN through traditional TBLB is not ideal, which may be less than 20%.[12] The ACCP lung cancer guidelines give preference to the selection of radial ultrasound-guided TBLB for diagnosis of SPN as an important mean.[11] Numbers of studies have also shown that compared with traditional TBLB, EBUS guided TBLB could significantly improve the diagnostic rate of peripheral pulmonary solitary lesions.[12] About 8% to 20.8% of the lesions were not reached, therefore some scholars considered that the radial ultrasound failed to realize self-navigation and positioning.[13,14]

Virtual navigation is one of the methods in currently clinical use to improve the diagnostic approach to peripheral small lesions. Scan data from multidetector chest CT acquired from patients before bronchoscopy were transferred to a workstation on which VBN software automatically created virtual bronchoscopic images. With the same pixel value range of endobronchial surface, the 3-dimensional reconstruction gives artificial pseudocolor and simulate endobronchial condition, obtaining the consecutive images as a bronchoscope in a monitor positioned beside the video-bronchoscopic screen. According to the chest CT, the path of the bronchoscope can be determined by the calibration of lung lesions. At present, virtual navigation technology can reach to the bronchus of grade 0 to 6. In this study, we found that the diagnostic yield of the VBN+EBUS group was higher than the EBUS group the difference between the 2 groups was not statistically significant.

Diagnostic yield of both the EBUS group and VBN+EBUS group were lower in lesions diameter <20 mm than the diameter ≥ 20 mm with statistically significant difference, showing that the diagnosis rate was positively correlated with the diameter of the lesion. In lesions diameter <20 mm, diagnosis yield of VBN +EBUS group was obviously higher than of the EBUS groups, reflecting the advantage of virtual navigation. In addition, the time for positioning lesions of the VBN+EBUS group was significantly less than that of the EBUS group, and the difference was statistically significant, suggesting that VBN could shorten the time of the targeting lesions. Finally, this study indicated that there is no difference of complication rate between the 2 groups, and no complications happened directly related to VBN, concluding that VBN is a safe and effective auxiliary technology.

Author contributions

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