Endoscopic ultrasound-guided fine needle aspiration and endobronchial ultrasound-guided transbronchial needle aspiration: Are two better than one in mediastinal staging of non–small cell lung cancer?

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Objective: The role of combined endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) with a single bronchoscope is poorly understood. The purpose of the present study was to elucidate the roles of EBUS-TBNA and EUS-FNA with a single bronchoscope in the preoperative hilar and mediastinal staging of non–small cell lung cancer (NSCLC).

Methods: A total of 150 patients with potentially resectable known or suspected NSCLC were enrolled in our prospective study. EBUS-TBNA was performed, followed by EUS-FNA, with an EBUS bronchoscope for N2 and N3 nodes ≥5 mm in the shortest diameter on ultrasound images, in a single session.

Results: EBUS-TBNA was performed for 257 lymph nodes and EUS-FNA for 176 lymph nodes. Of the 150 patients, 146 had a final diagnosis of NSCLC. Of these 146 patients, 33 (23%) had N2 and/or N3 nodal metastases. The sensitivity of EBUS-TBNA, EUS-FNA, and the combined approach per patient was 52%, 45%, and 73%, respectively (EBUS-TBNA vs the combined approach, $P = .016$, McNemar's test). The corresponding negative predictive value was 88%, 86%, and 93%. Two patients (1%) developed severe cough from EBUS-TBNA.

Conclusions: The combined endoscopic approach with EBUS-TBNA and EUS-FNA is a safe and accurate method for preoperative hilar and mediastinal staging of NSCLC, with better results than with each technique by itself. (J Thorac Cardiovasc Surg 2014;148:1169-77)

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Endoscopic ultrasound (EUS)-guided needle techniques, including endobronchial ultrasound-guided (EBUS) transbronchial needle aspiration (EBUS-TBNA) and EUS-guided fine needle aspiration (EUS-FNA), have been recommended as the test of choice for mediastinal staging of non–small cell lung cancer (NSCLC).[1] Although either EBUS-TBNA[2,3] or EUS-FNA[4,5] alone has been found to be an effective method, the combination of EBUS-TBNA and EUS-FNA has been reported to be more accurate than either method alone,[6-10] because EBUS-TBNA and EUS-FNA have complementary roles for mediastinal exploration.[11] However, the combination method has had some issues regarding the availability of expensive equipment and expertise. To overcome these problems, the utility of EUS-FNA with an EBUS bronchoscope in place of an EUS endoscope has been advocated.[12-14] Although the procedure requires some experience and skill, it can be performed by a bronchoscopist with an EBUS bronchoscope and thus enable a simple combined transbronchial and transesophageal endoscopic approach. To date, a few investigators[12,13] have suggested the efficacy of combined EBUS-TBNA and EUS-FNA with an EBUS bronchoscope in the mediastinal staging of NSCLC. However, because no prospective study has clearly demonstrated that the diagnostic value of the combined method is superior to that of each method alone, the roles remain unknown. The purpose of the present study was to elucidate the role of combined EBUS-TBNA and EUS-FNA with a single bronchoscope in preoperative hilar and mediastinal staging of NSCLC. The primary endpoint of the present study was to compare the diagnostic value of the combined method to that of each method by itself. The secondary endpoints were safety and the procedure duration.

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Abbreviations and Acronyms

CT = computed tomography
EBUS = endobronchial ultrasound
EBUS-TBNA = endobronchial ultrasound-guided transbronchial needle aspiration
EUS = endoscopic ultrasound
EUS-FNA = endoscopic ultrasound-guided fine needle aspiration
NSCLC = non–small cell lung cancer
TBNA = transbronchial needle aspiration

METHODS

Patients

We performed a prospective study that had been approved by the institutional review board of Nagoya Medical Center (identifier, 2009-251) and registered with the University Hospital Medical Information Network-Clinical Trials Registry (identifier, UMIN000002882). From December 2009 to August 2012, 150 patients with potentially operable, pathologically proven or clinical or radiologically suspected, NSCLC were enrolled in the present study. The operability was decided from the radiologic findings, including chest computed tomography (CT), positron emission tomography-CT, and brain magnetic resonance imaging, and the patients' condition. Patients with stage T4 or M1 disease according to the International Association for the Study of Lung Cancer staging system[15,16] were excluded. Patients with bulky N2 or N3 disease were also excluded. In our institution, we usually perform bronchoscopy for diagnosis and mediastinal staging in a separate setting; however, we sometimes perform EBUS-TBNA for highly suspicious mediastinal lymph nodes as an initial diagnostic test. Such patients with pathologically proven N2 or N3 disease were not included in the present study. All patients provided written informed consent. The baseline characteristics of the 150 patients are listed in Table 1.

