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A strategy to improve the yield of transbronchial needle aspiration

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Abstract
Background Transbronchial needle aspiration (TBNA) is a bronchoscopic technique that provides access to masses within the mediastinum. It is operator dependent, and factors such as needle type, lymph node site, and endobronchial ultrasosonography (EBUS) have been implicated as having an impact on its accuracy. This study aimed to develop a strategy for TBNA and specimen preparation techniques as the first step toward improving TBNA yield, and to determine whether EBUS can augment its application.
Methods Intervention included standardizing the use of the histology needle and the direct smear method. As competency improved, radial probe (RP) and linear EBUS were incorporated into TBNA.
Results The study assessed 35 conventional TBNA procedures before and 45 of these procedures after intervention as well as 45 RP-EBUS and 50 linear EBUS-guided TBNA procedures. Frequently sampled lymph node stations were 7, 4R, and 4L in the American Thoracic Society classification. The preintervention conventional TBNA yield was 43%, which improved to 82% after intervention. Although EBUS did not have an impact on TBNA yield ($p = 0.44$) compared with the intervention ($p = 0.001$), EBUS was useful for lymph nodes smaller than 2 cm ($p < 0.0001$). Linear EBUS did not confer higher diagnostic accuracy than RP-EBUS ($p = 0.47$).
Conclusion Proper TBNA and specimen preparation techniques are the first steps toward improving TBNA yield, and EBUS can be used to guide TBNA of small lymph nodes.

Keywords EBUS · Lung cancer · Lymph node · Staging · TBNA

Transbronchial needle aspiration (TBNA) is a well-validated bronchoscopic technique that provides access to masses and enlarged lymph nodes within the mediastinum [1–3]. When combined with bronchoscopic washing, brushing, and forceps biopsy, TBNA increases the diagnostic yield of lung cancer and may be exclusive when extrabronchial masses are encountered [4–6].

Despite its proven efficacy, TBNA remains underutilized and is not uniformly taught in training programs [7]. In fact, a bronchoscopy survey showed that 54% of respondents performed fewer than 10 TBNA procedures per year [8]. This apparent lack of interest was attributable to anecdotal comments by experienced bronchoscopists who were unable to reproduce in their own practices the high yields reported in the literature. Other factors cited were inadequate training for the bronchoscopist and assistant, needle problems, poor specimen preparation, fear of damaging the bronchoscope, and the risk of bleeding from the puncture of great vessels in the mediastinum [7, 9].

Transbronchial needle aspiration guided by computed tomography (CT), fluoroscopy [10], endoscopic and endobronchial ultrasonography (EBUS) [11, 12], and navigational bronchoscopy [13] has demonstrated improvements in yield. However, these procedures require logistic planning, costly equipment, and extensive operator training frequently limited to select centers. Conversely, training in TBNA and the method of specimen preparation does not need additional resources and are simple interventions that

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positively affect TBNA yield. We reviewed our experience in conventional TBNA to evaluate the impact of training on diagnostic yield as well as the role of EBUS as a complementary tool.

Methods and materials

Our study included all patients with enlarged mediastinal lymph nodes (>10 mm) shown on CT who had undergone TBNA for diagnosis and staging between 2003 and 2006. Clinical characteristics, site of primary tumor, lymph node stations according to American Thoracic Society (ATS) classification [14], size of the lymph node measured by short-axis diameter, TBNA technique, type of needle, number of passes, diagnosis, and complications were recorded. All patients gave informed written consent, and the study was conducted in accordance with protocol approved by institutional review boards.

All the patients underwent chest radiographs and CT with contrast enhancement at 5-mm cuts from the thoracic inlet to the carina and from the inferior pulmonary veins to the diaphragm. Transbronchial needle aspiration was performed using either no. 22 cytology or a no. 19/21 histology needle (Millrose, Mentor, OH, USA) via flexible videobronchoscopy with conscious sedation using intravenous midazolam and fetanyl. Care was taken to perform TBNA before any distal airway examination or specimen collection by minimizing suctioning to avoid inadvertent aspiration of respiratory secretions that may have been contaminated with exfoliated malignant cells. Selection of the lymph node for TBNA was left to the discretion of the bronchoscopist, and no CT fluoroscopy or rapid on-site cytologic evaluation was used.

