

Usefulness of virtual bronchoscopic navigation combined with radial endobronchial ultrasound for peripheral pulmonary lesions

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Abstract

Background: This study aimed to evaluate the diagnostic value of virtual bronchoscopic navigation combined with radial endobronchial ultrasound for peripheral pulmonary lesions (PPLs).

Methods: The 105 patients with PPLs identified by computed tomography in Nanjing Brain Hospital underwent radial endobronchial ultrasound (R-EBUS) with or without virtual bronchoscopic navigation (VBN) randomly from January 2015 to December 2017. The diagnostic yield, operation time and complications were evaluated in the two groups.

Results: There was no significant difference in the diagnostic yield between the VBN+R-EBUS group and the R-EBUS group (76.0% vs. 65.5%, $P = 0.287$). The operation time in VBN+R-EBUS group was less than that in R-EBUS group (20.6 ± 12.8 min vs. 28.6 ± 14.3 min, $P = 0.016$). No severe procedure related complications such as pneumothorax and hemoptysis were observed.

Conclusions: VBN cannot improve the diagnostic yield, but it can shorten the operation time. The VBN combined with R-EBUS is a safe and effective technique for PPLs.

Background

How to diagnose the peripheral pulmonary lesions (PPLs) quickly and accurately has always been a clinical difficulty [1]. CT-guided percutaneous lung biopsy has a high diagnostic yield and is recommended for the diagnosis of peripheral lung diseases, but it is often accompanied by pneumothorax, hemoptysis and other complications [2, 3]. Transbronchial lung biopsy (TBLB) has fewer complications, but the diagnostic yield of peripheral lung lesions with diameter ≤ 20 mm is lower [4]. In recent years, virtual bronchoscopic navigation (VBN) has been gradually applied in clinical practice. Several researches showed that [5–9], VBN combined with radial endobronchial ultrasound (R-EBUS) can improve the diagnosis yield of peripheral lung diseases, but VBN combined with R-EBUS is rarely used in PPLs. The purpose of this study was to investigate the diagnostic yield of pulmonary biopsy guided by VBN and R-EBUS in the diagnosis of PPLs, and to explore the clinical value of VBN and R-EBUS in the diagnosis of peripheral pulmonary nodules.

Methods

Patients

Total of 105 patients with PPLs were recruited, who underwent TBLB guided by R-EBUS alone or VBN combined with R-EBUS in the Nanjing Brain Hospital from January 2015 to December 2017. Inclusion criteria: the diameter of PPLs found by chest CT was less than or equal to 30 mm, and there was lesion were detected under bronchoscope. Exclusion criteria: Patients with cerebral hemorrhage and myocardial infarction in the past 3 months; patients with active hemorrhage and severe cardiopulmonary insufficiency can not tolerate bronchoscopy and do not cooperate with them. The patients were randomly

divided into VBN + R-EBUS group (50 cases) and R-EBUS group (55 cases). This study was approved by the ethics committee of Nanjing Brain Hospital. All subjects were fully informed of the examination content, risk and signed the informed consent.

Procedure

All patients underwent multi-slice spiral CT scan. The DICOM data of CT scan in VBN and R-EBUS group were imported into the computer, and the virtual bronchoscope image of the target bronchus was automatically created by VBN software (DirectPath v1.02, Cybernet systems), and the focus guidance path was established (Figure A, B). Two groups of patients were carried out under local anesthesia, fasting and water prohibition for 6 hours before operation, 2% lidocaine was inhaled by atomization, and 2% lidocaine was dripped into nose and trachea at the same time. In the VBN + R-EBUS group, bronchoscopy (Olympus BF-P260F, outer diameter 4.0 mm, working aperture 2.0 mm) was guided to the target's sub segment bronchi through the VBN system, and then the ultrasound probe (UM-S20-20R, Olympus) was extended to the corresponding sub segment. After detecting the low echo area (Figure C), the ultrasound probe was slowly withdrawn and the sub segment bronchus opening was measured to indicate the focus distance of the area. Then according to the measured distance, use the ultrasonic probe twice repeatedly to observe whether the operation path is correct. Withdraw the ultrasound probe and send it into the biopsy forceps along the positioning bronchial subsegment, and take the biopsy materials at the same location distance from the ultrasound focus. EBUS group: according to the location of the focus determined by preoperative chest CT, push the ultrasonic probe to the corresponding segment, the same as the operation steps of EBUS group. All the above groups were biopsied three times. Finally, the tissue samples were fixed with 4% formaldehyde solution and sent to pathological examination by smear (Figure D). Operation time: the time from arrival of bronchoscope to departure of bronchoscope from glottis.

