REVIEW ARTICLE

Endobronchial ultrasound-guided transbronchial needle aspiration

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KEY WORDS

ABSTRACT

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is an advance in bronchoscopy. It is a staging tool for nonsmall cell lung cancer (NSCLC) but also allows diagnosis of unexplained mediastinal lymphadenopathy due to malignant and benign disease. It is a minimally invasive procedure that is used to stage suspected NSCLC with hilar nodes, discrete N2 or N3 disease, or bulky mediastinal disease. After a negative EBUS-TBNA result, if the pretest probability of lung cancer is high, a mediastinoscopy is still recommended, although in the light of recent trial data this is likely to change. EBUS-TBNA is expensive, which may limit its development in resource-rationed health care systems. Conventional (without ultrasound) transbronchial needle aspiration (TBNA) still has a useful role in lung cancer staging, especially where EBUS-TBNA is not available; it can help avoid unnecessary mediastinoscopies.

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Introduction Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a minimally invasive mediastinal lung cancer staging and diagnostic procedure. Current surgical staging with mediastinoscopy is more invasive and expensive. EBUS-TBNA performs as well as mediastinoscopy in many respects and better than conventional transbronchial needle aspiration (TBNA). EBUS-TBNA can be useful in the diagnosis of unexplained mediastinal lymphadenopathy or masses. This review covers when EBUS-TBNA is considered, comparative mediastinal staging studies, procedural and training issues, as well as other applications.

Staging Quick diagnosis and accurate lung cancer staging are essential to allay patient anxiety, give the best chance of selection for radical treatment, and otherwise allow prompt palliative treatment. Mediastinal lymph node metastases determine prognosis, resectability, and survival (because mediastinal metastases in nonsmall cell lung cancer [NSCLC] correlate with extrathoracic metastases), and staging algorithms have therefore taken this into account.[1,2] Noninvasive staging by computed tomography (CT) and positron emission tomography (PET) has its problems, although it can give useful staging and guide where to obtain tissue for confirmation.[3]

Mediastinal sampling techniques include mediastinoscopy (and associated surgical staging techniques), EBUS-TBNA, and conventional TBNA. Mediastinoscopy is traditionally performed when radical treatment is considered, but it only accesses stations 2R, 2L, 4R, 4L, and 7 (see **FIGURE 1**). It performs well (78%–81% sensitivity, 91% negative predictive value in studies with mean prevalence of 39%)[4-10] and yields a large tissue core but is not without its problems. It takes a long time, is invasive with a small risk of important serious complications, and is expensive and rationed, requiring a thoracic surgical team, general anesthesia, and often overnight admission.[11] Conventional TBNA at flexible bronchoscopy samples the mediastinal nodes, is a less invasive technique, but its performance is inferior to mediastinoscopy (76–78% sensitivity, 71%–72% negative predictive value in studies with mean prevalence of 75%)[4-9] because the tissue size is smaller (although tissue cores from a 19-gauge needle can still be obtained) and sampling is not done under direct vision, although higher sensitivities of up to 82% have been reported in expert centers and also in newly developed services in higher prevalence cohorts (above 75%).[12,13]
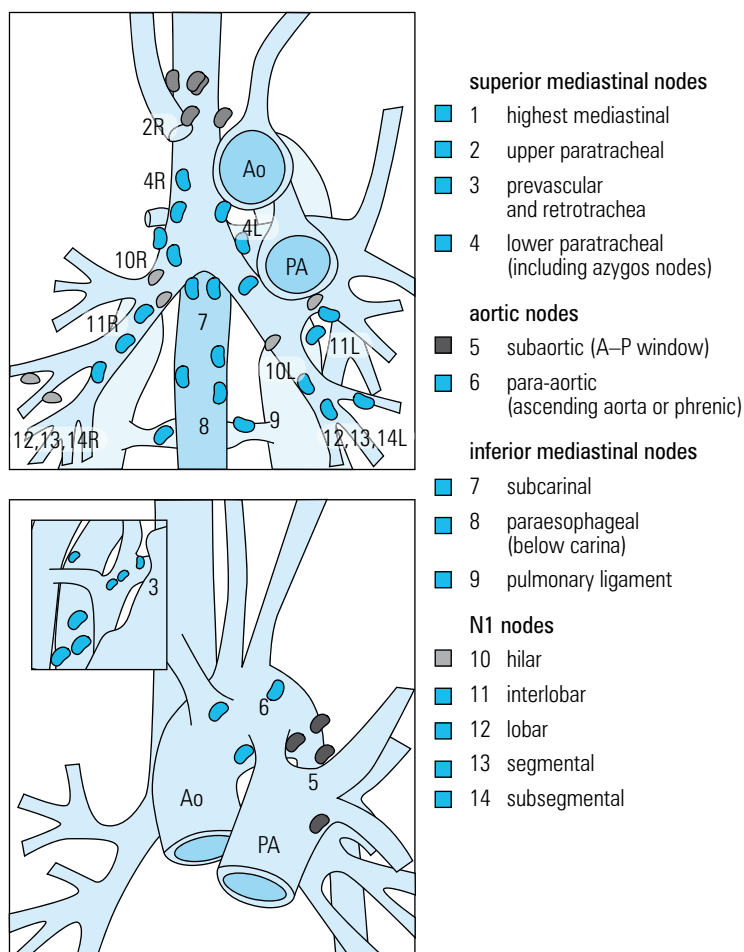
FIGURE 1 Regional lymph node map (reproduced with permission from: Mountain CF, et al. Regional lymph node classification for lung cancer staging. Chest. 1997; 111: 1718-1723)

