Original Article

Factors associated with increased diagnostic yield of endobronchial ultrasound-guided transbronchial needle aspiration: an observational single center study

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Background: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is an innovative tool for diagnosing mediastinal diseases. We investigated the factors affecting the diagnostic yield of EBUS-TBNA and evaluated whether the effects of these factors (number of biopsies, core tissue acquisition rate, and diameter and volume of tissue) vary depending on computed tomography (CT) and/or positron emission tomography (PET)/CT results.

Methods: We retrospectively analyzed lung cancer patients who underwent EBUS-TBNA at Korea University Ansan Hospital (January 2019–December 2022). Patients in whom EBUS-TBNA failed and those with missing diameter or volume data and no imaging data interpretation were excluded. Subgroup analysis was performed by dividing the patients into None (no cancer detected on CT or PET/CT), Either (cancer detected on either CT or PET/CT), and Both (cancer detected on both CT and PET/CT) groups.

Results: In all, 228 patients were enrolled; 351 lymph node stations were analyzed. The median age of the patients was 69 years (male, 76.8%). Adenocarcinoma (28.5%) was the most common diagnosis. EBUS-TBNA was predominantly performed at station #4R (30.5%). Each examination involved two stations with a total procedure time of 30 minutes. An increased number of passes led to a higher diagnostic yield for EBUS-TBNA (P<0.001). Additionally, successful tissue sampling was associated with a large diameter (P=0.016) and volume (P=0.002) of the tissue. The effect of these factors was modified by imaging results. In the None and Either groups, an increase in the pass number was correlated with an increased diagnostic yield (adjusted P=0.003 and 0.007, respectively). However, in the Both group, it was not significant and remained at a suggestive level (P=0.304). The diameter and volume did not differ significantly across subgroups (adjusted P>0.05).

Conclusions: Increasing the number of passes during EBUS-TBNA can maximize the diagnostic yield, especially when CT and/or PET/CT results are inconclusive.

Keywords: Accuracy; bronchoscopy; endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA); lung neoplasms; lymph nodes (LNs)

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Introduction

Background

Lung cancer is a significant global health problem, resulting in the highest number of cancer-related deaths. In 2020, there were 2.2 million new lung cancer cases, resulting in 1.8 million deaths. It has the highest morbidity and mortality rates among all malignant tumors (1). In cases of non-small cell lung cancer (NSCLC), which comprises 85% of primary lung cancer cases, assessing mediastinal lymph node (LN) metastasis is crucial for determining the need for surgery and predicting prognosis (2,3). Although non-invasive imaging tests such as computed tomography (CT) and positron emission tomography (PET)/CT are advancing rapidly, cytological or histological examination of mediastinal LN is essential because of issues such as low sensitivity and specificity as well as false positives and false negatives, respectively (4).

Rationale and knowledge gap

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) combines bronchoscopy and ultrasonography, allowing real-time visualization of the airway, mediastinum, and lungs during biopsy using a fine needle (5). EBUS-TBNA offers several advantages, such as high accuracy, minimal invasiveness, and cost-effectiveness (6), and is widely used for diagnosing thoracic malignancies (primary or metastatic), sarcoidosis, lymphoma, and tuberculosis (7-10). However, the diagnostic yield of EBUS-TBNA remains relatively low (11) and is influenced by factors such as lesion characteristics (size, location, and nature), operator experience, sample quality and adequacy, and the number of needle passes (12-15). Furthermore, the influence of external factors, such as CT or PET/CT findings, on these factors is unknown.

Objective

Our study aimed to investigate the impact of various factors, including sample diameter, sample volume, number of aspirations per LN station, and core tissue collection rate, on the diagnostic yield of EBUS-TBNA. We also evaluated how the effect of these factors was modified by the results of CT or PET/CT imaging. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1369/rc).

Highlight box

Key findings

- Increasing the number of passes during endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) can increase diagnostic yield. This effect is maximized when computed tomography (CT) and/or positron emission tomography/CT results are inconclusive.