Diagnostic criteria

The cases with malignant histology and/or cytology results are defined as positive cases, and the cases with non malignant pathological results are determined as follows according to the clinical situation: follow-up observation, anti infection, anti tuberculosis, percutaneous lung puncture, surgical biopsy, etc. to further clarify. All pathological results should be sent to the department of pathology for unified diagnosis. If there is any doubt, the second pathologist should cooperate in the diagnosis.

Statistical analysis

The data were processed by SPSS 20.0 software, the measurement data were described by mean \pm standard deviation, the comparison of measurement data was analyzed by single factor ANOVA, and the comparison between the count data groups was tested by χ^2 , with $P < 0.05$ as the difference.

Result

Clinical characteristics

Among the 105 patients with pulmonary nodules, there were 50 cases in VBN + R-EBUS group, 30 males and 20 females, with an average age of (55.8 ± 10.6) years and a diameter of (27 ± 3) mm. Among the 55 patients in R-EBUS group, 30 were male and 25 were female, with an average age of (56.5 ± 10.2) years and a diameter of (28 ± 2) mm. In VBN + R-EBUS group, there were 12 lesions in the right upper lobe (24.0%), 8 in the right middle lobe (16.0%), 15 in the right lower lobe (30.0%), 5 in the left upper lobe (10.0%), 10 in the left lower lobe (20.0%). In R-EBUS group, there were 15 lesions in the right upper lobe (27.3%), 8 in the right middle lobe (14.5%), 15 in the right lower lobe (27.3%), 5 in the left upper lobe (9.1%), and 12 in the left lower lobe (21.8%). There was no significant difference between the two groups (Table 1).

Table 1
□Baseline characteristics and final diagnosis

Variables	VBN + R-EBUS group	EBUS group	P
Age (years, median; range)	55.8 ± 10.6	56.5 ± 10.2	0.216
Gender (male/female)	30/20	30 /25	0.425
Lesion size (mm)			
< 20 mm,n (%)	20/50 (40.0%)	25/55 (45.5%)	
20–30 mm,n (%)	30/50 (60.0%)	30/55 (54.5%)	
Lesion location			
Right upper lobe, n (%)	12 (24.0%)	15 (27.3%)	
Right middle lobe, n (%)	8 (16.0%)	8 (14.5%)	
Right lower lobe, n (%)	15 (30.0%)	15 (27.3%)	
Left upper lobe, n (%)	5 (10.0%)	5 (9.1%)	
Left lower lobe, n (%)	10 (20.0%)	12 (21.8%)	
Final diagnosis			
Malignant disease			
Primary lung cancer n (%)	25 (50.0%)	23 (41.8%)	
Metastatic lung cancer n (%)	1 (2.0%)	2 (3.6%)	
Non-malignant disease			
Infectious disease n (%)	10 (20.3%)	10 (18.2%)	
Other benign condition n (%)	2 (4.0%)	1 (1.8%)	

Diagnostic yield

The diagnosis yield of VBN + R-EBUS group and R-EBUS group was 76.6% and 65.5% respectively, there was no significant difference between the two groups ($P = 0.287$). In the PPLs with diameter < 20 mm, the diagnostic yield of the VBN + R-EBUS group was 70.0%, higher than the diagnostic yield of the R-EBUS group of 40.0%. The difference was statistically significant ($P = 0.045$). Although the diagnostic yield of VBN + R-EBUS for benign lesions was higher than that of R-EBUS (80.0% vs. 55.0%), the difference was not statistically significant ($P = 0.123$). The diagnosis yield of malignant lesions in R-EBUS group and VBN + R-EBUS group was 71.4% and 74.3% respectively, and the difference was not statistically significant ($P = 0.788$). However, there was no significant difference in diagnosis yield between R-EBUS group and VBN + R-EBUS group in different location lesions (Table 2).

