Original Article

Additional benefit of endoscopic ultrasound with bronchoscope-guided fine needle aspiration to endobronchial ultrasound-guided transbronchial needle aspiration in the evaluation of lung cancer: a systematic review and meta-analysis

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Background: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and endoscopic ultrasound with bronchoscope-guided fine needle aspiration (EUS-B-FNA) are minimally invasive procedures for the diagnosis and staging of lung cancer. This study aimed to investigate the additional diagnostic value of EUS-B-FNA following EBUS-TBNA.

Methods: We performed a systematic literature review of PubMed, Embase, and the Cochrane Central Register databases and extracted the studies reporting the implementation of the combined EBUS-TBNA/EUS-B-FNA. A proportional meta-analysis was conducted to determine the pooled diagnostic yield of this procedure.

Results: We identified nine studies involving 2,375 patients. The overall pooled diagnostic yield of EBUS-TBNA alone and combined EBUS-TBNA/EUS-B-FNA was 0.87 [95% confidence interval (CI): 0.79–0.95, I^2=96.55%] and 0.92 (95% CI: 0.85–0.99, I^2=97.89%), respectively. Adding EUS-B-FNA to EBUS-TBNA increased the diagnostic yield by approximately 0.05. There was statistical heterogeneity among the studies (I^2=54.49%). Among the 832 patients in seven studies, additional diagnostic benefits of EUS-B-FNA were observed in 37 lesions. The most common diagnosed lesion was in station 4L (n=10), followed by station 5 (n=8) and station 7 (n=8).

Conclusions: In pooled estimates, the addition of EUS-B-FNA to EBUS-TBNA increased the diagnostic yield for the diagnosis and staging of lung cancer. Nodal station 4L, station 5, and station 8 were lesions frequently diagnosed by the addition of EUS-B-FNA. Because of statistical between-study heterogeneity, our findings should be interpreted with caution.

Keywords: Diagnostic imaging; bronchoscopy; endoscopic ultrasound-guided fine needle aspiration (EUS-FNA); lung neoplasms; mediastinal diseases

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Introduction

Lung cancer is the leading cause of cancer-related mortality worldwide (1). Accurate diagnosis and staging of lung cancer is essential to establish the most effective treatment strategy. Mediastinal evaluation of lung cancer requires optimal tissue sampling for either computed tomography or positron emission tomography–positive mediastinal lymph nodes (2). In the past, the investigation of mediastinal masses or lymphadenopathy was performed through surgical approaches such as mediastinoscopy, video-assisted thoracic surgery, and anterior left mediastinotomy (3). Currently, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) are used as minimally invasive modalities for mediastinal exploration (2,4,5).

EBUS-TBNA and EUS-FNA are complementary in the mediastinal approach; EBUS-TBNA can commonly access the paratracheal, subcarinal and hilar nodal stations, and EUS-FNA can access the subcarinal, aortopulmonary window and lower mediastinal nodal stations (6). The combination of EBUS-TBNA and EUS-FNA can cover nearly the entire mediastinum, and this approach has been reported to be more accurate than either individual method (7). However, because the combined EBUS-TBNA/EUS-FNA requires both an EBUS scope and an EUS scope, the availability of these procedures is limited. Since the EBUS bronchoscope can be introduced through the esophagus, EUS can be performed with a single EBUS scope by one bronchoscopist, facilitating the combined approach (8). This technique is referred to as endoscopic ultrasound with bronchoscope-guided fine needle aspiration (EUS-B-FNA) (8).

While several studies have reported the usefulness of the combined EBUS-TBNA/EUS-B-FNA for mediastinal exploration in lung cancer (8-10), the diagnostic yield of this procedure remains unclear. The purpose of the present study was to examine the pooled diagnostic yield of EUS-B-FNA following EBUS-TBNA through a systematic review and meta-analysis. We present this article in accordance with the PRISMA reporting checklist (11) (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-721/rc).