What is known and what is new?

- EBUS-TBNA is useful in diagnosing mediastinal diseases. However, diagnostic yield of EBUS-TBNA is low and influenced by several factors.
- This study investigated the effect of these factors on its diagnostic yield.

What is the implication, and what should change now?

- Given the time and cost-intensive nature of EBUS-TBNA, adjusting needle passes based on imaging findings is crucial for cost-effective accuracy enhancement.
- This approach could potentially improve precision in cost-effective EBUS-TBNA by better incorporating lesion characteristics and imaging results.

Methods

Study design and population

We retrospectively analyzed the medical records of patients who underwent EBUS-TBNA at a single university-affiliated hospital in South Korea between January 1, 2019 and December 31, 2022. All adult patients who underwent EBUS-TBNA due to abnormal findings in the mediastinal LN on chest CT and/or PET/CT imaging for various reasons were included in the study. The exclusion criteria were as follows: (I) cases in which EBUS-TBNA was attempted but was not performed; (II) missing data on tissue diameter or volume; (III) no interpretation result from the imaging; and (IV) diagnosis other than lung cancer. The chest CT and PET/CT data were independently interpreted by specialists in radiology

and nuclear medicine. General principles of interpretation were applied for assessing cancer findings in nodes. Factors such as the increasing size of nodes, irregular shape, central necrosis, and compression of adjacent structures were considered for CT. The interpretation considered the results of the maximum standardized uptake value for PET/CT. However, the decision to perform EBUS-TBNA was made independently by physicians, regardless of the interpretation of the imaging results. If the same patient underwent EBUS-TBNA two or more times on different dates during the study period, we recorded each procedure as a separate event.

The primary outcome was the relationship between the diagnostic yield of EBUS-TBNA and the number of passes, adequate tissue gain, maximum tissue diameter, and estimated tissue volume. A subgroup analysis was performed to evaluate the influence of CT and/or PET/CT results on this relationship.

Procedure and specimen handling

EBUS-TBNA was performed by a team of one bronchoscopist and two trained nurses; the bronchoscopist was replaced by three pulmonologists. The procedure was performed under topical anesthesia, and the scope was inserted via the oral route, followed by conscious sedation with midazolam and fentanyl. If a patient was inadequately sedated, propofol was administered at the discretion of the physician. EBUS-TBNA was performed using bronchoscopes (BF-1T260, BF-1TQ290, BF-Q290; Olympus, Tokyo, Japan) and an ultrasonic bronchoscope (BF-UC260FW; Olympus) with a dedicated 22-gauge needle (Vizishot 1; Olympus).

LN stations were named according to the International Association for the Study of Lung Cancer classification. Because rapid on-site cytological examination (ROSE) was not feasible at our institution, the appropriateness of sample collection was assessed visually by a trained nurse to confirm adequate sample collection. Specimens were placed in 10% formalin for cell block preparation and transferred to the pathology department. The cell blocks were embedded in paraffin, cut into 6-μm-thick sections, and stained with hematoxylin and eosin for pathological evaluation. Additional immunohistochemistry staining was performed at the discretion of the pathologists to determine the type of cancer.

Data collection and definition

Demographic data, CT and PET/CT findings, and smoking status data were also collected. The number of LNs obtained, LN stations, biopsy results, total procedure time, number of passes, percentage of core tissue, maximum diameter, and estimated volume were recorded.

In this study, the number of passes was defined as the number of needle punctures per LN, and the core tissue percentage was defined as the percentage of core tissue adequately obtained from all puncture attempts. The maximum diameter, representing the largest dimension of the acquired core tissue, was measured by a clinical pathologist when creating the slides. Tissue volume was estimated by multiplying the length, height, and width of the tissue. Successful biopsy was defined as a confirmed diagnosis of lung cancer using EBUS-TBNA, whereas biopsy failure was defined as either a benign result or an inadequate tissue sample for diagnosis.

