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Original article

The efficacy of transbronchial needle aspiration with endobronchial ultrasonography using a guide sheath for peripheral pulmonary lesions suspected to be lung cancer

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ABSTRACT

Background: The efficacy of transbronchial needle aspiration (TBNA) with endobronchial ultrasonography using a guide sheath (EBUS-GS) for cases of peripheral pulmonary lesions (PPLs) has not been well established. The purpose of this study was to evaluate the efficacy of TBNA with EBUS-GS for PPLs.

Methods: We evaluated 130 patients suspected to have lung cancer who underwent transbronchial brushing (brushing), transbronchial biopsy (TBB), and TBNA with EBUS-GS. The pathological diagnostic yields of TBNA were compared to that of TBB and brushing. The histological diagnosis of TBNA was compared to that of surgical specimens. The results of epidermal growth factor receptor (*EGFR*) gene mutation in TBNA samples were compared to that in TBB or surgical specimens.

Results: The diagnostic yields of this study were 62.9% for brushing, 80.0% for TBB, and 77.1% for TBNA. Histological diagnosis was 84.8% for TBB and/or TBNA and pathological diagnosis was 86.7% for all the procedures. TBB and TBNA had significance higher than brushing ($p < 0.05$). TBB and TBNA had a tendency of higher diagnostic yields than brushing if EBUS probe was adjacent to PPLs ($p = 0.058$). Histological evaluations were obtained from TBNA specimens from 50 of 105 patients (47.6%) and these were identical to those of surgical specimens from 29 of 32 patients (90.6%). The results of *EGFR* gene

Abbreviations: TBNA, transbronchial needle aspiration; EBUS-GS, endobronchial ultrasonography using a guide sheath; PPLs, peripheral pulmonary lesions; *EGFR*, epidermal growth factor receptor; TBB, transbronchial biopsy; brushing, transbronchial brushing

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mutation in TBNA specimens were identical to the same tissue obtained by surgery or TBB. *Conclusions:* TBNA with EBUS-GS for PPLs was a useful tool for accurate diagnosis and *EGFR* gene mutation analysis. This method may improve diagnostic accuracy and be useful for molecular testing.

This study was approved by the institutional review board (Date of approval: May 27, 2013, approval number: 2816) of Tokyo Women's Medical University Hospital.

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1. Introduction

Advances in computed tomography (CT) have resulted in the frequent detection of peripheral pulmonary lesions (PPLs). Various conditions, including lung cancer, malignant lymphoma, benign tumor, sarcoidosis, tuberculosis, and inflammation can manifest as PPLs. Transbronchial biopsy (TBB), transbronchial brushing (brushing), bronchoalveolar lavage, and instrument rinsing (IR) are widely used for the histological or cytological diagnosis of PPLs. The 3rd edition of the guidelines from the American College of Chest Physicians (ACCP) recommends the use of endobronchial ultrasonography (EBUS) to increase the diagnostic yields for PPLs [1]. TBB and brushing with EBUS using a guide sheath (EBUS-GS) are considered effective methods for PPLs. The diagnostic yields with EBUS-GS for PPLs are reported to range from 46.0% to 86.2% [2–9]. Furthermore, virtual bronchoscopic navigation with EBUS-GS has been used to obtain sufficient tissue from PPLs for improving the diagnostic yields [10]. However, successful sampling depends on the size and location of PPLs. Transbronchial needle aspiration (TBNA) for PPLs has obtained higher diagnostic yields than TBB [11–15]. TBNA with EBUS has reported higher diagnostic yields than TBB with EBUS [16]. Furthermore, TBNA with EBUS-GS and virtual bronchoscopy was found to be effective even when PPLs could not be visualized by EBUS-GS [17], and TBNA was established to obtain fragments of tissues [17,18]. However, its efficacy while undergoing TBNA with EBUS-GS remains unknown. The purpose of this study was to evaluate the efficacy and safety of TBNA with EBUS-GS to assess the PPLs of patients suspected to be lung cancer.

2. Patients and methods

2.1. Ethical considerations

This was a prospective study that was approved by the institutional review board (Date of approval: May 27, 2013, approval number: 2816) of Tokyo Women's Medical University Hospital. Informed consent was obtained from all patients before they were enrolled in this study.

2.2. Patients and study design

A total of 146 patients with clinically and radiologically suspected lung cancer were initially screened. However, 16 patients were excluded because they were identified with endobronchial tumor. Therefore, finally, the study included 130 patients who had undergone TBNA with EBUS-GS for a definitive diagnosis, from June 2013 to February 2014, at Tokyo Women's Medical University Yachiyo Medical Center. The eligible patients were aged 20 years or older who had PPLs suspected to be lung cancer. The exclusion criteria in this study were as follows: bleeding tendency, platelet count $< 20{,}000/mm^3$, pregnancy, obvious active infection, respiratory insufficiency, and refusal to participate in the study.

All PPLs were confirmed by CT, and 18F-fluorodeoxyglucose-positron emission tomography was performed to assess the lesion for suspected malignancy prior to TBNA with EBUS-GS. Each patient underwent bronchoscopy, and EBUS-GS was used for direct sampling by brushing, TBB, and TBNA. The specimens were used to assess and compare the diagnostic accuracy of each sampling method.

2.3. Procedures

A flexible fiber bronchoscope (BF-1T260; Olympus, Tokyo, Japan), guide sheath (SG201 C; Olympus), 1.4-mm 20-MHz radial probe (UM-S20-17S; Olympus), brush (BC-202D-2010; Olympus), forceps (FB-231D; Olympus), and a 1.3-cm 21-gauge needle with a side aperture (NA-201 SX-4022-A; Olympus) were used for this study. All procedures were performed using local anesthesia with 1% lidocaine via nebulizer, 2% lidocaine as bolus to the bronchus, and intravenous injection of 2–2.5 mg of midazolam and intramuscular injection of 35 mg pethidine hydrochloride for conscious sedation. During the procedure, all patients underwent monitoring for blood pressure, oxygen saturation, pulse rate, and electrocardiographic patterns.

2.4. Diagnostic samples

EBUS-GS was inserted into the bronchus associated with the PPLs. After identification of the PPLs by a combination of EBUS and radiographic fluoroscopy, the internal EBUS was removed, leaving behind the GS [3,4]. If the PPLs were not identified by EBUS, the EBUS probe was withdrawn and a curette was inserted into the GS to move into another target bronchus. The curette was withdrawn and the probe was reinserted into the GS to identify PPLs under fluoroscopy [3]. We performed all three procedures (brushing, TBB, and TBNA) in series, to obtain cytological materials and histological tissue, as follows: 1) The brush for brushing was inserted into the GS three times to obtain cytological materials; 2) The forceps used for TBB was inserted into the GS five times to

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