We evaluated all TBNAs performed before and after intervention. Included in the intervention were CT review and flipping of the films for their correlation with the tracheobronchial tree, and the TBNA approach was standardized to the use of "piggyback" or "jabbing" techniques as well as use of the histology needle in all cases. The number of needle passes per lymph node also was standardized to four if one ATS station was sampled and three if more than one station was sampled. On-the-job training focused on instruction in TBNA techniques by an experienced bronchoscopist (P.L.) and in the direct dry smear method for cytology specimen preparation. Communication between bronchoscopists and pathologists regarding TBNA adequacy also was increased through private discussions and clinicopathologic meetings.

To determine whether diagnostic accuracy could be further enhanced, EBUS using a radial probe (UM-B20R-26; Olympus, Tokyo, Japan) equipped with a 20-MHz transducer connected to driving unit MH-240 (Olympus, Tokyo, Japan) and processor EU-M20 (Olympus) was incorporated into conventional TBNA. This method involved insertion of a radial ultrasound probe (RP) through a 2.8-mm working channel followed by inflation of the balloon with sterile water to obtain a 360° cross-sectional image of the bronchus and the mediastinum. Enlarged hilar or mediastinal lymph node was identified, and its location in relation to the tracheobronchial tree was noted before the probe was withdrawn. Then TBNA was performed in the usual fashion.

Real-time puncture of lymph node can be performed using a dedicated needle inserted through the working channel of a linear EBUS bronchoscope equipped with 7.5-MHz-frequency ultrasound transducer at the tip and a balloon that can be filled with water to enhance the image quality [15]. After bronchoscopists had satisfied training requirements for RP-EBUS and linear EBUS-guided TBNA at centers with extensive experience, EBUS-guided TBNA was incorporated into the practice.

Statistical analysis

The data collected were entered onto a spreadsheet and analyzed with SPSS software (SPSS, Chicago, IL, USA). Median, interquartile range, and percentage values were computed. Comparisons between groups were performed with chi-square and Mann–Whitney U tests. A p value of 0.05 or less was considered significant.

Results

Preintervention

During a 2-year preintervention period, 2,200 bronchoscopy procedures were performed, 35 (1.6%) of which were TBNA. Besides chest X-ray and CT, complete blood count was performed for 91% of the patients ($n = 32$), coagulation study for 71% ($n = 25$), electrolytes for 77% ($n = 27$), and arterial blood gas for 20% ($n = 7$) before TBNA. The TBNA technique and the type of needle used were variable (Table 1). Assistants lacked proficiency in different TBNA approaches, in proper handling of the needles, and in specimen preparation.

The median size of the lymph nodes sampled was 3 cm (range, 2.5–3.5 cm). Only two lymph nodes measured less than 2 cm on CT. The ATS lymph node stations targeted were 7 and 4R, and a median of two needle passes were made per node. Specimens were submitted as dry smears ($n = 24$, 69%) and saline-diluted aspirates in alcohol ($n = 11$, 31%) to the pathologists for interpretation without prior defined criteria for TBNA adequacy. No complications were documented. The diagnostic yield achieved with conventional

Table 1 Type of procedures and lymph node stations performed pre- and postintervention