We also performed a subgroup analysis based on imaging findings. The None group had no cancer findings on either CT or PET/CT imaging, Either group had cancer findings on either CT or PET/CT imaging, and Both group had cancer findings on both CT and PET/CT imaging.

Ethical consideration

This study was conducted according to the ethical standards of the Declaration of Helsinki (as revised in 2013). The study protocol was approved by the Institutional Review Board of Korea University Ansan Hospital (IRB No. 2023AS0047), and the requirement for consent was waived owing to the retrospective nature of the study.

Statistical analysis

Categorical variables are presented as numbers and percentages, whereas continuous variables are presented as the median and interquartile range (IQR) or mean and standard deviation, depending on the distribution characteristics. Chi-square or Fisher's exact tests were used to determine the associations between categorical variables, and Student's *t*-test or Mann-Whitney *U* test was used to compare the means of continuous variables, depending on the normality of the distribution. We analyzed the relationship between the number of passes and diagnostic yield using the Cochran-Armitage trend test and logistic

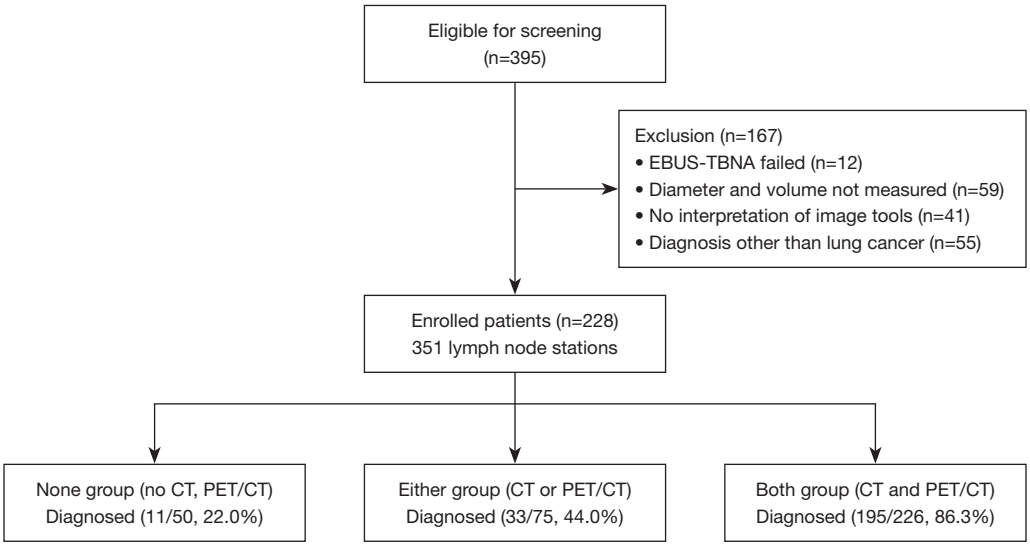

Figure 1 Flowchart of patient registration. EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; CT, computed tomography; PET, positron emission tomography.

regression analysis. We calculated the adjusted P values for subgroup analyses using the Bonferroni correction. Statistical P value was defined as a two-tailed P value <0.05, and all analyses were conducted using the SAS statistical software (ver. 9.4; SAS Institute, Cary, NC, USA) and R (ver. 4.0.3; The R Foundation, Vienna, Austria).

Results

During the study period, 395 patients underwent EBUS-TBNA, and 228 patients were finally registered after excluding 167 patients who did not meet the criteria (*Figure 1*). The median age of the patients was 69.00 years (IQR, 63.00–77.25 years), and 76.8% were male (n=175). Sixty-seven patients (29.4%) were current smokers, and 77 patients (33.8%) were former smokers, indicating that approximately two-thirds of the patients had a smoking history. Cancer was suspected in 159 patients (69.7%) based on CT findings, and 178 patients (78.1%) had cancer according to the PET/CT findings. A total of 351 LN stations were examined using EBUS-TBNA. The right lower paratracheal LN (#4R) was the most frequently examined node (30.5%), followed by the subcarinal LNs (#7) (27.4%). EBUS-TBNA was performed at a median of two stations, and the median procedure time was 30 minutes (IQR, 23–40 minutes). Adenocarcinoma was the most common type of lung cancer, identified at 100 stations (28.5%), and the proportion of benign LNs was 28.2%. No significant adverse events related to EBUS-TBNA were observed except for major bleeding that required endotracheal intubation for airway protection in one case. The most common complication was post-procedure fever, observed in 15.4%, followed by minor bleeding controlled with simple observation or local epinephrine use, which occurred in 7.9% (*Table 1*).

