Review Article

Bronchoscopy / Endobronchial ultrasound

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Abstract: Endobronchial ultrasound (EBUS) has emerged as a new diagnostic tool that allows the bronchoscopist to see beyond the airway. The radial probe EBUS was first introduced to evaluate the airway structure, which has been shown to be useful for identifying the extent of tumor invasion in the central airway. The newest development is the convex EBUS-transbronchial needle aspiration (TBNA) scope with a curvilinear electronic transducer on the tip of a flexible videoscope. Linear EBUS allows a real-time EBUS- guided TBNA.Although the main indication for EBUS-TBNA is lymph node staging, it can also be used for diagnosis of intrapulmonary tumors, of unknown hilar and/or mediastinal lymphadenopathy, and of mediastinal tumors. To date, there are no reports of complications related to EBUS-guided TBNA.It is a novel approach that has a good diagnostic yield with excellent potential in assisting safe and accurate diagnostic interventional bronchoscopy. The aim of this review is to highlight the current status of the EBUS-TBNA technique and to discuss the future direction of EBUS.

KeyWords: Bronchoscopy, Endobronchial ultrasound, Lung cancer, Lymph node metastasis, Mediastinoscopy, Staging, Transbronchial needle aspiration.

Lung cancer is one of the most common cancers. Despite the advances in surgical treatment and multimodality treatment, lung cancer is still the leading cause of death from malignant disease worldwide (1).

Accurate staging of the disease is important not only to determine the prognosis but also to decide the most suitable treatment plan. During the staging process, mediastinal lymph node staging is one of the most important factors that affect the patient outcome. Mediastinal staging can be divided into noninvasive staging (imaging) and invasive staging (sampling).

Computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET) and PET-CT are used for noninvasive imaging (2 -5).

Other imaging modalities include the use of esophageal ultrasound (EUS) and endobronchial ultrasound (EBUS) using a radial probe for detecting even small mediastinal lymph nodes (6-7). Invasive staging provides a de?nitive tissue diagnosis by surgical biopsy or needle biopsy. Mediastinoscopy is still the gold standard for mediastinal lymphnode staging (8-9).

However, it requires general anesthesia, and complications cannot be ignored. Various needle biopsy techniques exist, including conventional bronchoscopic transbronchial needle aspiration (TBNA), EUS-guided fine-needle aspiration (EUS-FNA), CT fluoroscopy-guided TBNA, and EBUS-guided TBNA using the radial probe (10-14). Each of these methods has its limitations.

There has been a need for a new modality with a high yield, enabling pulmonologists and thoracic surgeons to assess the mediastinum easily and safely. In 2003 a new endoscope with built-in linear probe ultrasound (US) on the tip enables real-time guidance during TBNA was available.

Compared to the radial probe EBUS, the linear US images are easier to understand. After preliminary studies showing the efficacy of EBUS-TBNA in surgical lung specimens (15), different groups reported the clinical use of EBUS-TBNA for the assessment of mediastinal and/or hilar lymph nodes.

EBUS-TBNA is now being performed in more than 500 centres around the world (16). Publications concerning the use of EBUS-TBNA in patients with respiratory disease indicate the effectiveness of this new modality. In this article, the role of EBUS-TBNA in the management of lung cancer is reviewed. In particular, its usefulness in the diagnosis and staging of lung cancer is discussed.

EBUS–TBNA: technique

The EBUS-TBNA scope is a US puncture bronchoscope with a 7.5-MHz convex transducer placed at the tip of a flexible bronchoscope (BF-UC260F-OL8; Olympus, Tokyo, Japan). This EBUS-TBNA is a linear curved array transducer that scans parallel to the insertion direction of the bronchoscope (Fig. 1). Images can be obtained by directly contacting the probe to the bronchial wall. The US image is processed in a US scanner and is visualized along with the conventional bronchoscopy image.

The outer diameter of the insertion tube of the EBUS-TBNA is

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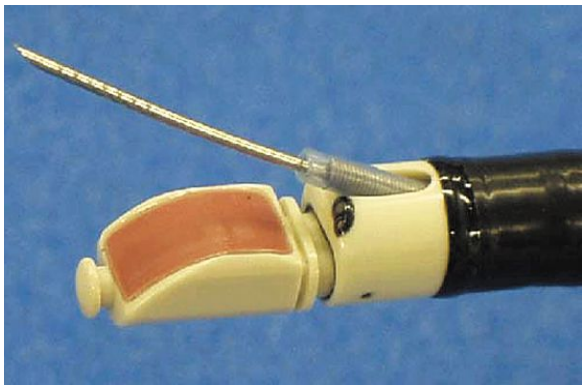

Fig. 1 Tip of the ultrasonic puncture bronchoscope and the 22–gauge transbronchial needle aspiration (TBNA) needle is inserted through the working channel to perform direct real–time endobronchial ultrasound–guided transbronchial needle aspiration (EBUS–TBNA)

6.2 mm, and that of the tip is 6.9 mm. The angle of view is 90° , and the direction of view is 35° forward oblique. The inner diameter of the instrument channel is 2.0 mm. A dedicated 22-gauge needle is used to perform EBUS-TBNA. The needle is also equipped with an internal sheath that is withdrawn after passing the bronchial wall, avoiding contamination during TBNA. This internal sheath is also used to clear out the tip of the needle after passing the bronchial wall.