Highlight box

Key findings

- The use of endoscopic ultrasound with bronchoscope-guided fine needle aspiration (EUS-B-FNA) with a single endobronchial ultrasound scope may complement endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) as minimally invasive modalities for mediastinal exploration.

What is known and what is new?

- The diagnostic yield of EUS-B-FNA following EBUS-TBNA remains still unclear.
- The pooled diagnostic yield of combining EUS-B-FNA with EBUS-TBNA for the diagnosis and mediastinal staging of lung cancer was 0.92, and the additional diagnostic yield of EUS-B-FNA was approximately 0.05.

What is the implication, and what should change now?

- EUS-B-FNA could be a procedure that provides additional diagnostic yield when combined with EBUS-TBNA.

Methods

Data sources and search strategy

We performed a systematic search of three electronic databases (PubMed, Embase, and the Cochrane Central Register) for relevant articles published before December 1, 2023. The following search terms were used: ((EBUS or EBUS-TBNA or endobronchial ultrasound or endobronchial ultrasonography) and (EUS or EUS-FNA or EUS-B-FNA or endoscopic ultrasound)) and (lung or pulmonary or mediastinal or lymphadenopathy or lymph node). This study was registered in PROSPERO, an international database of prospectively registered systematic reviews, with the registration number CRD42023470530. As this study was a systematic review of published articles, informed consent and ethics approval were not required.

Inclusion criteria

We included studies that met the following criteria in our systematic review and meta-analysis: (I) randomized controlled or observational trials for the utilization of the combined EBUS-TBNA/EUS-B-FNA; (II) studies for the evaluation the staging or diagnosis of lung cancer; and (III) studies that provided data regarding the diagnostic yield of the index tool. The search was limited to full-length studies or letters published in peer-reviewed English language journals. Review articles, case reports, editorials, and extension or *post-hoc* trials were excluded. Abstract form was not also included because the methods and results could not be analyzed in detail.

Data extraction and bias assessment

We independently screened studies that met the predefined criteria for eligibility through the title and abstract. After a thorough review of the full text, we extracted potentially eligible studies. References listed in relevant articles were manually reviewed for additional relevant data. The following information was retrieved from each study: first author's last name, year of publication, design, study country, study type, total number of subjects, subject demographic characteristics, the type of EBUS bronchoscope, sampled nodal size, the use of rapid on-site evaluation, needle size, number of aspirations per mediastinal nodal stations, study objectives, complications, and diagnostic yield. We investigated nodal stations that showed additional benefits through EUS-B-FNA. Prior to EBUS and EUS-B, selecting mediastinal lymph nodes for examination based on computed tomography or positron emission tomography was defined as the target approach, while making a decision for the procedure after conducting a full inspection of mediastinal lymph nodes by the bronchoscopist was defined as the systematic approach.

Two authors evaluated the potential risk of bias and applicability concerns using the revised tool for the quality assessment of diagnostic accuracy studies (QUADAS-2) (12). In the patent selection domain, the retrospective inclusion of patients was regarded as having a high risk of bias. The index test was EUS-B-FNA, and the reference standard was determined to be EBUS-TBNA. Publication bias was assessed through a funnel plot, and statistical significance was assessed based on Egger's regression test (13). Any discrepancies encountered during the study selection process, data extraction, or bias assessment were resolved through discussion.

Data synthesis and statistical analysis

A proportional meta-analysis was performed to calculate the pooled diagnostic yield of the combined EBUS-TBNA/EUS-B-FNA. The diagnostic yield was determined by dividing the number of malignancy-positive patients detected through the combined EBUS-TBNA/EUS-FNA by the total number of cases. The pooled proportions with 95% confidence intervals (CIs) for individual studies were also calculated. The diagnostic criteria for malignancy included both the diagnosis of lung cancer and histological confirmation of malignancy in mediastinal staging. Between-study statistical heterogeneity was assessed using I^2 statistics on a scale of 0–100% (14). When I^2 was greater than 50%, suggesting significant between-study heterogeneity, a random-effects model was employed; otherwise, a fixed-effects model was utilized (14). We additionally conducted meta-regression analyses to identify factors influencing diagnostic yield and to explore potential sources of bias associated with the input variables as follows: procedure approach (systematic *vs.* target), study design (prospective *vs.* retrospective), and number of patients (≥100 *vs.* <100).

