BRIEF REPORT

Diagnostic concordance rate between histologic and cytologic specimens of endobronchial ultrasound-guided transbronchial needle aspiration in lung cancer: A single institution experience

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Keywords

Concordance rate; cytology; EBUS-TBNA; histology.

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Abstract

Background: The aspirates from endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) were examined using the tissue core and cytology. We assessed that the tissue core was a more reliable specimen and attempted to analyze how many discrepancies were found between the two specimens. We investigated diagnostic concordance rate between histology and cytology.

Methods: From January 2011 to December 2011, a total of 267 consecutive patients with lung cancer, who underwent EBUS-TBNA, were included in this retrospective study.

Results: Of the 267 lung cancer patients, 207 (77.5%) were men. The median age was 65 years old. The most common pathologic type was adenocarcinoma (120, 44.9%), followed by squamous cell carcinoma (79, 29.6%). Among the 267 patients, 579 mediastinal and hilar lymph nodes were punctured. The right lower paratracheal (204, 35.2%) and subcarinal (172, 29.7%) lymph nodes were the most common nodal stations. Among the 579 lymph nodes, malignant cells were observed in 267 (46.1%) nodes, in either the histologic, cytologic or both slides: 209 in both histology and cytology, 37 in histology only, and 21 in cytology only slides. The diagnostic concordance rate between the tissue core and cytology was 90.0% (95% confidence interval CI, 87.1–92.2) ($\kappa = 0.79$).

Conclusions: The diagnostic concordance rate between the histology and cytology of EBUS-TBNA in lung cancer was 90.0% (95% CI, 87.1–92.2) ($\kappa = 0.79$).

Introduction

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has made great advances in the mediastinal staging of lung cancer.¹ Because of its high diagnostic accuracy, easy accessibility to hilar nodes, and minimal invasiveness, EBUS-TBNA has widely been applied in diagnostic bronchoscopy. Compared to transcervical mediastinoscopy, EBUS-TBNA can approach a wider range of mediastinal lymph nodes, and has a similar sensitivity and accuracy.²

Because of recent advances in the genetic diagnosis of lung cancer, obtaining a sufficient tissue core for immunohisto-

chemical staining and mutation studies is important.^{3–5} However, the aspirate specimen collected with EBUS-TBNA is relatively small; therefore, optimized specimen processing and efforts to avoid tissue loss during the process are necessary for an accurate diagnosis. The aspirates from EBUS-TBNA are processed into tissue cores for hematoxylin and eosin (H&E) staining and the remnant aspirates are used for Papanicolaou staining. Theoretically, histologic and cytologic slides are made from the same aspirates of EBUS-TBNA and the quantity of cellular components are more abundant in the tissue core for H&E staining than in the remnant aspirates for cytology; thus, histology is more reliable than the cytologic results.⁶ We investigated the diagnostic concordance rate

between histologic specimens and cytologic specimens, which were obtained from the same aspiration. Herein we attempt to explain the reason for the discordance.

Methods

Study population

Patients diagnosed with lung cancer or suspected recurrence of lung cancer in mediastinal or hilar lymph nodes underwent EBUS-TBNA for lung cancer staging or verifying the recurrence. The study duration was from January 2011 to December 2011 at the Seoul National University Hospital.

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA)

EBUS-TBNA was performed using a real-time linear probe (BF-UC260F-OL8; Olympus; Tokyo, Japan). A 22-gauge needle (NA-201SX-4022; Olympus; Tokyo, Japan) was used for transbronchial aspiration. EBUS-TBNA was performed by three pulmonologists. Local anesthesia (lidocaine) was applied to the tracheobronchial tree and patients were placed under conscious sedation (midazolam) in a supine position. After inspection of the mediastinal lymph nodes, the nodal stations selected at the judgment of the bronchoscopists were punctured. The nodal stations were classified according to the 7th Tumor Node Metastasis (TNM) classification.⁷

Specimen preparation of EBUS-TBNA

The aspirated specimen was expelled onto a glass slide. The tissue core was then identified and fixed in 10% formalin for H&E staining. The remaining aspirate was smeared and fixed with 95% alcohol for Papanicolaou staining. Rapid on-site cytology (ROSE) was not performed at our institution.