superior mediastinal nodes
- 1 highest mediastinal
- 2 upper paratracheal
- 3 prevascular and retrotrachea
- 4 lower paratracheal (including azygos nodes)

aortic nodes
- 5 subaortic (A–P window)
- 6 para-aortic (ascending aorta or phrenic)

inferior mediastinal nodes
- 7 subcarinal
- 8 paraesophageal (below carina)
- 9 pulmonary ligament

N1 nodes
- 10 hilar
- 11 interlobar
- 12 lobar
- 13 segmental
- 14 subsegmental

EBUS-TBNA is a logical development from TBNA allowing real-time sampling (with image capture for audit purposes), better safety, and improved performance comparable to mediastinoscopy in sensitivity (considering the higher disease prevalence in the studies) although its negative predictive value is inferior (88%–93% sensitivity, 76% negative predictive value in studies with mean prevalence of 68%),[4-9] so that mediastinoscopy should be performed in EBUS-TBNA-negative cases if there is a high clinical suspicion of malignancy. EBUS-TBNA is much quicker, performed as a day case out of theatre, and is less invasive than mediastinoscopy. The sonographic appearances at EBUS-TBNA can also help predict malignancy and additional pathology in the proximal pulmonary vasculature.[14,15] The closely related endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) can be performed at the same time as EBUS-TBNA and gives access to stations 4L, 5–9, as well as the left adrenal gland and left lobe of the liver. EBUS-TBNA does have its drawbacks compared to conventional TBNA: it costs much more, takes longer, and requires longer training. Occasionally, the EBUS-TBNA sample gets contaminated with bronchial epithelial cells, which affects the utility of some tumor markers.[16]

Changes to treatment The arrival of EBUS-TBNA with a superior negative predictive value to conventional TBNA offers potential changes to treatment approaches in N2 NSCLC. Its use in staging solitary or multiple discrete or bulky N2 disease in lung cancer staging offers the potential to stratify patients who may benefit from combination chemoradiotherapy and in whom surgery may not be the most appropriate treatment.

Endobronchial ultrasound-guided transbronchial needle aspiration vs. computed tomography and positron emission tomography Comparative studies are summarized in **TABLE 1**. Two studies have compared EBUS-TBNA with preoperative radiological staging in patients with a radiologically "normal" mediastinum.[17,18] EBUS-TBNA was superior to radiological staging in both studies (**TABLE 1**),[17,18] although nodal diameters were down to levels that would limit the utility of PET. EBUS-TBNA was also superior to radiological staging for nodes of between 5 and 20 mm (**TABLE 1**),[19] especially for adenocarcinoma, which is known to have a higher rate of mediastinal metastases[20] and lower PET activity.[21] Combined EBUS-TBNA/EUS-FNA was superior to either EBUS-TBNA or EUS-FNA alone for subcentimeter nodes on CT.[22] EBUS-TBNA may therefore have a role in preoperative staging and is superior to radiological staging but may be more effective when combined with EUS-FNA.