Statistical analyses were performed using Stata statistical software (Version 14.2, Stata Corp LP, College Station, TX, USA) and Review Manager (Version 5.3, Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark). Statistical significance was defined as a P value less than 0.05.

Results

Study search

Figure 1 displays a flow diagram outlining the study selection process. Initially, 1,386 records were identified. After removing duplicates, 1,147 articles were eligible for abstract review based on their titles. Subsequently, 32 articles underwent full-text review. Among these articles, 23 were excluded for reasons outlined in *Figure 1*. Finally, nine articles meeting the defined inclusion criteria were ultimately included (8-10,15-20).

Table 1 presents the characteristics of the studies included in this systematic review. A total of 2,375 patients were encompassed in the review and meta-analysis, and all studies were published between 2009 and 2022. The number of participants in each trial varied from 44 to 276. The mean patient age across studies ranged from 57.6 to 69 years, while the percentage of male participants ranged from 59.7% to 81.8%. Rapid on-site examination (ROSE) was performed in only one study (20). The systematic approach of EBUS and EUS-B-FBNA was performed in three studies (9,15,16), while the target approach was employed in six studies (8,10,17-20).

In the random effect model, the overall pooled diagnostic yield of EBUS-TBNA alone and combined EBUS-TBNA/EUS-B-FNA was 0.87 (95% CI: 0.79–0.95) and 0.92 (95% CI: 0.85–0.99), respectively (*Figure 2*). The diagnostic yield of EBUS-TBNA alone ranged from 0.73 to 0.96 across studies and that of combined EBUS-TBNA/EUS-B-FNA ranged from 0.76 to 1.00 across studies. There

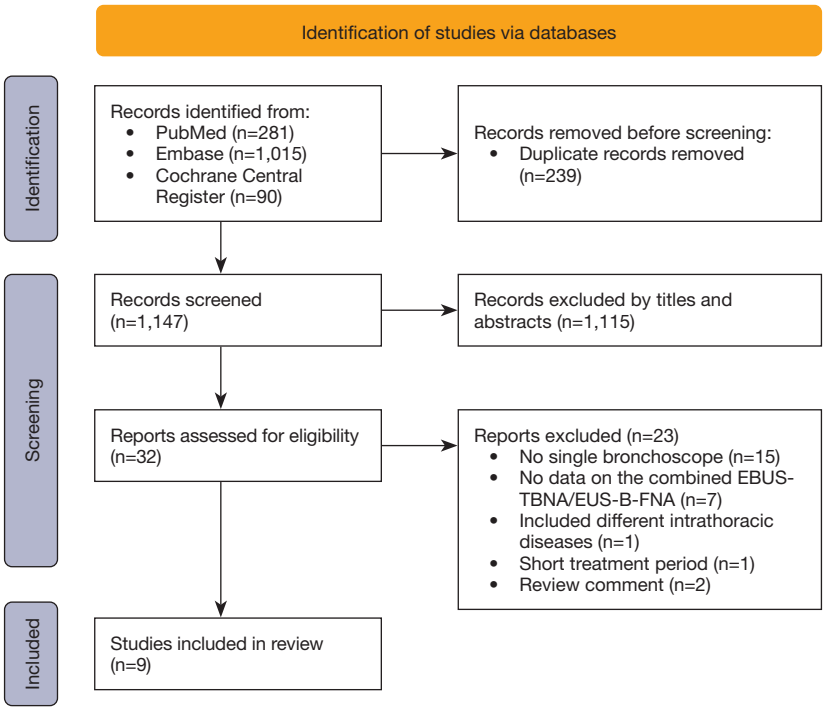

Figure 1 Flow diagram of the identification of eligible studies. EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; EUS-B-FNA, endoscopic ultrasound with bronchoscope-guided fine needle aspiration.

