

# An International Survey of Mediastinal Staging Practices amongst Interventional Bronchoscopists

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## Keywords

Endobronchial ultrasound · Endoscopic ultrasound · Mediastinal staging · Mediastinoscopy · Lung cancer

## Abstract

**Introduction:** In potentially curable non-small-cell lung cancer, different practice guidelines recommend invasive mediastinal staging in tumors larger than 3 cm, central, or hypermetabolic N1 lymph nodes. There is no consensus concerning the use of an endosonographic procedure or a mediastinoscopy in the first line in patients with a radiologically normal mediastinum, while in case of a mediastinal involvement, the latest European guidelines recommend the combination of endobronchial ultrasound (EBUS) and endoscopic ultrasound/endoscopic ultrasound with EBUS endoscope (EUS/EUS-B), using a systematic endosonographic procedure. This international survey was conducted to describe current medical practices in endoscopic mediastinal staging amongst interventional bronchoscopists. **Methods:** A survey was developed and sent to all members of different interventional pulmonology societies, with the purpose to describe

who, when and how an endoscopic mediastinal staging was performed. **Results:** One hundred and fifty-three bronchoscopists responded to the survey. Most of them practiced in Europe ( $n = 84$ , 55%) and North America ( $n = 52$ , 34%). In the first line, EBUS alone was the most widely used endoscopic procedure for mediastinal staging. Half of the responders performed a systematic endoscopic staging procedure, including a systematic examination of all accessible nodal stations and a sampling of all lymph nodes  $>5$  mm in the short axis at each station. A higher proportion of bronchoscopists who have completed a dedicated fellowship program performed systematic endoscopic mediastinal staging. Few endoscopists routinely perform combined EBUS/EUS(-B) for mediastinal staging and use the combination only in selected cases. **Conclusion:** There are several areas of divergence between published guidelines and current practices reported by interventional bronchoscopists. EBUS alone is the most widely used endoscopic procedure for mediastinal staging in lung cancer, and a combined endoscopic approach is frequently omitted by the responders. A fellowship program appears to be associated with a higher rate of systematic endoscopic staging procedures.

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## Introduction

Accurate mediastinal staging is fundamental to establish prognosis and a treatment plan in potentially curable lung cancer. Since their development, endobronchial ultrasound (EBUS), endoscopic ultrasound (EUS) and endoscopic ultrasound with EBUS endoscope (EUS-B) have changed the approach to mediastinal lymph node (LN) staging. Practice guidelines provided by the American College of Chest Physicians (ACCP) [1], the National Comprehensive Cancer Network (NCCN) [2] and the European Society of Thoracic Surgeons (ESTS) [3] recommend invasive mediastinal staging in patients with a radiologically normal mediastinum but central tumors, tumors larger than 3 cm and enlarged or hypermetabolic N1 LN. The latest guidelines from the European Society of Gastrointestinal Endoscopy (ESGE) in cooperation with the European Respiratory Society (ERS) and the ESTS [4] recommend the combination of EBUS and EUS/EUS-B over either test alone, but it is unclear whether combined endosonographic procedures (CEP) are widely adopted in clinical practice.

When mediastinal staging is performed, a systematic endosonographic procedure is recommended. This procedure should include at least the examination of LN 2, 4 and 7 with a systematic sampling of the largest LN  $\geq 5$  mm in the short axis at each station [3, 4]. A targeted procedure where only PET-CT or enlarged LN nodes are sampled is not recommended due to the risk of understaging [5–7]. It is unclear whether this systematic approach is implemented by most when performing mediastinal staging procedures.

We performed an international survey with the purpose to describe current medical practices in endoscopic mediastinal staging and evaluate concordance with current guidelines.

## Methods

An English language questionnaire of 42 items including single and multiple choice questions was developed to describe interventional bronchoscopists and how they perform endoscopic mediastinal staging (online suppl. Appendix 1; for all online suppl. material, see [www.karger.com/doi/10.1159/000507096](http://www.karger.com/doi/10.1159/000507096)). The questionnaire addressed mainly three aspects:

1. Description of respondents
2. Procedures performed, operator learning method and type of sedation used
3. When and how mediastinal staging is performed

An invitation to participate to this survey was sent by e-mail to all American Association for Bronchology and Interventional Pul-

monology, World Association for Bronchology and Interventional Pulmonology, European Association for Bronchology and Interventional Pulmonology, Canadian Assembly for Chest Procedure and Groupe d'Endoscopie de la Langue Française members in 2018. A reminder e-mail was sent 3 months later. These societies are composed of interventional bronchoscopists or physicians with an interest in bronchoscopy. The mailing list of these societies was composed at the time of 450, 3,000, 314, 34 and 175 members, respectively, likely with overlap between lists. The survey was completed by responders online on the platform Research Electronic Data Capture. Learning method was classified as "self-learning" (SL; no course or course of less than a week), "course >1 week" (course of more than a week or training program of less than 6 months) and "fellowship" (dedicated fellowship program or training program of more than 6 months).