Endobronchial ultrasound-guided transbronchial needle aspiration vs. conventional transbronchial needle aspiration EBUS-TBNA is superior to conventional TBNA although there are few comparative studies. On the basis of a recent systematic review, conventional TBNA had a 76% sensitivity[4] compared with 88% to 93% for EBUS-TBNA.[4-9] However, expert centers can achieve sensitivities of up to 82% in higher prevalence cohorts, although with a lower negative predictive value of 67%.[12] The impressive performance in this study reflects the expertise in TBNA but also the higher prevalence of disease. Conventional TBNA continues to have a role in centers where EBUS-TBNA is not available (because of the cost and training requirements) with the limitation of its lower negative predictive value.

Endobronchial ultrasound-guided transbronchial needle aspiration vs. mediastinoscopy There are only 3 comparative studies to date yielding differing results (**TABLE 2**), although the data from one of these studies are preliminary.[23,24] One study favored mediastinoscopy and 3 patients were upstaged by mediastinoscopy indicating that EBUS-TBNA may not completely replace it, although the prevalence of disease was lower.[24] More recent data from a randomized multicenter controlled trial (ASTER) of combined endosonography (EBUS-TBNA/EUS-FNA) followed by surgical staging (for negative findings) vs. surgical staging in potentially resectable NSCLC has revealed a higher detection of nodal metastases (50% vs. 35%) and a reduction in futile thoracotomies with no increase in complications.[25]

Noncomparative studies (**TABLE 2**) have not performed surgical staging in EBUS-TBNA-positive

TABLE 1 Studies evaluating endobronchial ultrasound-guided transbronchial needle aspiration and/or endoscopic ultrasound-guided fine needle aspiration in either normal mediastinum according to radiological staging: computed tomography and positron emission tomography or comparing to radiological staging

Study	No.	Technique	Sensitivity, %	Specificity, %	NPV, %	Prevalence, %	Node size, mm
Herth et al.[17]	97	EBUS-TBNA	89	100	98.9	8.2	<10 (mean 7.9)
Yasufuku et al.[18]	102	EBUS-TBNA	92.3	100	97.4	23.6	5–22 (mean 8.7)
		CT	76.9	55.3	87.5		
		PET	80.0	70.1	91.5		
Hwangbo et al.[19]	117	EBUS-TBNA	90.0	100	96.7	26	5–20
		PET/CT	70.0	59.8	85.2		
Szlubowski et al.[22]	120	EBUS-TBNA/EUS-FNA	68	98	91	22	<10

Abbreviations: CT – computed tomography, EBUS-TBNA – endobronchial ultrasound-guided transbronchial needle aspiration, EUS-FNA – endoscopic ultrasound-guided fine needle aspiration, NPV – negative predictive value, PET – positron emission tomography

TABLE 2 Comparative and noncomparative studies evaluating endobronchial ultrasound-guided transbronchial needle aspiration and mediastinoscopy

Study	No.	Technique	Sensitivity, %	Specificity, %	NPV, %	Prevalence, %	Node size, mm
comparative studies							
Ernst et al.[23]	66	EBUS-TBNA	87	100	78	89	>10
		MEDI	68	100	59		
Yasufuku et al.[24,a]	33	EBUS-TBNA	77	100	86	39	2–23 (mean 6.7)
		MEDI	85	100	90		
Tournoy et al.[25,a]	123	EBUS-TBNA/EUS-FNA + MEDI[b]	94	100	91	50	NA
	118	MEDI[b]	80	100	90	35	
noncomparative studies							
Szlubowski et al.[26]	206	EBUS-TBNA	89	100	83.5	61	5–23 (mean 13.8)
Rintoul et al.[27]	109	EBUS-TBNA	91	100	60	71	NA

a in abstract form (preliminary results), **b** surgical staging (includes mediastinotomy and video-assisted thoracoscopic surgery), used for EBUS-TBNA/EUS-FNA-negative cases only in endosonography group