was significant heterogeneity across studies (I^2=96.55% for EBUS-TBNA alone and I^2=97.89% for combined EBUS-TBNA/EUS-B-FNA, respectively). The addition of EUS-B-FNA to EBUS-TBNA increased diagnostic yield by approximately 0.05 (95% CI: 0.02–0.04). To determine factors affecting diagnostic yield and potential sources of the significant between-study heterogeneity, a meta-regression analysis was performed (*Table 2*). The analysis did not identify a correlation between the diagnostic yield of the modality and study design (P=0.84), number of patients (P=0.44), or procedure approach (P=0.25).

The benefits of additional EUS-B-FNA for lesions were described in seven studies (8-10,15-18). In the 832 patients, additional diagnostic benefits were observed in 37 lesions. The most common diagnosed lesion was in the 4L (n=10), followed by 5 (n=8), 7 (n=8), 8 (n=3), 2L (n=2), and 10L (n=2) (*Table 3*).

Major complications related to the procedure were observed in a total of three patients. After the procedure, one patient had fatal intracranial bleeding 48 hours later, assessed as unlikely to be procedure-related (9). Another patient developed a lymph node abscess following EBUS-TBNA (15). Additionally, pneumomediastinum was observed during the EBUS procedure in one patient, which resolved on its own without requiring specific treatment (16).

QUADAS-2 assessment results are presented in Figure S1. Overall, the studies were judged to be satisfactory in quality. Three studies had a high risk of bias in the patient selection domain (8,17,20). The studies showed unclear consecutive or random sampling of enrolled patients because of a retrospective study design. In the visual examination of the funnel plot, there was no evidence of asymmetry indicating publication bias (*Figure 3*), and the Egger test also showed no evidence of publication bias (P=0.18).

Discussion

We found that the pooled diagnostic yield of EBUS-TBNA alone for the diagnosis and mediastinal staging of lung cancer was 0.87, indicating a relatively high rate. The diagnostic yield was enhanced to 0.92 with the addition of EUS-B-FNA. Since its introduction in 2004, EBUS-TBNA has demonstrated a high diagnostic yield and a favorable safety profile (21). The ASTER trial reported comparable sensitivity between EBUS-TBNA and mediastinoscopy (85% *vs.* 79%, respectively), with lower complication rates

