

Endobronchial ultrasound-guided transbronchial needle aspiration: a maturing technique

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Accurate, quick pathological identification of a pulmonary or mediastinal mass is one of most challenging issues in thoracic oncology. This is particularly important when it comes to operable lung cancers in which a pre-surgical evaluation of mediastinal lymph node involvement is widely recognized as indispensable. For this purpose, mediastinoscopy was an accepted gold standard with 80% sensitivity and 100% specificity in the screening (1). Unfortunately, considerable invasiveness and the need for general anesthesia associated with mediastinoscopy limit the accessibility of this procedure to N2-3 lymph nodes; moreover, repetitive mediastinoscopy is hardly feasible owing to the formation of dense adhesions.

Endobronchial ultrasound (EBUS) is a procedure in which a miniature ultrasound probe is advanced into the airway lumen via fiberoptic bronchoscopy for real-time scanning, thus enabling study of histological characteristics as well as ultrasound imaging of the adjacent anatomy. In recent years, a novel EBUS-based technique, EBUS-guided transbronchial needle aspiration (EBUS-TBNA) has emerged (2), which can achieve precise aspiration biopsy of the peribronchial pulmonary lesions. In a number of studies, EBUS-TBNA has been shown to yield excellent diagnostic performance for central-type lung cancers without bronchial invasion, presurgical staging of mediastinal lymph nodes, and unexplained hilar or mediastinal masses (1,3,4). For example, the sensitivity of EBUS-TBNA is 85% to 95% and the specificity may be up to 100% in the staging of mediastinal lymph nodes and diagnosis of lung cancer (1,3). The real-time imaging with EBUS-TBNA enables accurate puncture that is difficult with mediastinoscopy, making it possible to biopsy a suspected lesion surrounding but not yet protruding into the bronchi; this is particularly relevant

for central-type lung cancers without airway invasion. In addition, EBUS-TBNA is associated with satisfactory safety of puncture (5). The complications are infrequent, and mainly include cough, bleeding, and hypoxemia, which can be readily corrected by application of local anesthesia, clotting agents, reduction of manipulation time, and enhanced oxygen inhalation. The use of EBUS with guide-sheath (EBUS-GS) or electromagnetic navigation may further improve the diagnosis rate of peripheral lung lesions (6,7). Conceivably, samples obtained with needle aspiration under ultrasound guiding may not suffice in size for a confirmatory pathological study. For this concern, rapid on-site evaluation (ROSE) has been used in TBNA of adenopathies and peripheral lesions; although, its significance in sampling centrally located lesions has not been validated. Several studies noted that ROSE of transbronchial aspirates by a cytopathologist during bronchoscopy may minimize the chance of inadequate biopsy and increase TBNA yield (8,9). However, for experienced endoscopic ultrasound specialists, ROSE seems to have no effect on the diagnosis rate with transesophageal-guided needle aspiration (10,11). Even when no cytological examination was performed on site, a diagnosis rate over 90% for mediastinal lymph nodes with EBUS-TBNA has been reported (12). The necessity and indications for rapid on-site evaluation in cases that undergo EBUS-TBNA require further clinical observation. In certain occasions, though, the harvested specimen does turn out to be insufficient owing to low tissue content and mechanical rupture, and it may be difficult to accurately and reliably distinguish between adenocarcinoma and squamous cell carcinoma based on morphology alone, especially in poorly

differentiated tumors. In such cases, immunohistochemical markers should be helpful to differentiate between adenocarcinoma and squamous cell carcinoma. Terry *et al.* (13) showed that combinations of biomarkers including TTF-1, p63, CK7, CK5/6, Napsin A, and mucicarmine can be fairly efficient for differential diagnosis between the two types of cancers.