	Preintervention *n* (%)	Postintervention *n* (%)	*p* Value
Total TBNA procedures	35	140	
Conventional TBNA	35	45	
EBUS-guided TBNA	0	95	
Prebronchoscopy tests			
Complete blood count	32 (91)	12 (9)	0.001[a]
Coagulation studies	25 (71)	11 (8)	0.001[a]
Electrolytes	27 (77)	4 (3)	0.001[a]
Arterial blood gas	7 (20)	1 (1)	0.02[a]
Type of needle			
Cytology, no. 22	11 (31)	0	
Histology, no. 19/21	24 (69)	90 (64)	
Dedicated EBUS needle (21-gauge)		50 (36)	
Size of lymph node: cm (range)	3.0 (2.5–3.5)	2.0 (1.8–2.4)	0.001[a]
Patients with lymph node stations sampled			
Subcarinal (ATS 7)	28 (80)	66 (47)	
Right paratracheal (ATS 4R)	7 (20)	73 (52)	
Left paratracheal (ATS 4L)	0	31 (22)	
Hilar	0	21 (15)	
More than 1 ATS station	0	51 (36)	
Conventional TBNA yield	15 (43)	37 (82)	0.001[a]
EBUS-guided TBNA yield	0	82 (86)	0.44

TBNA transbronchial needle aspiration, *EBUS* endobronchial ultrasosonography, *ATS* American Thoracic Society classification

[a] Statistically significant *p* value. Yield comparison between conventional and EBUS-guided TBNA in the postintervention period

TBNA was 43%. Most of the cases were due to lung cancer (69%), and right-sided tumors were more common (63%).

Postintervention

After the intervention, 45 conventional TBNA, 45 RP-EBUS TBNA, and 50 linear EBUS TBNA procedures were assessed (Table 1). Preprocedural testing was significantly reduced to 9% ($n = 12$) for complete blood count, 8% ($n = 11$) for coagulation studies, and 3% ($n = 4$) for electrolytes. A total of 193 lymph nodes were sampled, and the ATS stations were 7 ($n = 68$, 35%), 4R ($n = 73$, 38%), 4L ($n = 31$, 16%), and 10 ($n = 21$, 11%). The median size of the lymph nodes targeted was 2 cm (range, 1.8–2.4 cm).

Cytologic specimens were prepared using the direct smear method and fixed in 95% alcohol. Conventional TBNA procedures were performed with the histology needle for all the patients, and 27% of the patients ($n = 12$) had more than one lymph node station sampled.

Conventional TBNA provided a diagnosis in 82% of the cases. Most of the cases were due to lung cancer (83%), with right-sided tumors being more common (67%). Although the addition of EBUS resulted in improved yield, from 82% with conventional TBNA to 86% (Table 1), this improvement was not statistically significant ($p = 0.44$) compared with that resulting from intervention ($p = 0.001$). As shown in Table 2, EBUS was more useful than conventional TBNA in guiding TBNA of lymph nodes smaller than 2 cm ($p = 0.001$) (Table 2). There was, however, no difference in TBNA yield when lymph nodes smaller than 2 cm were sampled using linear EBUS or RP-EBUS ($p = 0.44$) (Table 3).

Table 2 Impact of endobronchial ultrasosonography (EBUS) on transbronchial needle aspiration (TBNA) yield per lymph node in the postintervention period

	EBUS-guided TBNA	Conventional TBNA	*p* Value
No of lymph nodes sampled	136	57	
Median size of lymph node: cm (range)	1.8 cm (1.6–2.0)	2.4 cm (2–2.8)	0.001[a]
Overall TBNA yield assessed per lymph node: % (*n*)	86 (117)	82 (47)	0.58
No. of lymph nodes <2 cm sampled:	93	12	0.001[a]
TBNA yield for lymph nodes <2 cm: % (*n*)	85 (79)	25 (3)	0.001[a]

[a] Statistically significant *p* value

Table 3 Comparison of radial probe (RP) endobronchial ultrasound (EBUS) with linear EBUS for lymph nodes smaller than 2 cm

	RP-EBUS	Linear EBUS	*p* Value
No. of lymph nodes sampled	49	44	
Median size of lymph node: cm (range)	1.6 (1.5–1.8)	1.7 (1.6–1.8)	0.14
TBNA yield per lymph node: % (*n*)	86 (42/49)	82 (36/44)	0.44
ATS lymph node stations			
4R	20	16	
4L	8	7	
7	18	11	
10R and 10L	3	10	

TBNA transbronchial needle aspiration, *ATS* American Thoracic Society classification

Discussion

Accurate mediastinal staging determines surgical resectability of non-small cell lung cancer and has an impact on survival. Although mediastinoscopy and mediastinotomy have high sensitivity (87%) and specificity (100%), they require general anesthesia and are associated with morbidity (1%) and mortality (0.2%) [16].