Table 1 Characteristics of the studies included in the meta-analysis

Study, year	Design	Country	Total subjects (number)	Mean age (years)	Male (%)	Sedation or anesthesia	Procedure time (mean)	Type of EBUS scope	Sampled nodule size (mean)	Use of rapid onsite examination	Needle size (gauge)	Number of aspirations per mediastinal nodal stations (mean)	Population	Study objectives
Crombag *et al.*, 2019 (9)	Prospective, multicenter	Netherlands and Belgium	229	67	65	Conscious, moderate or deep	20 min for the EBUS-TBNA and 10 min for the EUS-B-FNA	Pentax EB-1970UK, Olympus BF-UC180F, Fujifilm EB-530US	NA	No	22 or 25	NA	Suspected resectable NSCLC	To evaluate the diagnostic accuracy of a systematic EBUS procedure followed by EUS-B compared with a PET-CT-guided targeted EBUS approach
Herth *et al.*, 2010 (10)	Prospective, multicenter	Germany, Denmark, and USA	139	57.6	59.7	Moderate sedation or general anesthesia	14 min for the EBUS-TBNA and 16 min for the EUS-B-FNA	UF Olympus Medical	17 mm	No	NA	2.8 for the EBUS-TBNA and 1.7 for the EUS-B-FNA	Suspected lung cancer	To determine whether EBUS-TBNA and EUS-B-FNA could be performed through a single bronchoscope in the same setting by the same operator
Hwangbo *et al.*, 2009 (8)	Retrospective, single center	South Korea	84	66	70.2	Conscious sedation (midazolam)	Median 6.4 min and mean 7.8 min for the EUS-B-FNA	Olympus BF-UC260F-OL8	9 mm for short axis and 15 mm for long axis	No	22	1.7 for the EUS-B-FNA	The lesion was accessible by EUS-FNA but bronchoscopic procedures were impossible or difficult	To evaluate the feasibility and the additional role of EUS-B-FNA
Hwangbo *et al.*, 2010 (15)	Prospective, single center	South Korea	150	64.5	75.3	Conscious sedation (midazolam)	18.9 min for the EBUS-TBNA and 3.8 min for the EUS-B-FNA	Olympus BF-UC260F-OL8	7.8 mm for the EBUS-TBNA and 7.6 mm for the EUS-B-FNA (short axis size)	No	22	2.3 for the EBUS-TBNA and 1.4 for the EUS-B-FNA	Histologically confirmed or strongly suspected potentially operable NSCLC	To evaluate the diagnostic gain of EUS-B-FNA following EBUS-TBNA in the mediastinal staging of potentially operable lung cancer
Kang *et al.*, 2014 (16)	Prospective, single center	South Korea	80	63.2	78.8	Conscious sedation (midazolam and fentanyl)	38 min	Olympus BF-UC260F-OL8	NA	NA	22	NA	Histologically confirmed or strongly suspected potentially operable NSCLC	To investigate the impact of the primary procedure and procedure sequence on diagnostic values in the combination of EBUS and EUS in mediastinal staging of lung cancer
Lee *et al.*, 2014 (17)	Retrospective, single center	South Korea	44	66	81.8	Conscious sedation (midazolam)	40 min	Olympus BF-UC260F-OL8	10 mm for short axis and 14 mm for long axis	No	22	2	For staging and diagnosis of primary lung cancer, extrapulmonary malignancies, lymphoma, tuberculous lymphadenitis, and sarcoidosis	To compare the diagnostic performances of mediastinal N staging by EBUS-TBNA alone with that afforded by a combination of EBUS-TBNA and EUS-B-FNA
Oki *et al.*, 2014 (18)	Prospective, single center	Japan	150	68.3	68.7	Conscious sedation (midazolam)	29 min	Olympus BF-UC260F-OL8 or Olympus BF-UC260FW	NA	No	22	NA	Potentially operable pathologically proven or clinicoradiologically suspected NSCLC	To elucidate the roles of EBUS-TBNA and EUS-B-FNA in the preoperative hilar and mediastinal staging of NSCLC
Szlubowski *et al.*, 2014 (19)	Prospective, single center	Poland	106	61.5	73.6	Conscious sedation (midazolam)	15.2 min	Olympus BF-UC160F-OL8 and BF-UC180F	8.7 mm for short axis and 12.8 mm for long axis	NA	22	NA	NSCLC restaging in patients after induction therapy	To assess the diagnostic utility of combined EBUS-TBNA and EUS-B-FNA
Torii *et al.*, 2022 (20)	Retrospective, single center	Japan	276	69	67.8	Conscious sedation (midazolam and fentanyl)	NA	Olympus BF-UC260-OL8, Olympus BF-UC260FW BF-UC290, Fujifilm EB-530US	15.4 mm for short axis	Decided by the operator	19, 21, or 22	3	Accessible intrathoracic lesions	To evaluate the value of adding EUS-B-FNA to EBUS-TBNA

EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; EUS-B-FNA, endoscopic ultrasound with bronchoscope-guided fine needle aspiration; NA, not available; NSCLC, non-small cell lung cancer; PET-CT, positron emission tomography-computed tomography.

