ORIGINAL ARTICLE

Factors associated with the diagnostic yield of computed tomography-guided transbronchial lung biopsy

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Abstract

Background: Computed tomography (CT) may be useful for increasing the diagnostic yield of transbronchial lung biopsy (TBLB). However, only a few studies with small sample sizes have reported the diagnostic utility of CT-guided TBLB and the factors affecting the diagnostic accuracy of CT-guided TBLB are not well known. We evaluated the diagnostic yield of CT-guided TBLB and associated factors.

Methods: CT-guided TBLB was performed in 59 patients. Both conventional fluoroscopy and CT were used in all patients for TBLB. The biopsy forceps were advanced toward the lesion under conventional fluoroscopic guidance. CT was used to check whether the forceps were in the correct position.

Results: The average diameter of the lesions was 3.1 ± 1.0 cm. The biopsy forceps correctly reached the lesion in 43 patients by real-time CT. A diagnosis was made in 42 patients, and the overall diagnostic yield was 71.2%. The sensitivity for malignancy was 85.7%. In multivariate analysis, the only factor associated with diagnostic yield was forceps position assessed by CT scan (adjusted odds ratio 53.31; 95% confidence interval 5.31, 535.27; $P = 0.001$).

Conclusion: CT-guided TBLB is a useful diagnostic tool for pulmonary nodules or masses. The correct positioning of biopsy forceps using CT is valuable for successful CT-guided TBLB.

Introduction

Bronchoscopic procedures are used to visualize the tracheobronchial tree and obtain specimens of abnormal lesions. Transbronchial lung biopsy (TBLB) by either blind methods or under fluoroscopic guidance is a well-established method that has been used for more than 30 years. However, small and peripheral lung lesions are difficult to diagnose using these procedures.[1,2] The overall diagnostic yield of conventional fluoroscopic TBLB varies from 18% to 75%.[3–7]

Percutaneous transthoracic biopsy with computed tomography (CT) leads to a better diagnostic yield for peripheral lung lesions and pneumothorax is the most common complication.[8–10] Endobronchial ultrasound (EBUS)-guided TBLB also has a higher diagnostic yield than TBLB with conventional fluoroscopy for peripheral and small lung lesions.[11–13] However, EBUS-guided TBLB cannot be applied without the use of expensive endoscopic ultrasound systems or skilled operators.

Previous studies have reported a higher yield of CT-guided TBLB than conventional TBLB.[14–17] However, these studies had small sample sizes, and few have evaluated the factors associated with the diagnostic yield of CT-guided TBLB. Therefore, we evaluated the diagnostic yield of CT-guided TBLB and associated factors.

Methods

Study subjects

We retrospectively evaluated a total of 59 patients from January 2013 to April 2015. Chest CTs were performed in all patients before the bronchoscopic procedure. Only patients with measurable nodules or masses in the chest

CT were included in the study. We measured lesion size as the longest cross-sectional diameter. We also determined the location of the lesion in the upper, middle, or lower lobe. Air-bronchus sign was defined as air-filled bronchus surrounded by fluid-filled airspaces in the lesion. Distance from the hilum to the lesion was calculated by Pythagoras theorem. Horizontal distance was measured as the shortest distance from the hilum to the lesion. Vertical distance was calculated as the product of the number of CT slides from the lesion to the hilum and the thickness of the CT scan. Horizontal and vertical distance was applied to Pythagoras theorem to calculate the distance from the hilum to the lesion. Both conventional fluoroscopy and CT were used in all patients scheduled for TBLB. Informed written consent was obtained from all patients before bronchoscopic procedures. The Institutional Review Board of National Health Insurance Service Ilsan Hospital approved this study.