Abbreviations: MEDI – mediastinoscopy, NA – not available, others – see **TABLE 1**

cases. Transcervical bilateral extended surgical mediastinal lymphadenectomy was performed in all negative cases in a large prospective cohort study, and false-negative EBUS-TBNA results were attributed to proven small metastatic deposits.[26] A lower negative predictive value was noted in another larger prospective study (although sensitivity was comparable, see **TABLE 2**), indicating the need to surgically stage EBUS-TBNA--negative nodes when clinical suspicion is high.[27] Current guidelines recommend EBUS-TBNA for staging bulky mediastinal disease or discrete N2 or N3 disease.[5] Mediastinoscopy is still the preferred tool for radical treatment staging but given the findings from the recent ASTER trial, this position may need to be re-evaluated and the role for EBUS-TBNA/EUS-FNA is likely to extend into staging early-stage disease. Recommendations for restaging are less clear but mediastinoscopy leads to adhesions, which reduces the utility of re-mediastinoscopy, whereas initial staging with EBUS-TBNA/EUS-FNA may reduce adhesions.[28] Alternatively, EBUS-TBNA can restage with a 68% sensitivity and 78% negative predictive value with false negative results only in sub-5 mm nodes with small deposits.[29]

Unexplained mediastinal lymphadenopathy In addition to staging, another important application of EBUS-TBNA is to diagnose unexplained mediastinal lymphadenopathy due to malignant or benign disease. Many lung tumors are extraluminal and not always accessible via conventional bronchoscopic techniques; EBUS-TBNA is commonly the sole diagnostic method in lung cancer patients (22% in a typical real-world cohort of patients).[30] EBUS-TBNA can therefore reduce the need for other diagnostic procedures (CT-guided biopsy or diagnostic mediastinoscopy) in such situations and can be diagnostic in 45% of cases following on from a negative bronchoscopy and CT--guided biopsy.[31]

EBUS-TBNA has applications in the diagnosis of sarcoidosis although studies are limited largely to cohort studies with sensitivities from 71% to 93% depending on patient selection criteria (**TABLE 3**).[32-38] The lowest sensitivities were obtained in a selected cohort after a negative bronchoscopy and then using real-life criteria without a CT scan for all stages.[33,34] Higher sensitivities were achieved in patients with enlarged nodes on CT and stage 1–2 disease.[32,35,36] The one randomized trial did show superiority for EBUS-TBNA

TABLE 3 Studies (cohort unless specified) evaluating endobronchial ultrasound-guided transbronchial needle aspiration for the diagnosis of sarcoidosis

Study	No.	Criteria	Technique	Sensitivity, %	Node size, mm
Nakajima et al.[32]	31	stage 1	EBUS-TBNA	90.3	>10
Tournoy et al.[33]	80	initial negative FB	EBUS-TBNA	71	NA
Garwood et al.[34]	48	all stages	EBUS-TBNA	85	4–40 (mean 16)
Wong et al.[35]	65	stage 1–2	EBUS-TBNA	87.5	7–37 (mean 20.5)
Oki et al.[36]	15	stage 1–2	EBUS-TBNA	93	>10
Tremblay et al.[37]	50[a]	stage 1	EBUS-TBNA	83.3	>10
			TBNA	60.9	

a randomized controlled trial

Abbreviations: FB – flexible bronchoscopy, TBNA – conventional transbronchial needle aspiration, others – see **TABLES 1** and **2**

over conventional TBNA with a histology-gauge needle.[37]

EBUS-TBNA has other applications in benign disease. It can increase the diagnostic yield of smear-negative tuberculosis beyond bronchoalveolar lavage by use of molecular techniques on the EBUS-TBNA sample.[39] Similar application of limited esophageal EUS-FNA with an EBUS scope (even without molecular techniques) has been reported to have a high yield for tuberculosis in a recent case series of smear-negative cases.[40] EBUS-TBNA can enable diagnosis of hamartoma from the sonographic and histological appearances, avoiding more invasive procedures.[41]

In suspected mediastinal lymphoma, EBUS--TBNA is not the first-choice diagnostic tool (usually a larger tissue core is required by mediastinoscopy), but it can be diagnostic with the use of flow cytometry, which may be of particular help when the patient is unfit for a mediastinoscopy. In a small retrospective study, mediastinal lymphoma was diagnosed by EBUS-TBNA obtaining a 91% sensitivity.[42]

Procedural issues   Radial probe endobronchial ultrasound gives a 360º view using high frequencies (range 20–30 MHz) giving high resolution of less than 1 mm but lower depth penetration of 5 cm.[43,44] They are ideal for visualizing the airway wall and surrounding small parabronchial lesions in detail and are used for assessment of airway tumor infiltration to guide endobronchial therapy and peripheral pulmonary nodule sampling. Sampling is done sequentially and not in real time. The probes are smaller and can fit down a 2.8 mm working channel (or even 2 mm). The remainder if this discussion focuses on the linear probe.

