CHEST

Original Research

INTERVENTIONAL PULMONOLOGY

Real-time Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration in Mediastinal Staging of Non-Small Cell Lung Cancer*

How Many Aspirations Per Target Lymph Node Station?

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Objective: **The goal of this study was to determine the optimal number of aspirations per lymph node (LN) station during endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA) for maximum diagnostic yield in mediastinal staging of non-small cell lung cancer (NSCLC) in the absence of rapid on-site cytopathologic examination.**

Methods: **EBUS-TBNA was performed in potentially operable NSCLC patients with mediastinal LNs accessible by EBUS-TBNA (5 to 20 mm). Every target LN station was punctured four times.**

Results: **We performed EBUS-TBNA in 163 mediastinal LN stations in 102 NSCLC patients. EBUS-TBNA confirmed malignancy in 41 LN stations in 30 patients. Two malignant LN stations were missed in two patients. The sensitivity, specificity, positive predictive value, negative predictive value (NPV), and accuracy of EBUS-TBNA in predicting mediastinal metastasis were 93.8%, 100%, 100%, 96.9%, and 97.9%, respectively. Sample adequacy was 90.1% for one aspiration, and it reached 100% for three aspirations. The sensitivity for differentiating malignant from benign LN stations was 69.8%, 83.7%, 95.3%, and 95.3% for one, two, three, and four aspirations, respectively. The NPV was 86.5%, 92.2%, 97.6%, and 97.6% for one, two, three, and four aspirations, respectively. Maximum diagnostic values were achieved in three aspirations. When at least one tissue core was obtained by the first or second aspiration, the sensitivity and NPV of the first two aspirations were 91.9% and 96.0%, respectively.**

Conclusions: **Optimal results can be obtained in three aspirations per LN station in EBUS-TBNA for mediastinal staging of potentially operable NSCLC. When at least one tissue core specimen is obtained by the first or second aspiration, two aspirations per LN station can be acceptable.**

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Key words: endobronchial ultrasound; lung cancer; staging

Abbreviations: EBUS = endobronchial ultrasound; LN = lymph node; NPV = negative predictive value; NSCLC = non-small cell lung cancer; PET = positron emission tomography; PPV = positive predictive value; ROSE = rapid on-site cytopathologic examination; TBNA = transbronchial needle aspiration

Endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA) is a new bronchoscopic method that enables real-time aspiration of peribronchial or peritracheal lesions. Evidence of the usefulness of EBUS-TBNA in the diagnosis of mediastinal lymph nodes (LNs) is increasing.[1–9] EBUS-TBNA has a high sensitivity and a high negative predictive value (NPV) in the mediastinal staging of lung cancer.[3,8]

EBUS-TBNA is a recently introduced technique. Details of EBUS-TBNA methodology, such as the number of aspirations per target needed and the need for on-site cytopathologic support, have not been determined. According to Japanese reports[2,3,8]

about EBUS-TBNA, aspirates were evaluated by an on-site cytopathologist, and the median number of needle passes was two for each site. In some studies[1,4,5] not using rapid on-site cytopathologic examination (ROSE), one to three aspirates were obtained from the target lesion; judgment concerning the number of aspirates required was made according to the macroscopic appearance of the aspirate or arbitrarily by a bronchoscopist. In other studies[6,7] not using ROSE, two needle passes were made at every site. Some authors[10] suggest that three to four needle passes are associated with 90% sensitivity.

The goal of this study was to determine the optimal number of aspirations per LN station required during EBUS-TBNA for maximum diagnostic yield in the mediastinal staging of non-small cell lung cancer (NSCLC) when ROSE is not available.