Pathologic results

Pathologic results were classified as positive when malignant cells were present in the histologic or cytologic specimen. It was interpreted as negative when non-malignant cells (lymphocytes or lymphoid tissue only) and atypical cells were present. Two independent pathologists assessed the results of cases with positive results only in cytology in order to identify any difference in opinion between the pathologists. In order to calculate the diagnostic accuracy, lymph nodes were confirmed as benign only after surgical lung resection and mediastinal lymph node dissection, even though EBUS-TBNA had previously shown these to be benign.

Results

From a total of 267 lung cancer patients, 207 (77.5%) were men. Their median age was 65 years old (range 33–95). One

Table 1 Characteristics of the 267 patients and 579 lymph nodes

		Operation results		
		Positive	Negative	Total
EBUS-TBNA results	Positive	153	1	154
	Negative	9	104	113
	Total	162	105	267

Sensitivity = 94.4%; specificity = 99.0%; positive predictive value = 99.4%; negative predictive value = 92.0%. EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration.

hundred and ninety-four (72.7%) patients were current or ex-smokers. The most common pathologic type was adenocarcinoma (120, 44.9%), followed by squamous cell carcinoma (79, 29.6%) (Table 1). Among the 267 patients, 86 (32.2%) patients underwent curative lung resection. The sensitivity, specificity, negative predictive value and positive predictive value were 94.4, 99.0, 92.0, and 99.4%, respectively (Table 2). Sensitivity and specificity of histologic specimens alone were 84.0% and 99.0%, and those of cytologic specimens were 74.1% and 99.0%. Diagnostic accuracy of histologic specimens was higher than that of cytologic specimens (90.0% vs. 84.0%).

There were 579 punctured hilar and mediastinal lymph nodes. The most common nodal station was the right lower paratracheal lymph node (204, 35.2%), followed by the subcarinal lymph node (172, 29.7%) (Table 2). Of 579 lymph nodes, malignant cells were observed in 267 (46.1%). Among the 267 positive lymph nodes, malignant cells were found in 209 (36.1%) lymph nodes in both the histologic and cytologic specimens, 37 (6.4%) lymph nodes in the histologic specimens only and in 21 (3.6%) lymph nodes in the cytologic specimens only. The diagnostic concordance rate between the histologic and cytologic specimens was 90.0% (95% confidence interval [CI], 87.1–92.2) ($\kappa = 0.79$) (Table 3). The diagnostic concordance rate between the two procedures for lymph nodes ≤ 1 cm ($n = 184$) and > 1 cm ($n = 393$) was 94.0% (95% CI, 89.5–95.8) ($\kappa = 0.81$) and 88.1% (95% CI, 84.8–91.4) ($\kappa = 0.77$), respectively. The diagnostic concordance rates according to histologic subtypes were similar among adenocarcinoma ($\kappa = 0.79$) and squamous cell carcinoma ($\kappa = 0.77$).

In the 21 lymph nodes where malignant cells were only found in the cytologic specimens, histologic results were as follows: “negative” in 10 (47.6%), “atypical cells” in eight (38.2%) and “insufficiency for diagnosis” in three (14.2%) lymph nodes. To clarify the “atypical cells,” we requested the histology of those cells from two independent pathologists. One pathologist concluded that all eight of the lymph nodes were positive, and the other concluded that four lymph nodes were positive and the remaining were atypical cells.

Table 2 Diagnostic accuracy of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA)

Characteristics	Data
Male/female gender, No.	207/60
Age median, year (range)	65 (33–95)
Smoking history	
Never smoker	68 (25.5%)
Ex-smoker	117 (43.8%)
Current smoker	77 (28.8%)
Unknown	5 (1.9%)
Pathologic diagnosis	
Squamous cell carcinoma	79 (29.6%)
Adenocarcinoma	120 (44.9%)
Large cell carcinoma	4 (1.5%)
Non-small cell carcinoma, unspecified	28 (10.5%)
Small cell lung cancer	36 (13.5%)
Nodal station (n = 579)	579
1R	1 (0.2%)
2R	54 (9.3%)
2L	2 (0.4%)
4R	204 (35.2%)
4L	73 (12.6%)
7	172 (29.7%)
10R	44 (7.6%)
10L	10 (1.7%)
11R	14 (2.4%)
11L	5 (0.9%)
Median short-diameter of lymph node on the chest CT (mm)	12.0 (5.0–45.9)

CT, computed tomography; L, left; R, right.