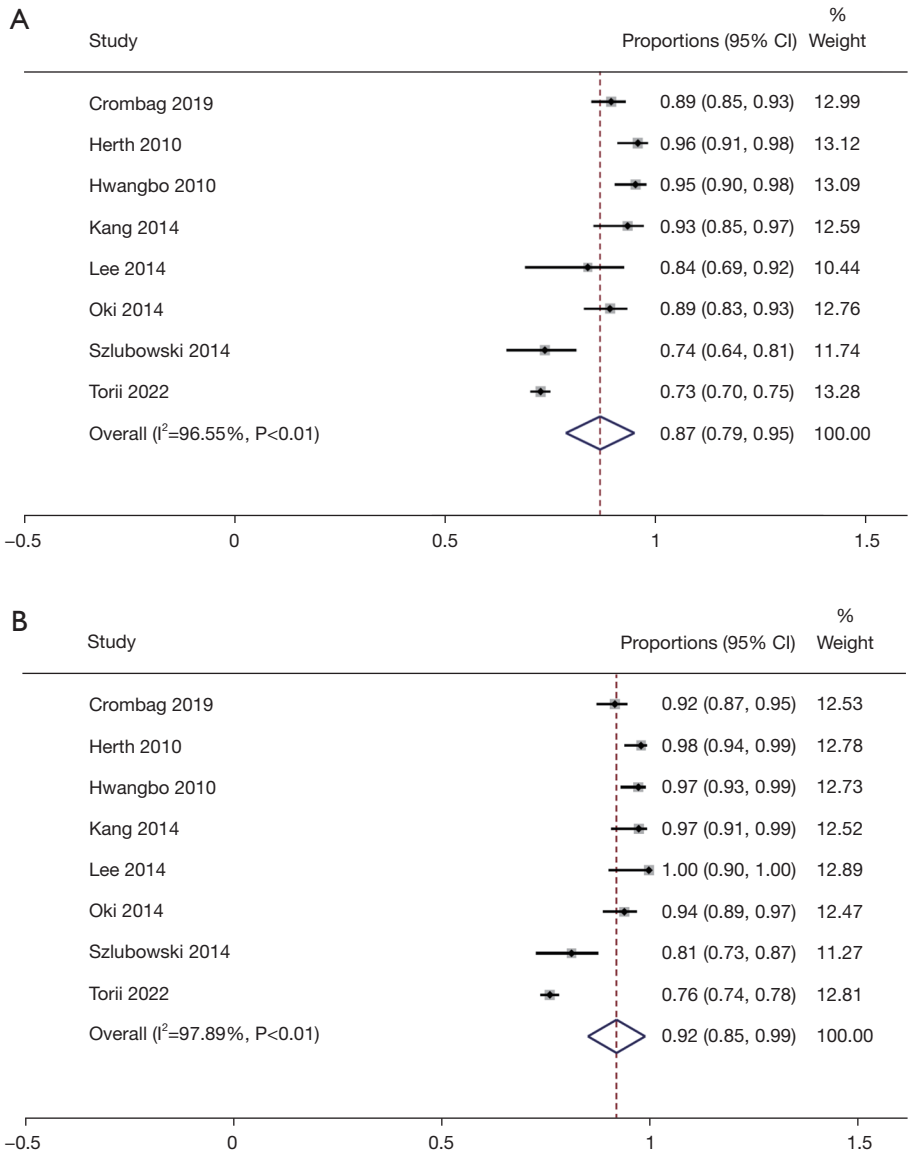

Figure 2 Forest plots of diagnostic yields for (A) EBUS-TBNA and (B) the combined EBUS-TBNA and EUS-B-FNA. CI, confidence interval; EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; EUS-B-FNA, endoscopic ultrasound with bronchoscope-guided fine needle aspiration.

Table 2 Univariate meta-regression analysis to identify potential sources of heterogeneity among studies

Covariates	Regression coefficient	Standard error	95% CI for coefficient	P value
Study design (prospective *vs*. retrospective)	−0.005	0.026	−0.072 to 0.061	0.84
Number of patients (≥100 *vs*. <100)	−0.021	0.025	−0.085 to 0.043	0.44
Procedure approach (systematic *vs*. target)	−0.030	0.023	−0.090 to 0.030	0.25

CI, confidence interval.