At present, the commonly used needle aspiration techniques in the field of thoracic disease include classical TBNA, transesophageal endoscopic ultrasound-guided fine needle aspiration (EUS-FNA), and transthoracic needle aspiration (TNA) (5,14-16). Transesophageal EUS-FNA allows examining lymph nodes of the aorta, pulmonary artery (group 5), around the esophagus (group 8), and pulmonary ligament (group 9), which are not accessible with EBUS-TBNA. Combination of EBUS-TBNA and transesophageal EUS-FNA can achieve complete mediastinal staging, and access any lymph-node station that cannot be accomplished by either alone. And the diagnostic sensitivity, has been reported to be 93-94% (17). In comparison, classical TBNA relies on chest computed tomography to locate the site for a blind puncture to sample the mediastinal tumor and lymph nodes, which is difficult to manipulate, far less accurate and successful, and hardly precedes mediastinoscopy in terms of its scope of application.

In addition, progress in EBUS has been made with respect to lung cancer treatment. EBUS can be used to implant radiation particles for local radiotherapy in lung cancer patients who are not candidates for surgery, and has shown satisfactory effects (18). Repeated EBUS-TBNA for patients has made a difference in the re-evaluation of hilar and mediastinal tumors and lymph nodes after neoadjuvant chemotherapy, which is an important aspect in determining the treatment response (19). However, the use of EBUS-TBNA for mediastinal re-staging after combination chemotherapy is not ideal; its diagnostic sensitivity was only 76% and the negative predictive value was 20% (19). Therefore, most researchers believe that the negative results of EBUS-TBNA should be confirmed by mediastinoscopy, surgical lymph node sampling, or clinical follow-up to compensate for the limitations of the technique (20). Subsequent studies have found a negative predictive value of 78% for EBUS-TBNA in mediastinal restaging after combination chemotherapy, and cases with negative results do not require further surgery for re-staging (21). Studies on large samples are needed to further investigate the negative predictive value of EBUS-TBNA for mediastinal

restaging after combination chemotherapy.

With respect to its use in other chest disorders, EBUS-TBNA showed diagnostic sensitivity of 91% for patients with clinically suspected lymphoma (22); the diagnostic rate achieved with EBUS-TBNA for sarcoidosis was 83-94% (23). EBUS can also be useful for unexplained recurrent hemoptysis (24) and drainage of mediastinal bronchogenic cysts (25). One study that focused on the learning curve for EBUS indicated that only ten training sessions were required to master the major know-how of this procedure (26,27).

In summary, EBUS-TBNA demonstrates high sensitivity and accuracy in diagnosis of lung cancers, mediastinal tumors and metastasis. Compared with many other investigational modalities, EBUS-TBNA is minimally invasive, safe, and cost-effective. This maturing technique adds to the armamentarium for management of thoracic diseases.

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References

1. Gompelmann D, Eberhardt R, Herth FJ. Endobronchial ultrasound. *Endosc Ultrasound* 2012;1:69-74.
2. Herth FJ. Endobronchial ultrasound: first choice for the mediastinum. *Endosc Ultrasound* 2013;2:179-80.
3. Ømark Petersen H, Eckardt J, Hakami A, et al. The value of mediastinal staging with endobronchial ultrasound-guided transbronchial needle aspiration in patients with lung cancer. *Eur J Cardiothorac Surg* 2009;36:465-8.
4. Zhang Y, Wang KP. Evolution of transbronchial needle aspiration - a hybrid method. *J Thorac Dis* 2013;5:234-9.
5. Zaric B, Stojsic V, Sarcev T, et al. Advanced bronchoscopic techniques in diagnosis and staging of lung cancer. *J Thorac Dis* 2013;5 Suppl 4:S359-70.
6. Schuhmann M, Eberhardt R, Herth FJ. Endobronchial ultrasound for peripheral lesions: a review. *Endosc Ultrasound* 2013;2:3-6.
7. Chee A, Stather DR, Maceachern P, et al. Diagnostic utility of peripheral endobronchial ultrasound with electromagnetic navigation bronchoscopy in peripheral lung nodules. *Respirology* 2013;18:784-9.
8. Tofts RP, Lee PM, Sung AW. Interventional pulmonology approaches in the diagnosis and treatment of early stage non small cell lung cancer. *Transl Lung Cancer Res*