The use of this sheath has significantly increased the yield of EBUS-TBNA. The exit of the needle is at 20° with respect to the outer covering of the insertion tube. The needle can be visualized through the optics and on the US image (Fig. 2) (17).

Because the endobronchial images obtained by the EBUS-TBNA scope is not as clear as the conventional flexible videoscope

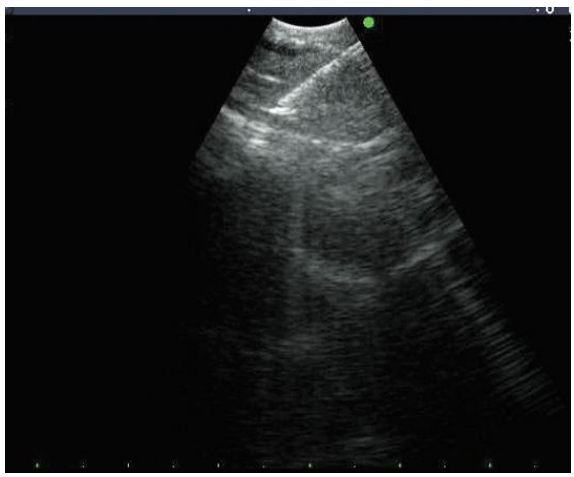

Fig. 2 Representative case of EBUS–TBNA. An EBUS scan demonstrates station 4r lymph node. The 22–gauge needle is seen in the lymph node.

image, most of the users prefer to examine the tracheobronchial tree using the conventional scopes.

All procedures can be performed under local anesthesia and conscious sedation (midazolam) (18). Nasal insertion may be diffi cult owing to the probe on the tip of the scope. After identifying the lesion of interest with EBUS-TBNA, the surrounding structures are visualized with the use of the Doppler mode to con?rm blood vessels (Fig. 3). The dedicated TBNA needle is inserted through the working channel of the bronchoscope, and the lesion is punc tured under direct EBUS guidance (EBUS-TBNA).

Fig. 3 Puncture of the Lymphnode in position 10r, the vessel is seen with the help of the Doppler mode

Indications for EBUS-TBNA are assessment of mediastinal and hilar lymph nodes, diagnosis of lung tumors, and diagnosis of mediastinal tumors. All of the mediastinal lymph nodes except for the subaortic and paraesophageal lymph nodes (levels 5, 6, 8, and 9) are assessable by EBUS-TBNA. Also the hilar nodes (10, 11, 12) are approachable (17)

Clinical results

To date, several papers have been published on this procedure. Krasnik et al. (15) reported on 11 patients in whom 15 lesions were punctured, without complications. The lesions were located as follows: 4 in region 10L, 4 in region 10R, 1 in region 4L, 3 in region 4R, 1 in region 1, 1 in region 7, and 1 in region 2R. The lesions ranged from 7 mm to 80 mm. Biopsies obtained through EBUS-FNA showed malignant cells in 13 lesions and benign cells in 2.

Yasufuku et al. (19) published his first experience in a few patients in 2004. In his second trial (20), he examined 70 patients with mediastinal (n=58) and hilar lymph nodes (n=12). The sensitivity, specificity, and accuracy of EBUS- TBNA in distinguishing benign from malignant lymph nodes were 95.7% , 100% , and 97.1%, respectively. There were no complications.

In a European paper by Rintoul et al. (21) EBUS-TBNA was used in 18 patients. Cytology revealed node (N)2/N3 disease in 11

patients and provided a primary diagnosis in 8 patients. Cytology results for EBUS-TBNA samples were negative in 6 patients, and mediastinoscopy or clinical follow-up confirmed this result in 4. Sensitivity, specificity, and accuracy for EBUS-TBNA were 85%, 100%, and 89%, respectively.