Bronchoscopic procedure

Patients received 0.5 mg of intramuscular atropine and 50 μg of intramuscular fentanyl before procedures. Dexmedetomidine (0.7 mg/kg/hour) was continuously infused during the procedure for sedation. The bronchoscope (240, P240, 40, P40; Olympus; Tokyo, Japan) was inserted through the nose into the trachea and bronchus. Patients received intranasal oxygen and breathed spontaneously during the procedure. Oxygen saturation, blood pressure, and electrocardiography were monitored in all patients.

After bronchoscopic insertion into the tracheobronchial tree, a full inspection was performed from the trachea to the segmental or subsegmental bronchus. The tip of the bronchoscope was placed into the suspected segmental bronchus thought to open through the lung lesions. After the tip of the bronchoscope was positioned, the biopsy forceps were inserted through the selected segmental bronchus under guidance by conventional fluoroscopy. Bronchoscopic procedure was performed in a CT-equipped angiography room.

Computed tomography procedure

A dynamic CT of the interventional angiography system (Artis Zee, Siemens, Germany) was used for real-time CT during the procedure. After the biopsy forceps were advanced toward the lung lesions, a brief dynamic CT scan was performed by a radiologist who then transmitted the images to a CT video monitor in real time. The bronchoscopist could check images displayed on a CT video monitor that was placed adjacent to the bronchoscopic video monitor. After confirming via CT images that the biopsy forceps had been placed within the target lesion images (Figs 1–2), TBLB was performed without additional CT
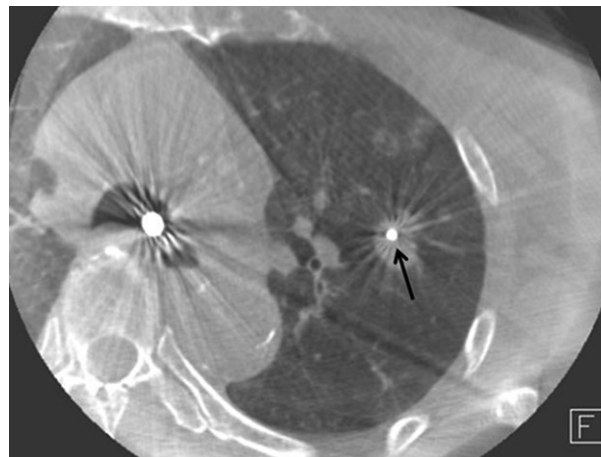

Figure 1 Computed tomography-guided transbronchial lung biopsy with biopsy forceps in a target lesion (black arrow).

scans. To minimize radiation exposure, a maximum of two CT scans were performed to check forceps position. If the forceps did not reach the lung lesions after two CT scans, TBLB was performed without additional CT confirmation of forceps positioning. Placement of the tip of the biopsy forceps into the lung lesions was considered to indicate successful targeting.

Final diagnosis

Biopsy specimens were immediately fixed in formalin and sent to pathology. Pathologic diagnoses were divided into four groups: non-specific inflammation, tuberculosis, malignancy, and other disease. Tuberculosis, malignancy, and other disease were considered as a definite diagnosis
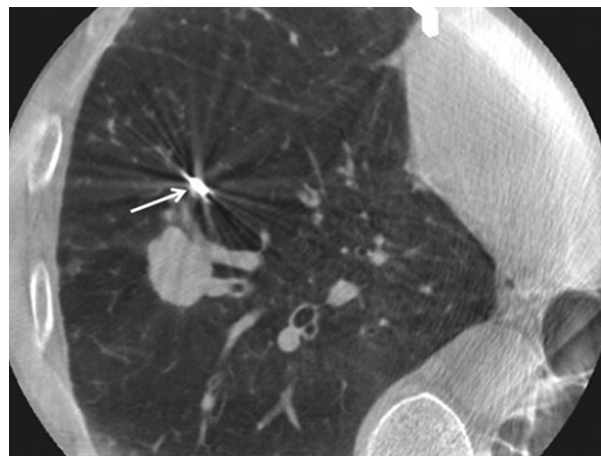

Figure 2 Computed tomography-guided transbronchial lung biopsy with the biopsy forceps failing to reach a target lesion (white arrow).