Table 2
□ Clinical factors associated with diagnostic yield

Factors	VBN + R-EBUS group	EBUS group	P
Diagnostic yields	38 / 50 (76.0%)	36/55 (65.5%)	0.287
Gender			
Male	22/30 (73.3%)	23/30 (76.7%)	0.766
Female	16/20 (80.0%)	13/25 (52.0%)	0.066
Lesion size (mm, median; range)			
< 20 mm, n (%)	14/20 (70.0%)	10/25 (40.0%)	0.045
20–30 mm, n (%)	24/30 (80.0%)	26/30 (86.7%)	0.488
Lesion location			
Right upper lobe, n (%)	11/12 (91.7%)	12/15 (80.0%)	0.396
Right middle lobe, n (%)	6/8 (75.0%)	3/8 (37.5%)	0.131
Right lower lobe, n (%)	10/15 (66.7%)	11/15 (73.3%)	0.690
Left upper lobe, n (%)	3/5 (60.0%)	2/5 (40.0%)	0.527
Left lower lobe, n (%)	8/10 (80.0%)	8/12 (66.7%)	0.484
Final diagnosis			
Malignant disease n (%)	26/35 (74.3%)	25/35 (71.4%)	0.788
Non-malignant disease n (%)	12/15 (80.0%)	11/20 (55.0%)	0.123

Operation time

The operation time of VBN + R-EBUS group was (20.6 ± 12.8) min, that of R-EBUS group was (28.6 ± 14.3) min, and that of VBN + R-EBUS group was significantly shorter than that of R-EBUS group ($P = 0.016$).

Complications

In the two groups, 12 patients had bleeding in the lumen, 4 in VBN + R-EBUS group and 8 in R-EBUS group, respectively. During the operation, the bleeding stopped after the treatment of 1:1000 ice salt water, adrenaline, thrombin, etc. through the bronchoscope biopsy channel, no moderate or severe bleeding and pneumothorax complications occurred.

Discussion

Histopathology is the "gold standard" for the diagnosis of the nature of peripheral pulmonary nodules. For the lesions near the chest wall, percutaneous lung biopsy can be guided by CT. However, for the lesions far away from the chest wall or with large blood vessels and other important organs around, the risks of pneumothorax and bleeding are difficult to implement. Conventional bronchoscopy can reach 4–5 grade bronchus. With the help of ultra-fine bronchoscopy, intratracheal ultrasound and virtual navigation, the operation field can be extended to 6, 7 grade or even more distal bronchus, which makes our positioning of pulmonary nodules more accurate. Lung tissue biopsy guided by multiple technologies may improve the diagnosis rate of pulmonary nodules.

The diagnostic yield of traditional lung biopsy for pulmonary nodules is not ideal, which may be lower than 20% [10]. According to ACCP lung cancer guidelines [9], radial ultrasound guided lung biopsy should be preferred in the diagnosis of pulmonary nodules, which can be used as an important means of diagnosis. A number of research results showed that [10], compared with the traditional lung biopsy technology, EBUS guided lung biopsy can significantly improve the diagnosis yield of peripheral pulmonary nodules. Some researcher considered that [11, 12], endobronchial ultrasound failed to achieve self navigation positioning, so 8% – 20.8% of the lesions could not be detected. Virtual navigation technology is one of the new technologies developed in recent years. The image data obtained by preoperative high-resolution thin-layer chest CT without septum scanning is guided into the virtual navigation software system. The three-dimensional reconstruction has the same pixel value range to the inner surface of the bronchus, endows artificial pseudo color and simulates the condition in the lumen, and obtains the dynamic reconstruction image similar to that in the lumen of the bronchus. Before operation, according to the prompt of chest CT, the operation path of bronchoscope can be determined by calibrating the focus of lung. At present, virtual navigation technology can observe the 0–6 grade bronchi. In this study, we found that the diagnostic yield of VBN combined with R-EBUS group was higher than that of R-EBUS group, which was basically consistent with the results of Ishida et al.