Responses were compared against current staging guidelines published by the ACCP, the ESTS and the ESGE in cooperation with the ERS/ESTS (Table 1).

Descriptive statistics were used to present the results. Data were compared using the  $\chi^2$  or Fisher tests for categorical variables. Statistical results were 2-sided, and a  $p$  value  $<0.05$  was considered significant. All analyses were performed with the Prism software (GraphPad Software Inc., CA, USA).

## Results

### *Description of Respondents*

One hundred and fifty-three interventional bronchoscopists responded to the survey (Table 2). One hundred and forty-six were respirologists (95.5%), and the remaining 7 were thoracic surgeons (4.5%). The majority ( $n = 112$ , 73.2%) practiced in academic environments. Respondents were mainly from Europe ( $n = 84$ , 55.0%) and North America (NA) ( $n = 52$ , 34.0%). France ( $n = 26$ , 31.3%), Italy ( $n = 10$ , 11.9%), Portugal ( $n = 6$ , 7.2%) and the UK ( $n = 6$ , 7.2%) were the most represented European countries while North American respondents were from the USA ( $n = 33$ , 63.5%) and Canada ( $n = 19$ , 36.5%) (online suppl. complete list Appendix 1).

Europeans reported having been in practice for more than 10 years more frequently than North Americans (67.9 vs. 38.5%) but reported less frequently having been performing EBUS for more than 10 years (13.0 vs. 30.8%) (Table 2). Most respondents had 5–10 years of experience performing EBUS (Europe 44.0%, NA 40.4%).

### *Procedures Performed, Operator Learning Method and Type of Sedation Used*

EBUS alone was the most widely used first intention procedure for mediastinal staging (Europe = 60.7%, NA = 75.0%), followed by the combination of EBUS + EUS-B (Europe = 27.4%, NA = 9.6%) and EBUS + EUS

**Table 1.** Summary of staging guidelines

	ACCP [1]	ESTS [3]	ESGE/ERS-ESTS [4]
Indications of invasive staging	Central tumor ( $\leq 1/3$ ) cN1 stage <sup>a</sup> cN2/3 stage	Central tumor ( $\leq 2/3$ ) Tumor $> 3$ cm cN1 and cN2/3 stage <sup>b</sup>	Central tumor ( $\leq 1/3$ ) Tumor $\geq 3$ cm cN1 and cN2/3 stage <sup>b</sup> FDG-non-avid tumor
First procedure	EBUS/EUS	cN0/N1: EBUS/EUS or mediastinoscopy cN2/N3: EBUS/EUS	EBUS/EUS(-B)
Systematic endosonographic procedure	No clear recommendation as to how staging should be performed	Complete assessment of mediastinal and hilar nodal stations Sampling the largest node $> 5$ mm on ultrasonography within each of these stations and PET-avid nodes within each of these nodal stations	Complete assessment of mediastinal and hilar nodal stations Sampling of at least three different mediastinal nodal stations (4R, 4L, 7) in cN2/N3 stage <sup>b</sup> and all abnormal lymph nodes <sup>b</sup>
Surgical staging if first procedure negative	When the clinical suspicion of mediastinal node involvement remains high <sup>c</sup>	cN2/3 stage <sup>b,d</sup>	Central tumor ( $\leq 1/3$ ) Tumor $\geq 3$ cm FDG-avid tumor cN1 and cN2/N3 stage <sup>b</sup> (CT or PET)

ACCP, American College of Chest Physicians; ESTS, European Society for Thoracic Surgery; ESGE, European Society of Gastrointestinal Endoscopy; ERS, European Respiratory Society;  $\leq 1/3$ , inner third of the lung;  $\leq 2/3$ , inner two thirds of the lung; FDG, fluorodesoxyglucose; CT, computed tomography; PET, positron emission tomography. <sup>a</sup>Node with a short axis  $> 10$  mm. <sup>b</sup>Node with a short axis  $> 10$  mm or node that is FDG-PET-avid. <sup>c</sup>With mediastinoscopy, video-assisted thoracic surgery, etc. <sup>d</sup>With video-assisted mediastinoscopy.