- 2013;2:316-31.
9. Chin R Jr, McCain TW, Lucia MA, et al. Transbronchial needle aspiration in diagnosing and staging lung cancer: how many aspirates are needed? *Am J Respir Crit Care Med* 2002;166:377-81.
 10. Cermak TS, Wang B, DeBrito P, et al. Does on-site adequacy evaluation reduce the nondiagnostic rate in endoscopic ultrasound-guided fine-needle aspiration of pancreatic lesions? *Cancer Cytopathol* 2012 Oct;120:319-25. PubMed
 11. Dietrich CF, Jenssen C. Endoscopic ultrasound-guided sampling in gastroenterology: European society of gastrointestinal endoscopy technical guidelines. *Endosc Ultrasound* 2013;2:117-22.
 12. Shimizu K, Okita R, Nakata M. Clinical significance of the tumor microenvironment in non-small cell lung cancer. *Ann Transl Med* 2013;1:20.
 13. Terry J, Leung S, Laskin J, et al. Optimal immunohistochemical markers for distinguishing lung adenocarcinomas from squamous cell carcinomas in small tumor samples. *Am J Surg Pathol* 2010;34:1805-11.
 14. Krishna SG, Ghouri YA, Suzuki R, et al. Uterine cervical cancer metastases to mediastinal lymph nodes diagnosed by endoscopic ultrasound-guided fine needle aspiration. *Endosc Ultrasound* 2013;2:219-21.
 15. Costache MI, Iordache S, Karstensen JG, et al. Endoscopic ultrasound-guided fine needle aspiration: from the past to the future. *Endosc Ultrasound* 2013;2:77-85.
 16. Ioncica AM, Bektas M, Suzuki R, et al. Role of EUS-FNA in Recurrent Lung Cancer: Maximum Results with Minimum (minimally invasive) Effort. *Endosc Ultrasound* 2013;2:102-4.
 17. Wallace MB, Pascual JM, Raimondo M, et al. Minimally invasive endoscopic staging of suspected lung cancer. *JAMA* 2008;299:540-6.
 18. Harley DP, Krinsky WS, Sarkar S, et al. Fiducial marker placement using endobronchial ultrasound and navigational bronchoscopy for stereotactic radiosurgery: an alternative strategy. *Ann Thorac Surg* 2010;89:368-73; discussion 373-4.
 19. Herth FJ, Annema JT, Eberhardt R, et al. Endobronchial ultrasound with transbronchial needle aspiration for restaging the mediastinum in lung cancer. *J Clin Oncol* 2008;26:3346-50.
 20. Almeida FA. Bronchoscopy and endobronchial ultrasound for diagnosis and staging of lung cancer. *Cleve Clin J Med* 2012;79 Electronic Suppl 1:eS11-6.
 21. Szlubowski A, Herth FJ, Soja J, et al. Endobronchial ultrasound-guided needle aspiration in non-small-cell lung cancer restaging verified by the transcervical bilateral extended mediastinal lymphadenectomy--a prospective study. *Eur J Cardiothorac Surg* 2010;37:1180-4.
 22. Kennedy MP, Jimenez CA, Bruzzi JF, et al. Endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of lymphoma. *Thorax* 2008;63:360-5.
 23. Chatterjee DK, Wolfe T, Lee J, et al. Convergence of nanotechnology with radiation therapy--insights and implications for clinical translation. *Transl Cancer Res* 2013;2:256-68.
 24. Patil S, Ayachit R. Unexplained intermittent hemoptysis with normal chest radiograph necessitates bronchoscopy?--mucoepidermoid carcinoma of lung: Case report. *J Transl Intern Med* 2014;2:40-4.
 25. Galluccio G, Lucantoni G. Mediastinal bronchogenic cyst's recurrence treated with EBUS-FNA with a long-term follow-up. *Eur J Cardiothorac Surg* 2006;29:627-9; discussion 629.
 26. Groth SS, Whitson BA, D'Cunha J, et al. Endobronchial ultrasound-guided fine-needle aspiration of mediastinal lymph nodes: a single institution's early learning curve. *Ann Thorac Surg* 2008;86:1104-9; discussion 1109-10.
 27. Ge N, Sun S. Endoscopic ultrasound: An all in one technique vibrates virtually around the whole internal medical field. *J Transl Intern Med* 2014;2:104-6.

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