In this study, we investigated the relationship between the diagnostic yield of EBUS-TBNA and various variables, such as the number of passes, core tissue percentage, maximal diameter, and estimated volume. The overall diagnostic yield was 68.1%, and it was found to significantly increase as the number of passes increased, with success rates of 52.6%, 61.3%, 77.5%, 87.9%, and 100.0% (P<0.001) (*Table 2*). Although the odds ratio (OR) for two passes compared to that for one pass was not statistically significant (P=0.327), the ORs for three passes and four or more passes showed significant increments [three passes: OR =3.09, 95% confidence interval (CI): 1.41–6.80, P=0.005; four or more passes: OR =7.65, 95% CI: 2.27–25.81, P=0.001] (Table S1). Additionally, the maximal diameter was significantly longer in the successful biopsy group (median, 1.50 cm; IQR, 1.00–2.00 cm) than that in the failed group (median, 1.00 cm; IQR, 1.00–1.50 cm) (P=0.016), and the tissue volume was also significantly larger in the successful biopsy group (median, 0.45 cm^3; IQR, 0.20–0.68 cm^3) than in the failed group (median, 0.20 cm^3; IQR, 0.10–0.45 cm^3) (P=0.002). However, there was no significant difference in the

Table 1 Baseline characteristics

Variables	Values
Sex (male)	175 (76.8)
Age (years)	69.00 [63.00–77.25]
Smoking status	
Current smoker	67 (29.4)
Former smoker	77 (33.8)
Never smoker	84 (36.8)
CT interpretation (suspicious lung cancer)	159 (69.7)
PET/CT interpretation (suspicious lung cancer)	178 (78.1)
Target location (351 stations)	
4R (right lower paratracheal lymph node)	107 (30.5)
7 (subcarinal lymph node)	96 (27.4)
Lung mass	34 (9.7)
11 L (left interlobar lymph node)	30 (8.5)
10 R (right hilar lymph node)	28 (8.0)
Others	56 (16.0)
Total number of target sites	2 [1–2]
Procedure time (minutes) (n=221)	30 [23–40]
EBUS-TBNA results (351 stations)	
Adenocarcinoma	100 (28.5)
Squamous cell carcinoma	60 (17.1)
Small cell carcinoma	48 (13.7)
Benign	99 (28.2)
Others	44 (12.5)
Complications	
Fever	35 (15.4)
Minor bleeding[†]	18 (7.9)
Desaturation	5 (2.2)
Hypotension	4 (1.8)
Major bleeding[‡]	1 (<1)

Categorical data are presented as number (%), and continuous data are presented as median [interquartile range], depending on the normality of the distribution. [†], minor bleeding is defined as cases where the bleeding stopped with simple observation or was controlled solely with topical epinephrine; [‡], major bleeding refers to cases where massive hemorrhage occurred, necessitating endotracheal intubation for airway protection. CT, computed tomography; PET, positron emission tomography; EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration.