(TBLB positive), while non-specific inflammation was not (TBLB negative). In cases of non-specific inflammation, patients underwent additional tests, including transthoracic needle aspiration or video-assisted thoracoscopic surgery, and lesions that resolved after antibiotic treatment were considered to be pneumonia.

Statistical analysis

Statistical analyses were performed using a SPSS version 21 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as the mean ± standard deviation, and categorical variables were expressed as number and percentage. Independent two-sample *t* test and chi-square or Fisher's exact tests were used to identify differences between groups. Logistic regression analysis was used to analyze the odds ratios of significant factors affecting the diagnostic yield of CT-guided TBLB. All statistical analyses were two-tailed and *P* values less than 0.05 were considered significant.

Results

Baseline characteristics

The enrolled patients included 41 men and 18 women with an average age of 65.5 ± 14.6 years (Table 1). All patients underwent chest CT scans before bronchoscopic procedures. The average size of the lesions was 3.3 ± 1.0 cm. Lung lesions are more frequent in upper than lower lobes.

Procedural results and pathologic diagnosis

All patients underwent CT-guided TBLB and were divided into two groups by pathologic results (Table 1). A total of 10 lung lesions were not visible on conventional fluoroscopy. The biopsy forceps were blindly advanced in these patients. The accuracy of forceps targeting was checked by dynamic CT (Figs 1–2). The average number of biopsies was 7.8 ± 2.9 and procedure duration was 33.7 ± 7.6 minutes. Successful targeting was confirmed in 43 patients (72.9%) by real-time CT. In 16 patients, lung lesions were not targeted by the biopsy forceps after a maximum of two CT scans. Pneumothorax occurred in two patients. Other factors, except lesion size, visibility by fluoroscopy, and forceps targeting by CT, were not significantly different between the two groups. Table 2 shows the pathologic diagnoses. The most common finding was malignancy in 30 patients. The second most common finding was non-specific inflammation in 17 patients. These patients underwent additional tests, including transthoracic needle aspiration or video-assisted thoracoscopic surgery. Other patients who could not undergo additional biopsies were followed up regularly after antibiotic treatment. Final diagnoses could not be confirmed in two patients.

Diagnostic yield and factors affecting diagnostic yield

The overall diagnostic yield of CT-guided TBLB was 71.2% (Table 3). For malignancy, the sensitivity of CT-guided TBLB was 85.7% and the negative predictive value was 81.5%. The diagnostic yield for lung nodules (<3 cm) was

Table 1 Baseline characteristics and clinical differences between TBLB results

	Total patients (*n* = 59)	TBLB positive (*n* = 42)	TBLB negative (*n* = 17)	*P*
Age (years)	65.5 ± 14.6	65.0 ± 15.1	66.8 ± 13.8	0.673
Male	41 (69.5)	29 (69.0)	12 (70.6)	0.907
Size (cm)	3.1 ± 1.0	3.3 ± 0.9	2.7 ± 0.9	0.022
Location				
Upper lobe	36 (61.0)	28 (66.7)	8 (47.1)	0.162
Middle or lower lobe	23 (39.0)	14 (33.3)	9 (52.9)	
Air-bronchus sign	17 (28.8)	14 (33.3)	3 (17.6)	0.344
Distance from hilum (cm)	5.3 ± 2.0	5.1 ± 2.1	5.7 ± 1.9	0.298
Conventional fluoroscopy				
Visible	49 (83.1)	38 (90.5)	11 (64.7)	0.026
Invisible	10 (16.9)	4 (9.5)	6 (35.3)	
Number of biopsies	7.8 ± 2.9	7.7 ± 2.5	8.1 ± 3.7	0.612
Forceps targeting by CT				
Success	43 (72.9)	38 (90.5)	5 (29.4)	<0.001
Failure	16 (27.1)	4 (9.5)	12 (70.6)	
Procedure duration (minutes)	33.7 ± 7.6	33.5 ± 7.8	34.2 ± 7.2	0.756
Pneumothorax	2 (3.4)	1 (2.4)	1 (5.9)	0.497

CT, computed tomography; TBLB, transbronchial lung biopsy. Data are shown as the mean ± standard deviation or number (%).