Table 3 Additional diagnostic yield of EUS-B-FNA

Author, year	Total subjects (number)	Patients diagnosed by additional EUS-B-FNA (number)	Diagnosed lesions [number]†	Approach
Crombag *et al.*, 2019 (9)	225	5	4L [2], 7 [2], 8 [2]	Systematic
Herth *et al.*, 2010 (10)	139	3	2L [1], 4L [1], 7 [1], 10L [1]	Target
Hwangbo *et al.*, 2009 (8)	68	6	4L [3], 5 [1], 9 [1], RLL mass [1], LLL mass [1]	Target
Hwangbo *et al.*, 2010 (15)	143	3	4L [1], 5 [3]	Systematic
Kang *et al.*, 2014 (16)	74	1	4L [1]	Systematic
Lee *et al.*, 2014 (17)	37	6	1R [1], 4L [1], 5 [2], 7 [1], 8[1]	Target
Oki *et al.*, 2014 (18)	146	7	2L [1], 4L [1], 5 [2], 7 [4], 10L [1]	Target
Szlubowski *et al.*, 2014 (19)	106	8	NA	Target
Torii *et al.*, 2022 (20)	1,437	48	NA	Target

†, allowed for overlapping. EUS-B-FNA, endoscopic ultrasound with bronchoscope-guided fine needle aspiration; L, left; R, right; RLL, right lower lobe; LLL, left lower lobe; NA, not available.

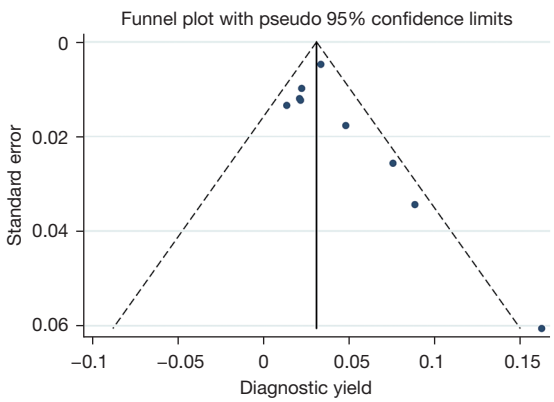

Figure 3 Funnel plot to assess publication bias.

and reduced instances of unnecessary thoracotomies for EBUS-TBNA (22).

EBUS-TBNA is currently a highly effective procedure for evaluating mediastinal lymphadenopathy, offering excellent access to pretracheal, subcarinal, and right paratracheal lesions. However, its ability to reach other mediastinal lymph nodes is somewhat limited. In particular, EBUS-TBNA cannot access the paraaortic or paraesophageal lymph nodes via a transbronchial approach. Additionally, it cannot effectively reach the deep left lower paratracheal station due to the limited angulation capabilities of bronchoscopy. EUS-FNA presents some benefits that surpass those of EBUS-TBNA. This tool enables access to lymph nodes in locations such as the inferior mediastinum, the left paratracheal nodal stations, and specific areas of the aortopulmonary window, which may be challenging to reach with EBUS-EBNA. And because the esophagus lacks cartilage and has a soft texture, tissue acquisition through EUS-FNA is facilitated (23). Considering these factors, our study revealed that EUS-B-FNA offered additional benefits for left paratracheal and subcarinal nodal stations that were inaccessible or difficult to access by EBUS-TBNA, as well as enabling independent access to lower paraesophageal lymph nodes. In the pooled estimates, the additional diagnostic yield of combining EUS-B-FNA with EBUS-TBNA was approximately 0.05. The advantages of employing additional EUS-B-FNA, as delineated in seven studies (8-10,15-18), were identified in 37 lesions. Some patients underwent EUS-B-FNA as a substitute when EBUS-TBNA was challenging because of poor respiratory conditions.