Table 2 Biopsy success percentage and ratio according to the number of passes

No. of passes	No. of stations	Failed, n (%)	Success, n (%)	Success percentage (%)	Success ratio	P value
1	38	18 (16.1)	20 (8.4)	52.6	1:1.11	<0.001
2	173	67 (59.8)	106 (44.4)	61.3	1:1.58	
3	102	23 (20.5)	79 (33.1)	77.5	1:3.43	
4	33	4 (3.6)	29 (12.1)	87.9	1:7.25	
5	5	0	5 (2.1)	100.0	All	
Total	351	112	239	68.1	1:2.13	

Number of passes was defined as the number of needle punctures per lymph node. The success percentage was calculated by dividing the number of successful stations by the total number of stations and multiplying it by 100. Success ratio was calculated as the ratio of failed to successful stations.

percentage of core tissue between the two groups (P=0.273) (*Table 3*).

We conducted a subgroup analysis to investigate how the CT and PET/CT results and other factors affect the diagnostic yield of EBUS-TBNA. We observed a significant difference in the success rate of EBUS-TBNA depending on the results of the imaging examination. The biopsy success rate was 22.0% (11 out of 50) in the None group, 44.0% (33 out of 75) in the Either group, and 86.3% (195 out of 226) in the Both group (Tables S2,S3). Additionally,

Table 3 Differences in each variable between successful and failed groups of cancer diagnosis

Variables	Total (n=351)	Success (n=239)	Failed (n=112)	P value
Core tissue percentage (%)	100.00 (75.00–100.00)	100.00 (75.00–100.00)	100.00 (100.00–100.00)	0.273
Maximal diameter (cm)	1.50 (1.00–1.75)	1.50 (1.00–2.00)	1.00 (1.00–1.50)	0.016
Volume (cm^3)	0.30 (0.12–0.68)	0.45 (0.20–0.68)	0.20 (0.10–0.45)	0.002

Core tissue percentage is defined as the percentage of core tissue adequately obtained from the total puncture attempts. Maximal diameter was the longest dimension of the obtained core tissue. Volume was estimated by multiplying the length, height, and width of the tissues. Data are presented as median (interquartile range).

Table 4 Relationship between the number of passes and success rate according to imaging subgroups

Subgroup	No. of passes	No. of stations, n (%)	Failed, n (%)	Success, n (%)	Success percentage (%)	Success ratio	P value	
							Raw	Adjusted
None	1	6 (12.0)	6 (15.4)	0 (0)	0	None	0.001	0.003
	2	28 (56.0)	25 (64.1)	3 (27.3)	10.7	1:0.12		
	3	13 (26.0)	7 (17.9)	6 (54.5)	46.2	1:0.86		
	4	3 (6.0)	1 (2.6)	2 (18.2)	66.7	1:2		
	Total	50	39	11	22.0	1:0.28		
Either	1	10 (13.3)	8 (19.0)	2 (6.1)	20.0	1:0.25	0.002	0.007
	2	38 (50.7)	25 (59.5)	13 (39.4)	34.2	1:0.52		
	3	19 (25.3)	7 (16.7)	12 (36.4)	63.2	1:1.71		
	4	8 (10.7)	2 (4.8)	6 (18.2)	75.0	1:3		
	Total	75	42	33	44.0	1:0.79		
Both	1	22 (9.7)	4 (12.9)	18 (9.2)	81.8	1:4.5	0.101	0.304
	2	107 (47.3)	17 (54.8)	90 (46.2)	84.1	1:5.29		
	3	70 (31.0)	9 (29.0)	61 (31.3)	87.1	1:6.78		
	4	22 (9.7)	1 (3.2)	21 (10.8)	95.5	1:21		
	5	5 (2.2)	0	5 (2.6)	100	All		
	Total	226	31	195	86.3	1:6.29		

Number of passes was defined as the number of needle punctures per lymph node. The success percentage was calculated by dividing the number of successful stations by the total number of stations and multiplying it by 100. Success ratio was calculated as the ratio of failed to successful stations. None group: defined as having cancer findings on neither CT or PET/CT readings; Either group: defined as having cancer findings on either CT or PET/CT scan; Both group: defined as having cancer findings on CT and PET/CT. CT, computed tomography; PET, positron emission tomography.

we found that the success rate of EBUS-TBNA significantly increased according to the number of needle passes in the None group, at rates of 0%, 10.7%, 46.2%, and 66.7% (adjusted P=0.003). In the Either group, the rates were 20.0%, 34.2%, 63.2%, and 75.0% (adjusted P=0.007), respectively. However, in the Both group, although the success rate tended to increase with the number of needle passes in both groups, the difference was not statistically significant (adjusted P=0.304) (*Table 4*). Lastly, we found no significant differences in the core tissue acquisition rate, maximum diameter, or estimated volume, depending on the image subgroup (all adjusted P>0.05) (*Table 5*).