Materials and Methods

Patients

This study was conducted between July 2006 and April 2007 at the Center for Lung Cancer, National Cancer Center, South Korea. Patients with strongly suspected or histologically confirmed potentially operable NSCLC were enrolled. To be included in the study, patients were required to have a mediastinal LN accessible by EBUS-TBNA with a short diameter of 5 to 20 mm on axial chest CT. LN status was classified according to the international staging system reported by Mountain and Dressler.[11] Tumor resectability was evaluated after an image-based staging workup for NSCLC, including CT of the chest and upper abdomen, brain MRI, whole-body positron emission tomography (PET)-CT, and/or bone scan. We excluded patients with M1 disease, inoperable T4 disease, evident N3 disease with spread to supraclavicular LNs, bulky mediastinal LN (short diameter > 2 cm on axial image of chest CT), or extranodal invasion of the mediastinal LN visible on chest CT. Patients with unresectable tumors diagnosed by white light bronchoscopy or patients with a Pancoast tumor were also excluded. Medical operability was assessed, and patients who were not physically suitable for surgery were excluded.

The ethical committee of our institute approved this study. Informed consent was obtained from all patients included in this study.

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EBUS-TBNA

EBUS-TBNA was performed with a flexible ultrasonic puncture bronchoscope with a linear scanning transducer (CP-EBUS, XBF-UC260F-OL8; Olympus; Tokyo, Japan). All EBUS-TBNA procedures were performed by the same bronchoscopist (B.H.). Local anesthesia (lidocaine) was applied. The procedure was performed under conscious sedation (midazolam). After full inspection of the mediastinal LNs accessible by EBUS-TBNA, target nodal stations considered to be necessary in mediastinal staging were selected by the judgment of a bronchoscopist. In selecting, we considered the likelihood of metastasis of the target nodal stations based on imaging studies and the potential pathway of lymphatic metastasis. We also considered the impact of metastasis of the target nodal station in deciding on treatment. Each target nodal station was aspirated four times with a dedicated 22-gauge needle (NA-201SX-4022; Olympus). We tried to target different areas of each nodal station for each aspiration to cover large parts of a nodal station (Fig 1). Different needles were used for different nodal stations to avoid contamination. N3 nodes were sampled first, and then N2 nodes were punctured. Procedure time was calculated from the insertion of the bronchoscope through mouth to the retrieval of the bronchoscope after the procedure.

The aspirate was expelled onto glass slides, smeared, and immediately fixed with 95% alcohol. We made three pairs of smear slides for each aspiration, if possible. Tissue cores (the solid substances in the aspiration needle obtained by EBUS-TBNA) were put into a solution of 10% neutral-buffered formalin. All specimens were numbered with respect to the order of aspiration. The remnants of each aspirate from the same nodal station were collected in one bottle filled with 95% alcohol for cell block. Smeared cytology slides were stained with hematoxylin-eosin and Papanicolaou. Tissue cores and cell blocks were stained with hematoxylin-eosin. Cytopathologic specimens were categorized as positive (presence of tumor cells), negative (lymphocytes or lymphoid tissue only), or inadequate (no cellular component, blood only, or cartilage or bronchial epithelial cells only). A pathologist (G.K. Lee), blinded to the details of the patients performed the cytopathologic examinations.

Treatment

Based on the EBUS-TBNA results, we recommended surgery for patients without mediastinal metastasis (open thoracotomy or video-assisted thoracic surgery including systematic LN dissection). Mediastinoscopy was not performed. We recommended chemotherapy (with or without radiotherapy) for patients with mediastinal metastasis with curative or neoadjuvant intent.

Statistical Analysis

The sensitivity, specificity, positive predictive value (PPV), NPV, and diagnostic accuracy of EBUS-TBNA were determined. The diagnostic consistency according to the number of aspirations was analyzed using the McNemar test. Differences in diagnostic values with respect to the presence of tissue core samples were examined with χ^2 or Fisher exact test; p values < 0.05 were considered statistically significant. All statistical analyses were performed using statistical software (STATA9, Stata Statistical Software Release 9; StataCorp; College Station, TX).

Results

Characteristics of Patients and LNs

We enrolled 105 patients in the study (Fig 2). Small cell lung cancer was diagnosed in three pa-