

Endobronchial ultrasound-guided transbronchial needle aspiration: unraveling myths of mass in the chest

Rui Wang, Guangqiao Zeng

State Key Laboratory of Respiratory Disease, National Clinical Center for Respiratory Diseases, Guangzhou Institute of Respiratory Diseases, First Affiliated Hospital, Guangzhou Medical University, Guangzhou 510120, China

Correspondence to: Prof. Guangqiao Zeng, State Key Laboratory of Respiratory Disease, National Clinical Research Center for Respiratory Diseases, Guangzhou Institute of Respiratory Diseases, First Affiliated Hospital, Guangzhou Medical University, 151 Yanjiang Road, Guangzhou 510120, China. Email: zgqiao@vip.163.com.

Submitted Nov 03, 2014. Accepted for publication Nov 21, 2014.

doi: 10.3978/j.issn.1000-9604.2014.12.02

View this article at: <http://dx.doi.org/10.3978/j.issn.1000-9604.2014.12.02>

Lung cancer is one of the most common neoplasms worldwide and a major cause of cancer death. Rapid diagnosis and accurate staging for patients with suspected lung cancer are essential to appropriate treatment. However, many of submucosal or parabronchial intrapulmonary lesions are invisible by bronchoscopy despite their adjacency to the central airway. Classical approaches in these cases, such as conventional bronchoscopy, transbronchial needle aspiration (TBNA) and computed tomography-guided transthoracic needle aspiration (TTNA), are of limited use in a sense of definitive diagnosis (1-3). With the advance in bronchoscopic diagnostics during the recent years, endobronchial ultrasound-guided TBNA (EBUS-TBNA) emerges as a novel technique for bronchoscopic sampling under ultrasound guidance. EBUS-TBNA enables real-time aspiration of lesions adjacent to the trachea or large bronchi (4). EBUS-TBNA circumvents the limitations of classical TBNA, making the technique safer and more precise in the diagnosis of lung cancer (5). Radial EBUS with a guide sheath and miniature ultrasound probe, or combined with electromagnetic navigation bronchoscopy, provides high diagnostic yield of peripheral pulmonary lesions (5,6). In a study by Zhao and colleagues, among 66 cases of intrapulmonary lesions unconfirmed by conventional bronchoscopy, 59 were finally confirmed by EBUS-TBNA (89.4%), with the sensitivity, specificity and accuracy being 93.7%, 100.0% and 93.9%, respectively (7). However, the low negative predictive value of this procedure render an indispensable need for further examination by other modalities in patients with no malignancy detected by EBUS-TBNA alone (7).

Since imaging alone is not adequately sensitive or specific for evaluation of lymph node metastases, mediastinal nodes are generally sampled when enlarged on CT (short axis >1 cm) and/or metabolically active on PET. Tissue sampling performed with invasive or minimally invasive techniques is crucial for the staging of lung cancer. Until recently, mediastinoscopy was considered as the gold standard for detection of mediastinal lymph node with a sensitivity of 80% and a specificity of 100% (8). However, mediastinoscopy can only access lymph node stations 1-4 and 7, while those at lower subcarinal regions can become a nightmare for this procedure. The compulsory need for mediastinoscopy to be performed under general anesthesia gives rise to significant rates of procedure-related morbidity (2%) and mortality (0.08%) (9). Furthermore, repeated mediastinoscopy by no means can be easy and acceptable in a same patient. By using EBUS-TBNA, sampling mediastinal nodes can be far less invasive with a satisfactory sensitivity of 85% to 95% and a specificity of 100% (8,10). During the procedure, certain ultrasonic features of the lymph nodes, such as circular appearance, distinct margin, heterogeneous echogenicity and signs of necrosis, can be of clinical use to predict metastasis of lung cancer (11). Compared with mediastinoscopy, EBUS-TBNA offers several advantages, such as lower risk of morbidity and mortality, wider accessible regions which include the hilar and interlobar lymph nodes (12). However, stations 5, 6, 8 and 9 are not accessible by this technique. On the other hand, endoscopic ultrasound fine needle aspiration (EUS-FNA) is useful for accessing the posterior mediastinal lesions but incompetent for evaluating lesions anterior to

the trachea (13-16). Therefore, combined use of EBUS-TBNA and EUS-FNA may result in highly accurate staging of lung cancer compared with either method used alone (17). Presently, needles for EBUS-TBNA are available in two sizes, 22-gauge (22G) and 21G. The differences between 22G and 21G needles in sample adequacy and diagnostic yield were not statistically significant, according to a retrospective study of 1,299 patients by Yarmus and coworkers (18). Mini-forceps offer a higher diagnostic yield than needle aspiration in EBUS guided sampling, especially when the histological samples are decisive for making diagnosis (19). Randomized controlled trials on this aspect are needed for validation. Rapid on-site evaluation (ROSE) handled by experienced cytologists plays an important role in ensuring the diagnostic yield of sampling procedure (20). Oki *et al.* reported that ROSE during EBUS-TBNA is associated with a lower need for additional puncture number other than diagnostic yield (21). More studies on the role of ROSE during EBUS-TBNA should be worthwhile. For patients who have received neoadjuvant chemo-radiotherapy, EBUS-TBNA can be an alternative in mediastinal restaging. Subsequent determination by surgical staging is recommended in cases of negative EBUS-TBNA sampling (22). However, another study looking at a consecutive group of 61 patients with non-small cell lung cancer (N2) showed a negative predictive value of 67% and concluded that it is not necessary to re-stage the mediastinal nodes following a negative EBUS-TBNA (23). Further studies are required to address the debate and to improve the negative predictive value of EBUS-TBNA.