Table 5 Differences in variables between success and failure according to imaging subgroups

Subgroup	Variables	Total, median (interquartile range)	Success of biopsy	Median (interquartile range)	P value	
					Raw	Adjusted
None	Core tissue percentage (%)	100.00 (75.00–100.00)	Success (n=11)	100.00 (66.70–100.00)	0.214	0.641
			Failed (n=39)	100.00 (100.00–100.00)		
	Maximal diameter (cm)	1.00 (1.00–1.50)	Success (n=11)	1.50 (1.00–2.00)	0.129	0.386
			Failed (n=39)	1.00 (0.80–1.50)		
	Volume (cm^3)	0.20 (0.10–0.45)	Success (n=11)	0.23 (0.15–1.20)	0.095	0.285
			Failed (n=39)	0.20 (0.10–0.39)		
Either	Core tissue percentage (%)	100.00 (75.00–100.00)	Success (n=33)	100.00 (66.70–100.00)	0.621	>0.99
			Failed (n=42)	100.00 (100.00–100.00)		
	Maximal diameter (cm)	1.00 (1.00–1.50)	Success (n=33)	1.50 (1.00–2.00)	0.168	0.505
			Failed (n=42)	1.00 (1.00–1.50)		
	Volume (cm^3)	0.20 (0.10–0.45)	Success (n=33)	0.23 (0.20–0.60)	0.186	0.559
			Failed (n=42)	0.20 (0.10–0.45)		
Both	Core tissue percentage (%)	100.00 (75.00–100.00)	Success (n=195)	100.00 (75.00–100.00)	0.668	>0.99
			Failed (n=31)	100.00 (83.35–100.00)		
	Maximal diameter (cm)	1.50 (1.00–2.00)	Success (n=195)	1.50 (1.00–1.80)	0.723	>0.99
			Failed (n=31)	1.50 (1.00–2.00)		
	Volume (cm^3)	0.45 (0.20–0.68)	Success (n=195)	0.45 (0.20–0.68)	0.856	>0.99
			Failed (n=31)	0.45 (0.13–0.80)		

Core tissue percentage is defined as the percentage of core tissue adequately obtained from the total puncture attempts. Maximal diameter was the longest dimension of the obtained core tissue. Volume was estimated by multiplying the length, height, and width of the tissues. None group: defined as having cancer findings on neither CT or PET/CT readings; Either group: defined as having cancer findings on either CT or PET/CT scan; Both group: defined as having cancer findings on CT and PET/CT. CT, computed tomography; PET, positron emission tomography.

Discussion

Key findings

Our study demonstrates that the diagnostic yield of EBUS-TBNA increased with the number of needle passes. Furthermore, we observed that a higher maximum diameter or estimated volume of the target lesion rather than the acquisition of core tissue was correlated with a higher diagnostic yield. Importantly, the significance of additional needle passes became evident when imaging studies such as CT or PET/CT yielded inconclusive results.

Explanation of findings and comparison with similar research

Accurate LN staging is crucial for determining prognosis and developing an optimal treatment plan. The 2007 guidelines of the European Society of Thoracic Surgeons recommend a combination of imaging, endoscopic, and surgical techniques for LN staging (16). Among these approaches, imaging techniques such as CT and PET/CT are first-line non-invasive methods. Chest CT is a conventional tool used for identifying and staging lung cancer and plays an essential role in the diagnostic process.