On the other hand, TBNA is a well-established bronchoscopic method for patients with CT evidence of enlarged mediastinal lymph nodes adjacent to the airways. However, conventional TBNA has a variable yield of 20–89% and is the most operator dependent of all the bronchoscopic techniques [17, 18]. Increasing experience and practice have been shown to improve yield [9].

Because conventional TBNA is a blind procedure in which needle placement within the desired lesion cannot be confirmed by imaging and failure to target abnormality leads to false-negative results, some investigators have proposed performing up to seven passes per nodal station [19]. The introduction of rapid on-site cytology evaluation (ROSE) has obviated the need for an excessive number of aspirations and reduced procedural time correspondingly [20, 21]. However, ROSE incurs additional labor costs and may not be available in all hospitals.

Thus, new technologies that allow real-time imaging such as CT fluoroscopy, EBUS, endoscopic ultrasound, and navigational bronchoscopy [10–13] appear attractive because they facilitate location of the target and guide needle entry. However, acquisition of the equipment would incur considerable expenses. Moreover, performing TBNA with CT fluoroscopy requires logistic planning, and excessive exposure of patients and staff to irradiation is a valid concern.

Our study showed that for enlarged lymph nodes, standardization of TBNA technique, use of the histology needle, and proper specimen preparation were the first steps toward improving the TBNA yield. Careful review of CT, which served as a road map to the location of lymph nodes, and flipping of the films for better correlation with the endoscopic view of the tracheobronchial tree were in our opinion useful in determining the appropriate sites for TBNA puncture. Different TBNA approaches have been described, and although no data exist for comparison of these methods [17, 18], "jabbing" and "piggyback" techniques were chosen in our study to expedite expertise acquisition. We also standardized use of the histology needle exclusively to obtain aspirate and core biopsy [22], instructed our assistants in proper specimen preparation using the direct smear method and 95% alcohol fixation [1, 23], and adopted the ATS lymph node classification [14] to facilitate communication among our colleagues in pathology and thoracic surgery. It was a multiprong intervention that had improved our TBNA yield.

Notwithstanding our study's limited sample size, we did not observe a significant impact on the overall TBNA yield when EBUS was incorporated into our practice, which concurred with the findings of Shannon et al. [24], who showed no additional benefit with EBUS when the baseline sensitivity of conventional TBNA was high. There was also no difference in diagnostic accuracy between RP-EBUS and linear EBUS.

However, when we evaluated lymph nodes smaller than 2 cm, application of RP- EBUS to locate and confirm the appropriate site for puncture and use of the linear EBUS bronchoscope for real-time TBNA conferred a higher yield than conventional TBNA. This finding could be explained by a recent report demonstrating significant lymph node displacements in the craniocaudal, mediolateral, and ventrodorsal axes, and movement of the carina by as much as 8 mm during respiration [25]. The degree of lymph node and carina displacement during respiration could not be factored into the preprocedural planning because appropriate sites for TBNA in relation to the tracheobronchial tree were selected based on CT images acquired during breathhold.

Our study revisited the importance of CT reading and knowledge of how the enlarged lymph nodes relate to the tracheobronchial tree, proper TBNA, and specimen preparation techniques. It also validated a simple strategy that incorporates the histology needle to obtain a core biopsy and the optimal number of needle passes required per lymph node (4 per lymph node station and 3 if more than 1 station is sampled). In our opinion, these are the first steps toward improving conventional TBNA yield at no additional cost [26]. As shown, EBUS complements conventional TBNA by allowing more precise targeting of lymph nodes smaller tan 2 cm sited at challenging locations.

Disclosures Ghee Chee Phua, Kyung-Jae Rhee, Mariko Koh, Chian Min Loo, and Pyng Lee have no conflicts of interest or financial ties to disclose.

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