The largest trial reported the results of the method in 502 patients (12). 572 lymph nodes were punctured, and 535 (94%) resulted in a diagnosis. Biopsies were taken from all reachable lymph node stations (2l, 2r, 3, 4r, 4l, 7, 10r, 10l, 11r and 11l. Mean (SD) diameter of the nodes was 1.6 cm (0.36 cm) and the range was 0.8 to 3.2 cm. Sensitivity was 92%, specificity was 100%, and the positive predictive value was 93%. Like in all other trials no complications occurred.

The danish-german group (23) examined in addition the accuracy of EBUS-TBNA in sampling nodes less than 1 cm in diameter. Among 100 patients 119 lymph nodes with a size between 4 up to 10 mm were detected and sampled. Malignancy was detected in 19 patients but missed in 2 others; all diagnoses were confirmed by surgical findings. The mean (SD) diameter of the punctured lymph nodes was 8.1 mm. The sensitivity of EBUS-TBNA for detecting malignancy was 92.3 %; the specificity was 100%; and the negative predictive value was 96.3 %. Again no complications occurred. They summarized, that EBUS-TBNA can sample even small mediastinal nodes, therefore avoiding unnecessary surgical exploration in 1 of 5 patients who have no CT evidence of mediastinal disease. Potentially operable patients with clinically nonmetastatic NSCLC may benefit from presurgical EBUS-TBNA biopsies and staging.

A study comparing EBUS-TBNA, CT, and PET for lymph node staging of lung cancer showed a high yield for EBUS-TBNA (24). Altogether, 102 potentially operable patients with proven (n = 96) or radiologically suspected (n = 6) lung cancer were included in the study. CT, PET, and EBUS-TBNA were performed prior to surgery for the evaluation of mediastinal and hilar lymph node metastasis. The sensitivities of CT, PET, and EBUS-TBNA for the correct diagnosis of mediastinal and hilar lymph node staging were 76.9%, 80.0%, and 92.3%, respectively; the specificities were 55.3%, 70.1%, and 100%, respectively; and the diagnostic accuracies were 60.8%, 72.5%, and 98.0%, respectively. EBUS-TBNA was proven to have high sensitivity and speci?city, compared to CT or PET, for mediastinal staging in patients with potentially resectable lung cancer.

Restaging of the mediastinum is another area of growing interest for the treatment strategy of lung cancer. In cases of advanced lymph node stage lung cancer, induction chemotherapy prior to surgical resection is an option. Mediastinoscopy is considered the gold standard for staging the mediastinum. However, re-medi astinoscopy can be technically difficult and is therefore not commonly performed. The ability to perform multiple, repeat biopsies using EBUS-TBNA allows restaging of the mediastinum after the introduction of chemotherapy.

A group of 124 consecutive patients with tissue-proven IIIA-N2 disease who were treated with induction chemotherapy underwent mediastinal restaging by EBUS-TBNA. The sensitivity, specificities, positive predictive value, negative predictive value, and diagnostic accuracy of EBUS-TBNA for mediastinal restaging following induction chemotherapy were 76%, 100%, 100%, 20%, and 77%, respectively. EBUS TBNA is an accurate, minimally invasive test for mediastinal restaging of patients with NSCLC. However, because of the low negative predictive value, tumor-negative findings should be confirmed by surgical staging (24).

EBUS-TBNA can be also used for the diagnosis of intrapulmonary nodules as well as mediastinal and hilar lymph nodes. The limitation is the reach of EBUS-TBNA, which depends on the size of the bronchus. Usually the EBUS-TBNA can be inserted as far as the lobar bronchus. Lung tumors located adjacent to the airway within reach of EBUS-TBNA can be diagnosed with EBUS-TBNA. Tornouy et al. (26) have reported there experience is this indication. In 60 patients, who have had a nondiagnostic bronchoscopy before, they were able to establish the defintive diagnosis in 77% without any complication.

Complications

Complications related to the procedure are similar to those of conventional TBNA including bleeding from major vessels, pneumomediastinum, mediastinitis, pneumothorax, bronchospam and laryngospasm. All authors have not encountered complications related to EBUS-TBNA and to date there are no major complications reported in the literature. Although EBUS has enabled the bronchoscopist to see beyond the airway, one must be aware of the possible complications related to the procedure (27, 28).

Conclusion

EBUS-TBNA has emerged as a new instrument that enables real-time TBNA of the mediastinum, hilum, and intrapulmonary nodules. It is a minimally invasive, safe procedure that is useful and effective for the diagnosis and staging of NSCLC. More prospective data describing the diagnostic yield of EBUS-TBNA compared to conventional tools are needed to support the value of this new modality. However, based on thecurrent experience, EBUS-TBNA can be used as the first test for patients with undiagnosed mediastinal lymphadenopathy either with or without a lung mass. It is an attractive procedure that allows simultaneous lymph node staging as well as diagnosis.

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