EUS-B-FNA provides additional advantages by enhancing procedural comfort for patients and facilitating the procedures. For patients with poor respiratory conditions or performance status, bronchoscopic procedures may be inappropriate. EUS-FNA, conducted via the esophagus rather than the airway, offers a relatively safe alternative in such cases (24). This approach reduces patient coughing, allows for multiple tissue punctures, and facilitates the retrieval of sufficient tissue (24). Given that a significant number of lung cancer patients are diagnosed at advanced stages unsuitable for surgical resection, obtaining an ample tissue sample for molecular analysis becomes

crucial. EUS-FNA offers benefits in these regards.

Previous studies using systematic review and meta-analysis have been reported that evaluated the added value and diagnostic accuracy of EBUS-TBNA combined with EUS-FNA or EUS-B-FNA for diagnosing and staging mediastinal diseases (7,25,26). These meta-analyses showed that the sensitivity of EBUS was approximately 0.87, and the combination of the two procedures provided greater sensitivity than each individual procedure in mediastinal diseases (7,25,26). However, EUS-FNA typically requires a separate EUS scope rather than an EBUS scope and is commonly performed by gastroenterologists. This leads to increased costs as well as time-consuming procedures. In the present analysis, we included only studies in which a single EBUS scope was used for both transbronchial and transesophageal approaches. The research design of a prior meta-analysis study was similar to our study design (27). Notably, among the ten studies included in the previous research, data on EBUS-TBNA were missing in five studies, which precluded an accurate assessment of the additional diagnostic benefits of EUS-B-FNA (27).

Among the subjects in our study, three patients underwent significant complications from the procedure, such as fatal intracranial bleeding, a lymph node abscess, and pneumomediastinum. Even though these major complications occurred at a low rate of 0.3%, there are still concerns regarding the infectious complications of combined EBUS-TBNA/EUS-B-FNA. In a recent study, 33 (0.48%) out of 6,826 patients who underwent EBUS-TBNA were reported to have developed infectious complications like pneumonia and mediastinal infections (28). And procedures combined with EUS-B-FNA were independently associated with infectious complications of EBUS-TBNA (adjusted odds ratio, 3.19; 95% CI: 1.47–6.88; P=0.003) (28). Attention is warranted regarding potential infectious complications when conducting EUS-B-FNA.

We analyzed the data using diagnostic yield instead of diagnostic accuracy for the following reasons. Some of the studies included in our analysis did not report two-by-two tables, preventing us from determining the true negative results and the diagnostic accuracy. Additionally, some studies relied on clinical and radiological follow-up to establish the final diagnosis. This follow-up might not be a substitute for tissue sampling, such as surgical biopsy, which could have affected the number of true negatives.

Our study has a strength in providing reliable estimates by incorporating updated reports through a rigorous literature search. This study also has some limitations. First, in the pooled estimates, substantial heterogeneity was observed among the included studies. Heterogeneity is frequently encountered in systematic reviews of diagnostic test accuracy studies (29). Despite our efforts to evaluate factors influencing the diagnostic yield of this procedure by incorporating covariates into the bivariate model utilized in the meta-regression analysis, we were unable to identify potential sources of heterogeneity. Second, the indications for performing EUS-B-FNA among the included studies were diverse and not clearly delineated. Third, the diagnostic yield of EUS-B-FNA may be influenced by the systematic or target approach employed. However, due to missing data in the included studies, we were unable to investigate relevant findings.

Conclusions

Our study suggests that EUS-B-FNA may be a beneficial procedure that enhances the diagnostic yield of EBUS-TBNA. While we performed meta-regression analysis to address the substantial between-study heterogeneity, we could not identify the potential sources of this heterogeneity. Our results should be interpreted with caution, and further large-scale studies are warranted.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-721/rc

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-721/prf

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-721/coif). J.L. reports that this work was supported by a research grant from Jeju National University Hospital in 2023 (to J.L.). The other author has 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.

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