



Efficacy of endobronchial ultrasound-guided transbronchial needle aspiration repeat-biopsy

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Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has been considered as a novel and accurate method for precise sampling of mediastinal lymph nodes and peribronchial lesions with a diagnosis yield of about 93–97% (1,2). So far, some studies have reported that EBUS-TBNA may not precisely diagnose mediastinal lymph nodes and peribronchial lesions for some situations. Therefore, to avoid a repeat sampling procedure, a better method of biopsy should be applied. However, given the high sensitivity and specificity of EBUS-TBNA method, repeat EBUS-TBNA (repeat-biopsy) may yield satisfactory results (3). Here, we retrospectively reviewed data of patients who underwent multiple EBUS-TBNA at The First Affiliated Hospital of Guangzhou Medical University from January 2012 to June 2020. The study was approved by the Institutional Ethic Committee of the First Affiliated Hospital of Guangzhou Medical University (#2020131).

Among 4,911 patients who received EBUS-TBNA, 140 patients (2.85%) underwent multiple procedures. Specifically, 131 patients received two procedures, eight patients received three procedures, and one patient received four procedures. Except 44 patients show received multiple procedures with the aim of reviewing disease or genetic testing. Ninety-six patients received repeat biopsy due to unexpected or non-diagnostic results in the first biopsy. These patients were further divided into 3 groups based on reasons for the repeat-biopsy: (I) 55 patients showed atypical results, i.e., abnormal cytopathology results with no diagnostic significance; (II) 24 patients had negative results; (III) 17 patients underwent repeat biopsy due to poor

quality of samples. All patients were followed up for a long period to confirm the diagnosis. The final diagnosis which was based on pathological analysis was considered as the correct diagnosis. The characteristics of patients followed up are shown in *Table 1*.

This report focuses on two main questions: (I) does repeat-biopsy improve the rate of correct diagnosis? (II) What are the factors influencing the diagnostic accurate of repeat-biopsy?

Overall, the correct diagnosis rate of repeat-biopsy was 67.7% (65/96), but there were significant differences in correct rates between groups. Patients who showed negative results in the first EBUS-TBNA procedure had a lower correct rate [45.8% (11/24)] in repeat-biopsy compared with those with atypical sample [72.7% (40/55)] and those who had samples with poor quality [82.4% (14/17)] ($P < 0.001$). It was found that site of biopsy may greatly affect the correct rate. Consequently, repeat-biopsy for peribronchial lesions achieved a correct rate of 93.8% (15/16) whereas that for lymph nodes had a correct rate of 62.5% (50/80).

For the 24 patients who had negative results, their CT scans were examined to analyze the gross features of the biopsied lymph nodes. Notably, small lymph nodes (short axis < 10 mm) were punctured in 3 patients. The main characteristics of the biopsied nodes were inhomogeneous density [37.5% (9/24)] and irregular margins [50% (12/24)].

In the subsequent sections, we discuss a patient who received EBUS-TBNA 4 times. The patient was a 51-year-old man who was admitted to the hospital due to a mass in the left lung. PET-CT scans confirmed the presence

Table 1 Baseline and correct rate of included patients

Characteristic	Result	P value
Included patients (n)	96	
The location of the biopsy (n)		
Lymph nodes	80	
Peribronchial lesion	16	
Reasons of re-biopsy (n)		
Negative biopsy	24	
Atypical biopsy	55	
Poor quality sample	17	
Operating factors in re-biopsy (n)		
Change/add biopsy points	69	
Replacement of operator	62	
Final diagnosis (n)		
Malignant disease	51	
Squamous cell carcinoma	16	
Adenocarcinoma	24	
Lymphoma	6	
Other	5	
Benign disease	45	
Sarcoidosis	3	
Pulmonary infect	6	
Tuberculosis	17	
Other	19	
Correct rate of re-biopsy (%)		
Overall	67.7 (65/96)	
Negative biopsy	45.8 (11/24)	<0.001
Atypical biopsy	72.7 (40/55)	
Poor quality sample	82.4 (14/17)	
Malignant disease	68.6 (35/51)	>0.05
Benign disease	66.6 (30/45)	
Lymph nodes	62.5 (50/80)	<0.001
Peribronchial lesion	93.8 (15/16)	
Change/add biopsy points	63.7 (44/69)	>0.05
Replacement of operator	66.1 (41/62)	

of a central lung neoplasm in the left upper lung with multiple mediastinal lymph node metastases. The initial EBUS-TBNA performed in 4R and 7# lymph nodes showed negative results. To prevent false negatives, a second lymph node biopsy was carried out. Similar to the first biopsy, the result was negative on repeat-biopsy, and even mediastinoscopic biopsy found no tumor. The patient received conservative therapy for two weeks but his symptoms did not improve. The patient was advised to undergo surgery to confirm the diagnosis, but he refused. Therefore, EBUS-TBNA was repeated twice and a small group of heteromorphic cells was found, but no tumor was confirmed. Finally, the patient was diagnosed with a special pathogen infection. After long-term follow-up, the result showed that there was no significant progress in lung mass. This case demonstrates poor efficacy of EBUS-TBNA repeat-biopsy for an initially negative result.

Although EBUS-TBNA has extremely high sensitivity and specificity, it has been reported to obtain negative results across different diseases. Therefore, it is important to develop a standard protocol for handling cases where patients show negative EBUS-TBNA results. Overall, compared with the unstable diagnostic yield of conventional-TBNA (which ranges from 20% to 80%) (4), repeat-biopsy achieves a correct diagnosis rate of 66.7%. However, the application of EBUS-TBNA should be decided based on the actual patient situation. The present case shows that repeat EBUS-TBNA can lead to a successful diagnosis for patients with atypical pathological results or poor-quality samples. For negative results, repeat-biopsy had a low rate of correct diagnosis, hence a more effective biopsy modality should be considered. Rapid on-site evaluation (ROSE) is a simple procedure that can provide an immediate and accurate assessment of benign and malignant samples. Moreover, the procedure can avoid additional sampling (5). However, there is no consensus on the necessity of ROSE in combination with EBUS-TBNA. Recently, EBUS-guided intranodal forceps (EBUS-INF) biopsy has been shown to provide larger histologic tissue samples. Using samples from EBUS-INF to perform genetic analysis may avoid repeat-biopsy for cases where the tissue sample is insufficient. Meanwhile, for suspected false-negative EBUS-TBNA results, EBUS-INF can be an alternative method for confirmation purposes (6).

Other factors that may also influence the efficacy of EBUS-TBNA include CT image characteristics, such as inhomogeneous density and irregular margins. A recent report indicated that PET/CT can increase the diagnostic efficacy of EBUS-TBNA (7), and choosing a PET-positive lymph node may improve the correct rate of repeat-biopsy.

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Footnote

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