The diagnosis yield of VBN combined with R-EBUS group and R-EBUS group in the lesions with diameter < 20.0 mm was lower than that of the lesions with diameter ≥ 20.0 mm, the difference was statistically significant. It can be seen that the diameter of the lesions was positively correlated with the diagnosis

yield. In the lesions with diameter < 2.0 cm, the diagnosis yield of VBN combined with R-EBUS group was significantly higher than that of R-EBUS group, reflecting the accuracy of virtual navigation. In addition, the operation time of VBN combined with R-EBUS group was significantly shorter than that of R-EBUS group, suggesting that VBN can shorten the operation time. Finally, this study suggests that there is no difference between the two groups of complications, and no complications directly related to VBN are found. It can be seen that VBN is a safe and effective auxiliary technology.

Conclusion

In conclusion, VBN combined with R-EBUS has a high diagnostic value for peripheral pulmonary nodules, which can reduce the operation time of tracheoscopy and provide a safe and effective method for the diagnosis of peripheral pulmonary nodules.

Declarations

Acknowledgements

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Authors' contributions

CHX and WW were responsible for designing the study, writing the protocol and report, screening potentially eligible studies. CHX, CZC, QZ, LL and QY were responsible for conducting the search, writing the protocol, and report. CHX, WW and RSY contributed to data extraction and provided feedback on the report. All authors read and approved the final manuscript.

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Availability of data and materials

The data used to support the findings of this study were supplied by Chunhua Xu under license and so cannot be made freely available. Requests for access to these data should be made to Chunhua Xu, Department of Respiratory Medicine, The Affiliated Brain Hospital of Nanjing Medical University, 215 Guangzhou Road, Nanjing, China, 210029, E-mail: xuch2188@163.com.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of The Affiliated Brain Hospital of Nanjing Medical University and were in accordance with the Helsinki Declaration.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

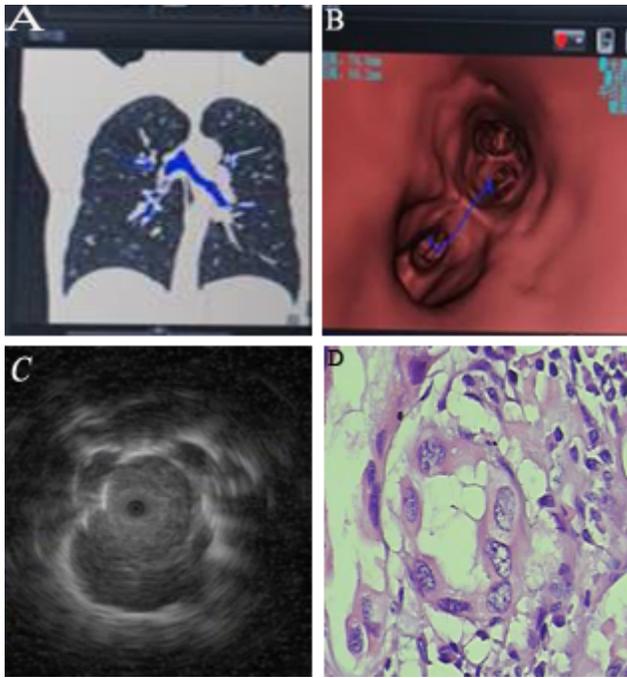


Figure 1

(A) The coronal position setting navigation path. (B) VBN demonstrated a precise route to the peripheral nodule (mm). (C) R-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 R-EBUS-guided TBLB.