However, its sensitivity and specificity are relatively low at 60% and 77%, respectively (17). Additionally, it is important to note that approximately 40% of the nodes suspected to be malignant based on CT criteria (short-axis diameter >10 mm) are benign, while 20% of the nodes that are considered benign (short-axis diameter ≤10 mm) turn out to be malignant (18). In contrast, PET measures the uptake of 2-[^{18}F]fluoro-2-deoxy-D-glucose, which is higher in cancer cells with increased glycolytic rates than in normal cells (19). The sensitivity and specificity for identifying mediastinal metastases were higher when CT was combined with PET (93% and 95%, respectively) than when CT was used alone (75% and 63%, respectively) (20). However, PET/CT has drawbacks such as high cost, additional radiation exposure, and the possibility of false-positive and false-negative results (4). Therefore, despite advancements in non-invasive techniques, further sampling and evaluation of mediastinal nodes are required to ensure accurate confirmation of node involvement and avoid unnecessary thoracotomies.

EBUS has become the first-choice tool for diagnosing mediastinal diseases and for LN staging in lung cancer, particularly since the introduction of linear probes in the early 2000s (21). This method allows for easy tissue sampling using a dedicated needle while visualizing the airways, mediastinum, and lungs in real time using an integrated convex ultrasound probe during bronchoscopy. EBUS-TBNA has several advantages, such as high diagnostic accuracy, minimal invasiveness, and safety. Unlike conventional TBNA using CT or fluoroscopy, EBUS-TBNA does not expose the operator to radiation. However, it is not possible to access the LN in the aortopulmonary window (#5), para-aortic window (#6), para-esophageal window (#8), and pulmonary ligament (#9) using this technique, and the diagnostic accuracy depends on the experience of the operator (22,23). Additionally, EBUS-TBNA showed a relatively low negative predictive value and the possibility of false negatives. Therefore, efforts are needed to improve diagnostic accuracy (24-26).

Our study found that the diagnostic yield significantly increased as the number of passes increased, consistent with the results of previous studies. Lee *et al.* conducted EBUS-TBNA on 163 LN stations in 102 patients with NSCLC not having undergone ROSE and observed that the diagnostic value increased as the number of passes increased, suggesting that three aspirations would be the optimal number (27). Yarmus *et al.* investigated the number of needle passes required to obtain sufficient tissue for molecular profiling in 85 patients with NSCLC. They reported that with the use of ROSE, a minimum of four passes was sufficient for molecular marker analysis in 96% of the cases (28). Overall, our results and those of previous research indicate that increasing the number of passes improves the diagnostic yield. However, the optimal number of passes may vary depending on the specific diagnostic purpose and use of ROSE.

EBUS-TBNA has several advantages; however, the tissue sample size is a concern because of the use of a fine needle. Generally, a larger tissue sample size yields higher diagnostic accuracy and increases the risk of complications. Recently, molecular profiling has become necessary to determine treatment strategies and the use of immune checkpoint inhibitors by evaluating biological factors such as specific genetic mutations or protein expression levels (29,30). An insufficient sample size decreases the diagnostic accuracy and reliability of molecular testing, leading to errors in treatment decisions. Our study showed that the tumor diameter and volume were significantly higher in the EBUS-TBNA successful group. Recent report suggested that using a nineteen-gauge needle is more appropriate for obtaining larger tissue samples and making histological diagnoses safely (31). However, another study has not reported the superiority of the 19-gauge needle in obtaining tissue core samples and instead have shown that it leads to more blood contamination (32). Obtaining large samples is time-consuming and laborious, and it is unclear whether this truly improves diagnostic accuracy. Further studies are required to confirm the benefits of obtaining large tissue samples.