Table 2 Pathologic diagnosis by TBLB and final diagnosis

	Number of patients
Pathologic diagnosis by TBLB	
Non-specific inflammation†	17
Tuberculosis	11
Adenocarcinoma	18
Squamous cell carcinoma	5
Small cell carcinoma	6
Non-small cell carcinoma	1
Aspergilloma	1
Final diagnosis	
Pneumonia	9
Tuberculosis	12
Adenocarcinoma	20
Squamous cell carcinoma	6
Small cell carcinoma	7
Non-small cell carcinoma	2
Aspergilloma	1
No final diagnosis	2

†Final diagnosis of non-specific inflammation: pneumonia (9), tuberculosis (1), adenocarcinoma (2), squamous cell carcinoma (1), small cell lung cancer (1), non-small cell lung cancer (1), no final diagnosis (2). TBLB, transbronchial lung biopsy.

Table 3 Overall diagnostic yield and sensitivity, specificity, PPV, and NPV for malignancy†

Factor	Result (%)
Diagnostic yield	71.2
Sensitivity	85.7
Specificity	100.0
PPV	100.0
NPV	81.5

†Two patients with no final diagnosis were excluded from analyses of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

58.6%. The factors associated with diagnostic yield of CT-guided TBLB are shown in Table 1. Lesion size, visible lesions by fluoroscopy, and proper forceps position confirmed by real-time CT were associated with diagnostic yield. However, the only significant factor in multivariate analysis was confirmation of forceps position by real-time CT (Table 4). The diagnostic yield was 53.31 times greater when CT could confirm the position of the biopsy forceps

in the lung lesions than when the forceps failed to find the lesions.

Discussion

Our results suggest that CT-guided TBLB is suitable for the diagnosis of lung nodules or masses. The overall observed diagnostic yield was 71.2%, and sensitivity for malignancy was 85.7%. The most important factor associated with diagnostic yield was confirmation of the position of the biopsy forceps in lung lesions by real-time CT.

Most previous studies of CT-guided TBLB have been small case series, most without control groups. The overall diagnostic yield of CT-guided TBLB reported in these studies ranged from 62% to 75%.[16–21] Only two studies evaluated CT-guided TBLB with controls. Tsushima *et al.* retrospectively compared 82 patients who underwent CT-guided bronchoscopy to 78 patients treated with fluoroscopy-guided bronchoscopy.[19] The two groups had undergone bronchoscopy during different time periods (2001–2003 vs. 1999–2001) and at different hospitals, but all procedures were performed by the same bronchoscopist. In that study, CT-guided bronchoscopy demonstrated superior results in terms of lesion size (<15 mm in diameter). Ost *et al.* prospectively compared 26 patients who underwent CT-guided bronchoscopy to 24 patients treated with fluoroscopy-guided bronchoscopy.[21] They evaluated CT-guided bronchoscopic performance for the diagnosis of peripheral lung nodules and mediastinal lymph nodes. Although they failed to demonstrate any benefits of CT-guided TBLB compared with fluoroscopy, they reported that CT-guided TBLB might yield superior diagnosis of mediastinal lymphadenopathy compared with conventional bronchoscopy.