The linear probe visualizes mediastinal lymph nodes, masses, and proximal vasculature in particular and allows real-time sampling, giving a larger tissue core than conventional TBNA (**FIGURE 2A** and **2B**). In clinical practice, a separate flexible bronchoscopy is sometimes done because the white light endoscopic image is inferior on the EBUS-TBNA scope, and the scope is also larger in external diameter limiting full examination of the distal tracheobronchial tree. The supine

patient is normally intubated orally from behind under either conscious sedation or general anesthesia with a laryngeal mask. The probe can be sheathed with an inflatable balloon to improve ultrasonic image quality but in clinical practice, this is often unnecessary. It uses a lower frequency range of about 7.5 MHz, giving good depth penetration of about 9 cm at the expense of some loss in resolution, although newer linear probes have a frequency range of 5 to 20 MHz.

The endoscopic image is not the same as encountered at conventional bronchoscopy and is at an obliquely angled view of 30º forward with the ultrasonic image (**FIGURE 3**, M-mode with optional power Doppler to avoid vascular puncture) at an angled forward view of 90º parallel to the EBUS bronchoscope shaft. The EBUS-TBNA needle is a sheathed 22-gauge needle (although 21-gauge has been used too, but not 19-gauge as sometimes used for conventional TBNA) (**FIGURE 4**) with an internal removable stylet (**FIGURE 5**), and the technique is similar to conventional TBNA with some modifications: firstly, the length of needle expulsion is determined using the calibrator at the side of the sonographic image and set on the needle operating system (**FIGURES 3** and **6**); secondly, it is important to agitate the stylet when in the node to remove debris before sampling. Serpiginous tissue cores are deemed "optimal" and 2 samples alone if "optimal" are sufficient,[45] but many centers perform up to 4 passes if samples are not "optimal" subject to patient tolerance as studies suggest additional benefit here.[46] The higher stage nodes are sampled first (N3, then N2) to prevent upstaging by contamination.

Many centers use liquid cytology bottles for samples, supported by a recent study.[47] Conventional TBNA studies suggest that the smear technique (smearing the sample onto glass slides and fixing in alcohol) is superior, resulting in less cellular distortion (**FIGURE 2B**), which may potentially be of value in sarcoidosis and tuberculosis for example.[48-50] Rapid on-site evaluation for cytopathology improves the diagnostic yield of TBNA but is not routinely available in many centers.[51,52] For histology tissue cores, formalin and saline (for microbial culture) pots are used.
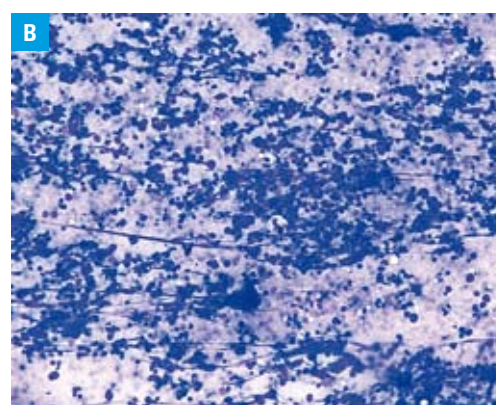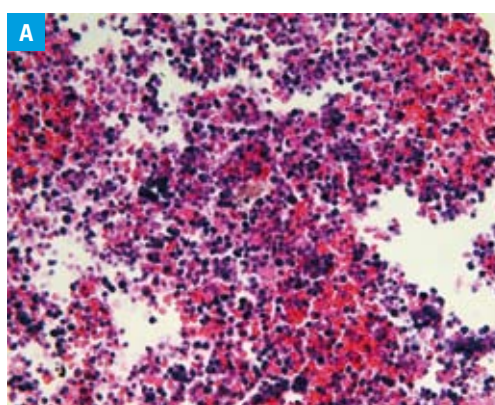
EBUS-TBNA has a similar safety profile to conventional flexible bronchoscopy and is well tolerated.[53,54] A postprocedure chest radiograph (CXR) is not usually performed as pneumomediastinum, pneumothorax, and hemomediastinum (avoided by real-time sampling usually) are very rare, although some centers do perform a CXR after hilar node sampling.[55,56] Infectious complications can occur including mediastinal abscess[57] and bacteremia, but the latter are usually asymptomatic.[58,59] More recent data suggest that metal particles can be released into lymph nodes when using EBUS-TBNA needles, but not from conventional TBNA. This may result from friction between the stylet and needle; the significance of this is currently unknown but requires further study.[60]