TABLE 1. Patient and lesion characteristics

Characteristic	Value
Patients (n)	150
Gender	
Male	103 (69)
Female	47 (31)
Age (y)	
Mean ± standard deviation	68.3 ± 8.6
Range	33-83
Smoking history	
Never	30 (20)
Former	52 (35)
Current	68 (45)
Primary lesion location by bronchopulmonary segment	
Right upper lobe	51 (34)
Right middle lobe	3 (2)
Right lower lobe	24 (16)
Left upper lobe	34 (23)
Lingula	7 (5)
Left lower lobe	31 (21)
Final histopathologic classification	
Non–small cell lung cancer	
Adenocarcinoma	89 (59)
Squamous cell carcinoma	48 (32)
Large cell carcinoma	3 (2)
Adenocarcinoma + squamous cell carcinoma	2 (1)
Adenocarcinoma + large cell carcinoma	1 (1)
Squamous cell carcinoma + small cell carcinoma	1 (1)
Adenocarcinoma + small cell carcinoma	1 (1)
Sarcomatoid carcinoma	1 (1)
Other	
Small cell carcinoma	2 (1)
Tuberculosis	1 (1)
Organizing pneumonia	1 (1)
Preprocedural diagnosis for non–small cell lung cancer	
Diagnosed	137 (91)
Undiagnosed, but suspected	13 (9)

Data presented as n (%), unless otherwise noted.

Procedures

For EBUS-TBNA and EUS-FNA, a convex probe ultrasound bronchoscope (BF-UC260F-OL8 or BF-UC260FW; Olympus, Tokyo, Japan) and 22-gauge needles (NA-201SX-4022; Olympus) were used. The endoscopic procedures were performed with the patient under local anesthesia with lidocaine and conscious sedation with intravenous midazolam by staff pulmonologists or supervised pulmonary residents. EBUS-TBNA was performed first, followed by EUS-FNA, in a single session.

EBUS-TBNA was performed in the manner similar to the one we have previously described.[17] The procedure was performed with the patient in the supine position. After anesthetizing the upper airway with lidocaine, an EBUS bronchoscope was inserted into the trachea through the mouth, and lidocaine was administered into the trachea and bronchus through the working channel. Next, a balloon attached to the transducer was inflated with saline solution. It was then brought into contact with the airway wall and moved in all directions to identify the lesions for sampling. Once the target lesion had been visualized by ultrasound, a dedicated needle was passed through the working channel of the EBUS bronchoscope and advanced through the tracheobronchial wall into the lesion under real-time ultrasound visualization. After the central stylet had been removed, suction was applied using a syringe while manipulating the needle back and forth within the lesion. After sampling, the suction was released slowly, and the needle was retracted. The specimen collected in the lumen of the needle was first pushed out with the central stylet and then blown by air with a syringe onto a glass slide. The visible tissue fragment on the glass slide was then collected and transferred into numbered separate containers filled with formalin for histologic examination. The remaining specimen on the glass slide was smeared with another glass slide and fixed in 95% alcohol for cytologic examination. To clarify the role and diagnostic ability of each needle aspiration procedure, rapid on-site cytologic examination was not used. EBUS-TBNA was performed for N3 nodes, followed by the N2 nodes that were ≥5 mm in the shortest diameter on the ultrasound images. N1 nodes were examined after the N2 nodes if the attending physician or examiner considered it necessary. Two punctures were made for each lymph node, as previously reported by Herth and colleagues.[18] The lymph node location examined and the duration of the procedure from insertion to removal of an EBUS bronchoscope were recorded.

After EBUS-TBNA, EUS-FNA was performed at the left lateral position, as previously described.[19] An EBUS bronchoscope was inserted and advanced through the esophagus while examining the structure around the esophagus by ultrasound. Once the target lesion had been identified, it was punctured through the esophagus with another needle to avoid contamination from the EBUS-TBNA samples under real-time ultrasound guidance. Next, the needle was manipulated back and forth within the lesion