(Europe = 7.1%, NA = 11.5%) (Table 2). Only 4% reported that mediastinoscopy was the first intention procedure used in their institution. Responses were varied when bronchoscopists were asked which procedure or combination had the best negative predictive value: EBUS + EUS-B 38.0% (Europe = 45.2%, NA = 26.9%); EBUS + EUS 32.7% (Europe = 28.6%, NA = 32.7%); videomediastinoscopy 28.7% (Europe = 44.0%, NA = 28.8%); and EBUS alone 17.6% (Europe = 8.3%, NA = 32.7%).

All respondents perform EBUS (Table 3). The majority have an experience of 5–10 years (Europe = 44.0%, NA = 40.4%) or 1–5 years (Europe = 29.8%, NA = 26.9%) with EBUS. In NA, the majority of respondents learned EBUS through a fellowship (75.0%) while only a minority in Europe (29.7%) did.

Respectively 55.9 and 42.4% of respondents in Europe and NA perform EUS-B. The majority (Europe = 61.7%, NA = 59%) have less than 5 years of experience with this procedure. Learning through a fellowship was more frequent in NA than Europe (63.6 vs. 10.7%). Respectively 7.1 and 11.5% of respondents in Europe and NA perform EUS. Europeans less frequently learned EUS through a fellowship than North Americans (16.7 vs. 83.3%) (Table 3).

68.6% of the respondents have access to CEP in their institution (Europe = 70.0%, NA = 69.2%) (Table 4). Among them, 25.7% use CEP systematically during staging procedures (Europe = 37.3%, NA = 13.9%) while the

majority (Europe = 62.7%, NA = 86.1%) perform CEP in selected situations which represent less than 5% of their cases. The main indication for CEP when used selectively was the presence of a suspicious LN on imaging only accessible by EUS or EUS-B (92.3%).

49.0% reported performing endoscopic procedures under general anesthesia (GA) (Europe = 49.0%, NA = 52.0%). The use of GA varied largely when comparing North American countries (Canada 0%, USA 85%). When respondents reporting using GA were asked the reasons for this choice, their most frequent answers were patient comfort (66.6%) and possibility of achieving a more complete staging (84.0%). 27.0% of respondents using conscious sedation (CS) believed that GA did not allow a better staging, and 66.6% used CS because it was more resource efficient.

#### *When and How Mediastinal Staging Is Performed*

Bronchoscopists were asked to select amongst a list of indications the ones they felt to be appropriate indications for invasive mediastinal staging. Suspicious N2/N3 LN on imaging (67.0%), suspicious N1 LN on imaging (60.0%), central tumor (52.3%) and tumor  $\geq 3$  cm (47.7%) were the most frequent indications selected for invasive mediastinal staging. No differences in indications selected were observed when comparing respondents who learned through a fellowship and self-learning (Fig. 1).