Training Conventional TBNA should be performed for proximal enlarged mediastinal adenopathy at the same time as bronchoscopy (even if there is an endobronchial lesion) because it is cheap compared with EBUS-TBNA, easier to learn,[61] well tolerated,[62] and available, providing diagnostic and staging information.

Conventional TBNA can also avoid mediastinoscopy in 35% of cases[63,64] and save costs (£560 per patient when used as a new service in a real-world

United Kingdom cohort).[13] EBUS-TBNA differs from conventional bronchoscopy and TBNA. There are 2 different (often simultaneous) views. The ultrasonic image needs to be acquired, interpreted correctly, and maintained. The endoscopic white light view has less resolution than at conventional bronchoscopy and the distal tracheobronchial tree cannot be accessed (due to the higher external diameter of the scope). The scope itself is more fragile, heavier, and thicker at its end with an altered angle of endoscopic view. Training bodies recommend between 40 to 50 supervised procedures with a minimum 5 to 25 procedures annually to maintain level of skill but this refers to radial probe EBUS. The British Thoracic Society is in the process of issuing new guidance.

Although the learning curve has traditionally been thought to be short, backed up by good results from newly developed EBUS-TBNA services (although performance is influenced by node size, disease prevalence, and tumor histology),[30,65-67] more recent data suggest learning can take much longer even among experienced bronchoscopists,
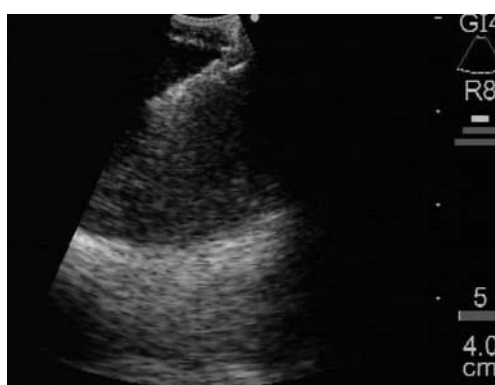
FIGURE 3 Typical sonographic image (M-mode but power Doppler off) during endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) of large 2cm subcarinal node. Calibrator on right denotes 1cm markings. EBUS-TBNA needle shown coming in from top right into node under real-time imaging

FIGURE 4 Typical 22-gauge endobronchial ultrasound-guided transbronchial needle aspiration needle shown extruding from sheath

FIGURE 5 Internal stylet extruding from needle operating system

FIGURE 6 Endobronchial ultrasound-guided transbronchial needle aspiration needle operating system with needle controller, manual calibrator to alter depth of needle extrusion with hub and needle system locks

and Cusum analysis is a useful technique to illustrate this.[68]

Regarding EUS-FNA (a useful surrogate to EBUS-TBNA for training because it has been used in clinical practice for much longer), the American Society for Gastrointestinal Endoscopy (ASGE) recommends 100 EUS-FNA procedures based on experience from esophageal cancer.[69,70] The United Kingdom Endoscopic Ultrasound Users Group recommend training is undertaken in units doing more than 200 endoscopic ultrasound (EUS) procedures annually[71] with learning of EUS-FNA only after 50 EUS procedures.[72] Data suggest that tuition from an experienced EUS-FNA mentor cannot be replaced by mechanical models or courses.[73] Some pulmonologists perform a more limited esophageal EUS-FNA with the same EBUS scope with the advantage of cost-saving if a separate EUS scope is not available; this is likely to require less training as the same scope is used, but there are no formal guidelines on this particular technique.[40,74] Other pulmonologists perform complete EUS-FNA in conjunction with gastroenterologists, interventional radiologists, or surgeons, and the ASGE guidelines are likely to be more relevant here.