EBUS-TBNA can also be useful for definitive diagnosis and classification of malignant lymphoma and non-neoplastic lesions in patients with mediastinal lymphadenopathy. Differential diagnosis sometimes relies much on EBUS-TBNA in certain thoracic disease entities that may be mimickers of tumors [such as sarcoidosis, ground glass opacity pulmonary lesions (24)] or rarely encountered (such as histoplasmosis). With advances in technology, endoscopic ultrasound is becoming an important tool in natural orifice transluminal endoscopic surgery (25-27), and has evolved from a purely diagnostic imaging modality to an interventional procedure.

In conclusion, EBUS-TBNA has been increasingly popular as a widely adopted procedure for evaluating a variety of chest diseases, in particular, for the diagnosis and staging of lung cancers. Despite more studies pending to improve the clinical performance of EBUS-TBNA, encouraging outcomes in diagnostics and therapeutics with

this procedure mark a milestone and have lightened up a hope for the patients. A beam of sunlight is visible at the horizon of tomorrow, when the darkness of malignancy in the chest is fully unraveled with on-going refinement of this technique.

Acknowledgements

Disclosure: The authors declare no conflict of interest.

References

1. Dasgupta A, Jain P, Minai OA, et al. Utility of transbronchial needle aspiration in the diagnosis of endobronchial lesions. *Chest* 1999;115:1237-41.
2. Haponik EF, Shure D. Underutilization of transbronchial needle aspiration: experiences of current pulmonary fellows. *Chest* 1997;112:251-3.
3. Arslan S, Yilmaz A, Bayramgürler B, et al. CT- guided transthoracic fine needle aspiration of pulmonary lesions: accuracy and complications in 294 patients. *Med Sci Monit* 2002;8:CR493-7.
4. 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.
5. Zhang Y, Wang KP. Evolution of transbronchial needle aspiration - a hybrid method. *J Thorac Dis* 2013;5:234-9.
6. Schuhmann M, Eberhardt R, Herth FJ. Endobronchial ultrasound for peripheral lesions: a review. *Endosc Ultrasound* 2013;2:3-6.
7. Zhao H, Xie Z, Zhou ZL, et al. Diagnostic value of endobronchial ultrasound-guided transbronchial needle aspiration in intrapulmonary lesions. *Chin Med J (Engl)* 2013;126:4312-5.
8. Lee BE, Kletsman E, Rutledge JR, et al. Utility of endobronchial ultrasound-guided mediastinal lymph node biopsy in patients with non-small cell lung cancer. *J Thorac Cardiovasc Surg* 2012;143:585-90.
9. Detterbeck FC, Jantz MA, Wallace M, et al. Invasive mediastinal staging of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest* 2007;132:202S-20S.
10. 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.
11. Fujiwara T, Yasufuku K, Nakajima T, et al. The utility of

- sonographic features during endobronchial ultrasound-guided transbronchial needle aspiration for lymph node staging in patients with lung cancer: a standard endobronchial ultrasound image classification system. *Chest* 2010;138:641-7.
12. Tournoy KG, Keller SM, Annema JT. Mediastinal staging of lung cancer: novel concepts. *Lancet Oncol* 2012;13:e221-9.
 13. 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.
 14. 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.
 15. 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.
 16. Sharma SS, Jhaharia A, Maharshi S, et al. Mediastinal paraganglioma: specific endoscopic ultrasound features. *Endosc Ultrasound* 2013;2:105-6.
 17. Vilmann P, Krasnik M, Larsen SS, et al. Transesophageal endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) biopsy: a combined approach in the evaluation of mediastinal lesions. *Endoscopy* 2005;37:833-9.
 18. Yarmus LB, Akulian J, Lechtzin N, et al. Comparison of 21-gauge and 22-gauge aspiration needle in endobronchial ultrasound-guided transbronchial needle aspiration: results of the American College of Chest Physicians Quality Improvement Registry, Education, and Evaluation Registry. *Chest* 2013;143:1036-43.
 19. Chrissian A, Misselhorn D, Chen A. Endobronchial-ultrasound guided miniforceps biopsy of mediastinal and hilar lesions. *Ann Thorac Surg* 2011;92:284-8.
 20. Dietrich CF, Jenssen C. Endoscopic ultrasound-guided sampling in gastroenterology: European society of gastrointestinal endoscopy technical guidelines. *Endosc Ultrasound* 2013;2:117-22.
 21. Oki M, Saka H, Kitagawa C, et al. Rapid on-site cytologic evaluation during endobronchial ultrasound-guided transbronchial needle aspiration for diagnosing lung cancer: a randomized study. *Respiration* 2013;85:486-92.
 22. 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.
 23. 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.
 24. Izumo T, Sasada S, Chavez C, et al. The diagnostic utility of endobronchial ultrasonography with a guide sheath and tomosynthesis images for ground glass opacity pulmonary lesions. *J Thorac Dis* 2013;5:745-50.
 25. Téllez-Ávila FI, Romano-Munive AF, Herrera-Esquivel Jde J, et al. Central is as effective as bilateral endoscopic ultrasound-guided celiac plexus neurolysis in patients with unresectable pancreatic cancer. *Endosc Ultrasound* 2013;2:153-6.
 26. Drigo JM, Castillo C, Wever W, et al. Endoscopic ultrasound practice survey in latin america. *Endosc Ultrasound* 2013;2:208-18.
 27. Fusaroli P, Ceroni L, Caletti G. Forward-view Endoscopic Ultrasound: A Systematic Review of Diagnostic and Therapeutic Applications. *Endosc Ultrasound* 2013;2:64-70.

Cite this article as: Wang R, Zeng G. Endobronchial ultrasound-guided transbronchial needle aspiration: unraveling myths of mass in the chest. *Chin J Cancer Res* 2014;26(6):732-734. doi: 10.3978/j.issn.1000-9604.2014.12.02