Computed tomography-guided TBLB has shown better diagnostic yield for small peripheral lesions; however, overall diagnostic yield remains 60–70%. Therefore, the identification of factors related to the diagnostic yield of CT-guided TBLB is important. Shinagawa *et al.* reported that diagnostic sensitivity was related to the locations of lesions, bronchial generation inserted by bronchoscopy, and the presence of a bronchus close to the lesion.[20] In

Table 4 Multivariate analyses of factors associated with diagnostic yield

	Adjusted odds ratio	95% confidence interval	*P*
Forceps targeting	53.31	5.31 –535.27	0.001
Visibility by conventional fluoroscopy	0.62	0.06 –6.32	0.687
Size	2.74	0.98 –7.63	0.054
Air-bronchus sign	5.15	0.60 –44.47	0.136
Distance from hilum	0.77	0.48 –1.23	0.272

their study, the method had low diagnostic sensitivity for lesions in the left superior segment compared with other locations. An ultrathin bronchoscope that could be inserted into the fifth or higher generation of a bronchus had high diagnostic sensitivity, and lesions connected to a bronchus or an artery could be detected with sensitivity. In our study, targeting of the biopsy forceps by CT scan, lesions visualized by conventional fluoroscopy, and lesion size were correlated with diagnostic yield. Among these, positioning of the biopsy forceps in the lung lesions by CT scan was the most important predictor of accurate diagnosis in multivariate analysis. Predicting the success of biopsies is important because it allows clinicians to prepare another option for evaluation or to explain to patients that the biopsy may fail before results are reported.

The most important problem associated with CT-guided TBLB is radiation exposure. Previous studies have reported that CT-guided TBLB causes acceptable levels of radiation exposure. Hautmann *et al.* found that low-dose CT guided TBLB had high diagnostic yield and low radiation exposure.[17] The average number of CT scans was 4.1, and the mean effective dose of radiation was 0.55 mSv, equivalent to the radiation dose of three chest X-rays. Another previous study also reported that the radiation exposure associated with real-time multi-slide computed tomography (MSCT)-guided TBLB is low.[19] The radiation dose associated with MSCT fluoroscopy is at least double that of conventional fluoroscopy. Unlike conventional fluoroscopy, MSCT fluoroscopy employs a tightly collimated beam that is confined to a narrow area. In our study, a maximum of only two CT scans were performed per procedure to minimize radiation exposure. However, we were unable to calculate exact radiation doses because the necessary program was not in use in our hospital during the study period.

Computed tomography-guided transthoracic needle aspiration or EBUS-guided biopsy are alternative options for the diagnosis of lung lesions. However, CT-guided transthoracic needle aspiration leads to decreased diagnostic accuracy and an increased risk of pneumothorax when the target is distant from the pleura.[22] EBUS-guided biopsies that have higher diagnostic yield do not cause radiation exposure.[11–13] However, such procedures are not widely available and only possible if clinicians receive specialized training. Moreover, small nodules without solid components are difficult to detect with ultrasound-guided biopsy.[23,24]

Our study has several limitations. First, we included a wide range of patients. The higher diagnostic yield in this study may be a result of including relatively large lung lesions. However, separate analyses of small nodules showed an acceptable diagnostic yield, similar to previous studies. Second, this is a single center study. Other institutions may not use real-time CT-guided TBLB. However,

CT is a widely used diagnostic tool and institutions that perform bronchoscopy and CT may perform this procedure without difficulty. Third, we only retrospectively analyzed patients who underwent CT-guided TBLB. Therefore, we cannot directly compare diagnostic yield between conventional fluoroscopy-guided and CT-guided TBLB. Multicenter studies with large sample sizes are needed to validate the effectiveness of CT-guided TBLB. Finally, we could not analyze for ground glass nodules because we only enrolled patients with solid nodules or masses. Further studies will be needed to determine the diagnostic yield of CT-guided TBLB for ground glass nodules.

In conclusion, we found that CT-guided TBLB provides a good diagnostic yield for pulmonary nodules or masses, with a relatively low risk of radiation exposure and low rate of complications. The positioning of biopsy forceps under the guidance of real-time CT can predict successful biopsy results. In selected patients, CT-guided TBLB is a suitable alternative for the diagnosis of lung lesions that are difficult to evaluate by other procedures.

Acknowledgments

Disclosure

No authors report any conflict of interest.

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