Miscellaneous EBUS has other potential applications by allowing imaging of the proximal pulmonary vasculature, allowing accessing the mediastinal nodes in other malignant diseases, assessing airway wall caliber (using the radial probe), and assessing other nonmalignant mediastinal abnormalities accessible from the airway. Specific examples of these include detection of central pulmonary emboli (although this would require further validation),[15] staging malignant mesothelioma in conjunction with EUS-FNA,[75] and measuring airway wall thickness in asthmatics,[76]

sampling substernal thyroid nodules where standard EUS-FNA is not possible.[77]

Summary EBUS-TBNA is a minimally invasive staging technique for NSCLC but also allows diagnosis of unexplained mediastinal lymphadenopathy. When radical treatment is contemplated, mediastinoscopy is still mostly used for staging but this may be replaced in the future by EBUS-TBNA given more recent trial data. Currently, mediastinoscopy is still advisable for EBUS-TBNA-negative nodes when the pretest probability of lung cancer is high.

EBUS-TBNA requires training and has a definite learning curve even for experienced bronchoscopists. EBUS-TBNA can avoid unnecessary mediastinoscopies or other diagnostic procedures. A combined EBUS-TBNA/EUS-FNA service accessing all nodal stations is feasible with sufficient expertise and patient throughput. For centers without EBUS-TBNA, conventional TBNA should be performed because it is cheap, well tolerated, learnable, and performs no worse than EBUS-TBNA for large proximal nodes.

Summary for internists and primary care practitioners From the perspective of the internist or primary care practitioner, mediastinoscopy is the most invasive technique used by the thoracic surgeon under general anesthetic for staging the mediastinum when radical treatment is contemplated. It gives the largest amount of tissue but cannot access all the mediastinal stations, can have complications, and is most expensive but has remained the gold standard. Conventional TBNA offers a local anesthetic minimally

invasive procedure done by the pulmonologist, allowing access to the hilar stations as well with good results (slightly inferior to mediastinoscopy), especially in specialist centers with experienced operators, although a negative result is not as reliable. Similarly, EBUS-TBNA offers a a local anesthetic minimally invasive procedure done by pulmonologists, but allowing more reliable access to smaller, more distant nodes in the mediastinum and real-time sampling to reduce bleeding. It performs as well as mediastinoscopy in many respects but further studies are needed to clarify how reliable a negative result is, and its development is limited by cost and training requirements.

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Ultrasonografia wewnątrzoskrzelowa z przezoskrzelową biopsją igłową

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STRESZCZENIE

Przezoskrzelowa biopsja igłowa wykonywana pod kontrolą ultrasonografii wewnątrzoskrzelowej (*endobronchial ultrasound-guided transbronchial needle aspiration* – EBUS-TBNA) to najnowsze osiągnięcie w bronchoskopii. Jest narzędziem służącym do oceny stopnia zaawansowania niedrobno-komórkowego raka płuc (*nonsmall cell lung carcinoma* – NSCLC), ale pozwala także na diagnozowanie powiększonych węzłów chłonnych śródpiersia o nieznanej etiologii w przebiegu choroby nowo-tworowej lub nienowotworowej. Jest procedurą minimalnie inwazyjną, stosowaną do oceny stopnia zaawansowania przy podejrzeniu NSCLC z zajęciem węzłów chłonnych wnęki, cechą N2 lub N3, bądź obecnością masywnego guza w śródpiersiu. Jeżeli istnieje duże prawdopodobieństwo raka płuca, a wynik EBUS-TBNA jest ujemny, nadal zaleca się wykonanie mediastinoskopii, jednak w świetle ostatnich wyników badań wytyczne te mogą się zmienić. EBUS-TBNA jest drogą procedurą, co może ograniczyć jej zastosowanie w systemie opieki zdrowotnej, który ma ograniczone nakłady finansowe. Klasyczna (bez użycia ultrasonografii) przezoskrzelowa biopsja igłowa nadal odgrywa istotną rolę w ocenie stopnia zaawansowania raka płuca, szczególnie tam, gdzie EBUS-TBNA jest niedostępna. Pozwala ona uniknąć wykonywania zbędnych mediastinoskopii.