Discussion

EBUS-TBNA is a safe and accurate technique to evaluate mediastinal and hilar lymph nodes in non-small cell lung cancer (NSCLC). As the aspirated specimens from EBUS-TBNA are usually small, optimizing the process for small specimens is essential. We processed the obtained specimens into tissue cores for histology and remnants for cytology, as described previously.⁸ We investigated the diagnostic concordance rate between histologic specimens and cytologic specimens per lymph node, rather than per patient, and analyzed 267 patients and 579 lymph nodes. We report a

Table 3 Comparison between histologic and cytologic results from the same endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) specimens

		Histologic results		
		Positive	Negative	Total
Cytologic results	Positive	209 (36.1%)	21 (3.6%)	230
	Negative	37 (6.4%)	312 (53.9%)	349
	Total	246	333	579

Kappa value = 0.79.

high concordance rate of 90.0% (95% CI, 87.1–92.2) ($\kappa = 0.79$) between histologic and cytologic specimens from EBUS-TBNA in lung cancer, regardless of the size of the lymph node, or the subtype of NSCLC. Casal *et al.*⁹ prospectively compared EBUS-TBNA with EBUS-guided transbronchial needle capillary sampling, which was fine needle sampling without the use of suction. In this study, no difference in adequacy, diagnosis, or quality between the two techniques was found. Our data strengthened the previous study. We found that the diagnostic value of cytologic specimens matched that of histologic specimens. Considering both our study and the previous study, cytology has been revealed to have significant diagnostic value in cases where histologic specimens are not available, such as ROSE or low quality samples.

Because the diagnostic results were influenced by the diagnostic accuracy of EBUS-TBNA, the sensitivity, specificity, negative predictive value, and positive predictive value were calculated with the results shown above. The overall diagnostic accuracy was 96.3%; thus, we consider the results of the EBUS-TBNA as reliable. As mentioned above, in 21 lymph nodes, malignant cells were observed in cytologic specimens only. Among them, an appropriate diagnosis could not be reached for three histologic slides because of an insufficient tissue volume, while sufficient malignant cells were observed in the cytologic slides. These lymph nodes showed low attenuation in the computed tomography scan (Fig 1). The tissue core obtained from these nodes was brittle to the naked eye directly after aspiration. Thus, we were concerned about the possibility of tissue loss during histologic processing if the lymph nodes had necrotic characteristics.

This study had some limitations. First, ROSE was not performed. In the literature review, the advantages of ROSE during EBUS-TBNA were as follows: a reduced rate of non-diagnostic sampling and a reduced need for additional bronchoscopic procedures, punctures and time, and cost effectiveness,^{10–12} and increased sensitivity of EBUS-TBNA.¹³ Second, we could not assess all of the cases analyzed by the two independent pathologists; therefore, we could not evaluate the possibility of discrepancies in the positive cases. However, in the literature review^{14,15} and in our previous study,¹⁶ the negative predictive values of EBUS-TBNA were almost 100%. Thus, it was assumed that the possibility of false positives was negligible.

Conclusion

In conclusion, the diagnostic concordance rate between the histology and cytology of EBUS-TBNA in lung cancer was as high as 90% (95% CI, 87.1–92.2) ($\kappa = 0.79$). No difference was detected in the concordance rate, regardless of lymph node size and subtype.

Figure 1 Necrotic subcarinal lymph node on chest computed tomography (CT) and endobronchial ultrasound (EBUS). Enlarged and centrally necrotic subcarinal lymph node on the chest CT (arrow) and EBUS. The tissue core obtained at this lymph node was more fragile than in the other cases. The histologic result of this lymph node was a few atypical cells in the necrotic background, and the cytologic result was metastatic adenocarcinoma, thus, only positive in the cytology specimen. The necrotic feature of the lymph node is one of the possible causes of the negative histologic result.

Disclosure

No authors report any conflict of interest.

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