We conducted a subgroup analysis of how the diagnostic yield of EBUS-TBNA changed according to the non-invasive imaging results. EBUS-TBNA showed the highest diagnostic yield in both groups, where a cancer diagnosis was suspected based on CT and PET/CT. When patients with suspected cancer visit a clinic, CT or PET/CT is the first non-invasive and relatively accurate test to be performed. However, CT or PET/CT has the drawbacks of false negatives, and there are cases where metastasis is confirmed through tests such as EBUS-TBNA or surgical LN biopsy, even if cancer is not suspected on imaging tests (33). Through subgroup analysis, we searched for a solution and found that increasing the number of needle passes to obtain tissue samples was more effective than it was in obtaining core tissue or collecting large or voluminous specimens. In particular, increasing the number of needle passes to collect tissue is important when CT and PET/CT yield negative results or when only one modality yields positive results.

Based on these results, we suggest that when CT or PET/CT results are unclear, it is important to take the time to increase the number of needle passes and collect the tissue samples.

Strengths and limitations

The strength of our study is that this is the first to attempt a subgroup analysis based on CT and PET/CT results while confirming the variables associated with the diagnostic yield of EBUS-TBNA. However, this study has several limitations. First, it was conducted at a single institution, making it difficult to generalize the results. In addition, because this was a retrospective study, missing values may have affected the results. Secondly, we focused only on the number of passes and did not measure the number of needle revolutions inside the LNs. However, our institution has standardized the technical method by performing ten to 30 revolutions per LN, and one study found no difference in the diagnostic success rate or specimen adequacy by increasing needle revolutions (34). Thirdly, we could not perform ROSE; therefore, the appropriateness of the core tissue acquisition was assessed by trained nurses. However, because ROSE is often not possible in actual clinical situations, the results of this study are useful. Finally, although this study was conducted in patients with lung cancer, EBUS-TBNA can be performed in various benign conditions and can be useful in lymphoma or metastatic cancer. Therefore, caution is needed before generalizing the results.

Conclusions

Our study demonstrated that the diagnostic yield of EBUS-TBNA is associated with the number of passes, diameter, and volume rather than with the core tissue acquisition rate. We also observed that the diagnostic yield increased with an increase in the number of passes. This phenomenon was more pronounced when non-invasive imaging tests, such as CT and PET/CT, did not clearly indicate cancer. Therefore, increasing the number of passes may improve the diagnostic yield of EBUS-TBNA when imaging results are inconclusive. However, further large-scale prospective studies are necessary to generalize our findings.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1369/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1369/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Korea University Ansan Hospital (IRB No. 2023AS0047) and individual consent for this retrospective analysis was waived.

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Supplementary

Table S1 The association between number of passes and biopsy success

No. of passes	No. of stations	Odds ratio (95% confidence interval)	P value
1	37	As reference	–
2	173	1.42 (0.70–2.89)	0.327
3	103	3.09 (1.41–6.80)	0.005
≥4	38	7.65 (2.27–25.81)	0.001

Number of passes was defined as the number of needle punctures per lymph node.

Table S3 *Post-hoc* analysis between imaging subgroups

Subgroup	P value	
	Raw	Adjusted
None *vs.* Either	0.012	0.035
None *vs.* Both	<0.001	<0.001
Either *vs.* Both	<0.001	<0.001

None group: defined as having cancer findings on either CT or PET/CT; Either group: defined as having cancer findings on either CT or PET/CT scan; Both group: defined as having cancer findings on CT and PET/CT. CT, computed tomography; PET, positron emission tomography.

Table S2 Differences in the success rate according to the imaging subgroup

Subgroup	No. of stations (%)	Biopsy				P value
		Failed, n (%)	Success, n (%)	Success percentage (%)	Success ratio	
None	50 (14.2)	39 (34.8)	11 (4.6)	22.0	1:0.28	<0.001
Either	75 (21.4)	42 (37.5)	33 (13.8)	44.0	1:0.79	
Both	226 (64.4)	31 (27.7)	195 (81.6)	86.3	1:6.29	
Total	351	112	239	68.1	1:2.13	

None group: defined as having cancer findings on either CT or PET/CT; Either group: defined as having cancer findings on either CT or PET/CT scan; Both group: defined as having cancer findings on CT and PET/CT. CT, computed tomography; PET, positron emission tomography.

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