**Table 2.** Characteristics of the bronchoscopists

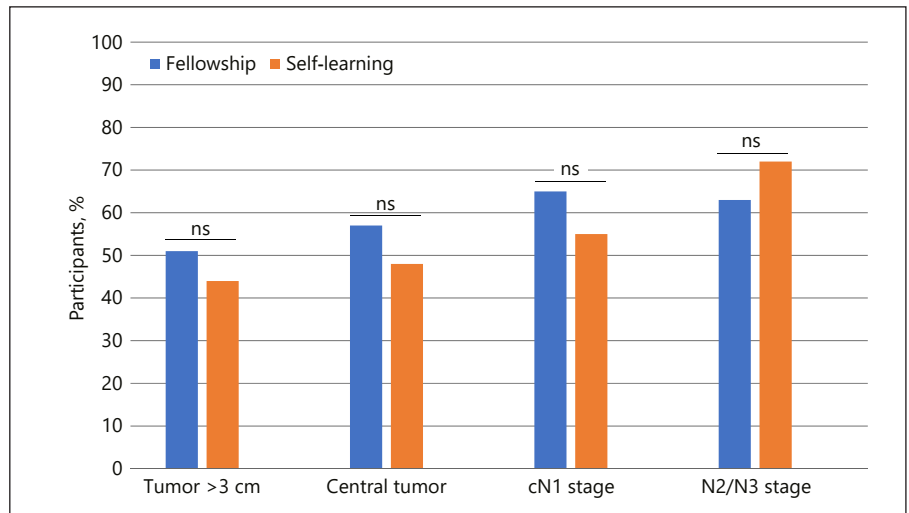
	Europe	North America	Total
Respondents, <i>n</i> (%)	84 (55)	52 (34)	153
Medical specialty			
Pulmonology	80 (95.2)	49 (94.2)	146 (95.5)
Thoracic surgery	4 (4.8)	3 (6.8)	7 (4.5)
Practice years			
<5 years	7 (8.3)	17 (32.7)	28 (18.3)
5–10 years	20 (23.8)	15 (28.8)	41 (26.8)
>10 years	57 (67.9)	20 (38.5)	84 (54.9)
Practice in academic hospital			
Yes	62 (73.8)	39 (75)	112 (73.2)
Techniques mainly used for a mediastinal staging in the institution <sup>1</sup>			
EBUS only	51 (60.7)	39 (75)	86 (56.2)
EBUS and EUS-B	23 (27.4)	5 (9.6)	32 (21)
Nodal dissection during surgery	1 (1.2)	6 (11.5)	13 (8.5)
EBUS and EUS	6 (7.1)	6 (11.5)	12 (7.8)
Mediastinoscopy	3 (3.6)	1 (1.9)	6 (4)
EUS only	0	0	4 (2.5)
Procedure with best negative predictive value <sup>1</sup>			
EBUS with EUS-B	38 (45.2)	14 (26.9)	58 (38)
EBUS with EUS	24 (28.6)	17 (32.7)	50 (32.7)
Videomediastinoscopy	37 (44)	15 (28.8)	44 (28.7)
EBUS alone	7 (8.3)	17 (32.7)	27 (17.6)
Anesthesia (EBUS, EUS(-B))			
General anesthesia	41 (49)	28 (52)	75 (49)
Conscious sedation	43 (51)	24 (48)	78 (51)
Reasons for general anesthesia <sup>1</sup>			
Allows a better staging	37 (90.3)	21 (75)	63 (84)
Patient's comfort	29 (70.7)	17 (60.7)	50 (66.6)
No access to conscious sedation	5 (12.2)	1 (3.6)	7 (9)
Reasons for conscious sedation <sup>1</sup>			
Less resource-consuming	23 (53.5)	21 (87.5)	52 (66.6)
General anesthesia does not allow a better staging	13 (30.2)	8 (33.3)	21 (27)
No access to general anesthesia	13 (30.2)	5 (20.8)	21 (27)

<sup>1</sup> More than one answer allowed.

**Table 3.** Endosonographic procedures performed and operator learning method

	EBUS		EUS-B		EUS	
	Europe	NA	Europe	NA	Europe	NA
Respondents, <i>n</i> (%)	84 (100)	52 (100)	47 (55.9)	22 (42.4)	6 (7.1)	6 (11.5)
Practice years						
<1 year	7 (8.3)	1 (1.9)	5 (10.6)	0	0	0
<5 years	25 (29.8)	14 (26.9)	29 (61.7)	13 (59)	2 (33.3)	1 (16.7)
5–10 years	37 (44)	21 (40.4)	11 (23.4)	5 (22.7)	2 (33.3)	3 (50)
>10 years	15 (13.9)	16 (30.8)	2 (4.3)	4 (18.3)	2 (33.3)	2 (33.3)
Learning method						
Course >1 week	16 (19.1)	1 (2)	4 (8.5)	0	0	0
Fellowship	25 (29.7)	39 (75)	5 (10.7)	14 (63.6)	1 (16.7)	5 (83.3)
Self-learning	43 (51.2)	12 (23)	38 (80.8)	8 (36.4)	5 (83.3)	1 (16.7)

Course >1 week, course of more than a week or training of less than 3 months; fellowship, dedicated fellowship program or a training of more than 6 months; self-learning, own learning and/or course of less than a week; NA, North America.



**Fig. 1.** Indications for mediastinal staging according to learning method. ns, nonsignificant.

**Table 4.** Combined use of EBUS-transbronchial needle aspiration and EUS or EUS-B fine needle aspiration

	Europe	NA	Total
Respondents, <i>n</i> (%)	59 (70)	36 (69.2)	105 (68.6)
Systematically during a staging procedure	22 (37.3)	5 (13.9)	27 (25.7)
In selected cases	37 (62.7)	31 (86.1)	78 (76.3)
Proportion of patients			
<5%	21 (56.7)	28 (90.3)	52 (66.7)
5–25%	15 (40.5)	3 (8.7)	22 (28.2)
26–50%	1 (2.8)	0	4 (5.1)
>51%	0	0	0
Indications <sup>a</sup>			
Left lung tumor	0	3 (9.7)	7 (8.9)
Positive LN (CT or PET-CT) only accessible by EUS/EUS-B	33 (89.2)	30 (96.8)	72 (92.3)
Other	7 (18.9)	1 (3.2)	8 (10.3)

NA, North America; LN, lymph node; CT, computed tomography; PET, positron emission tomography.  
<sup>a</sup> More than one answer allowed.

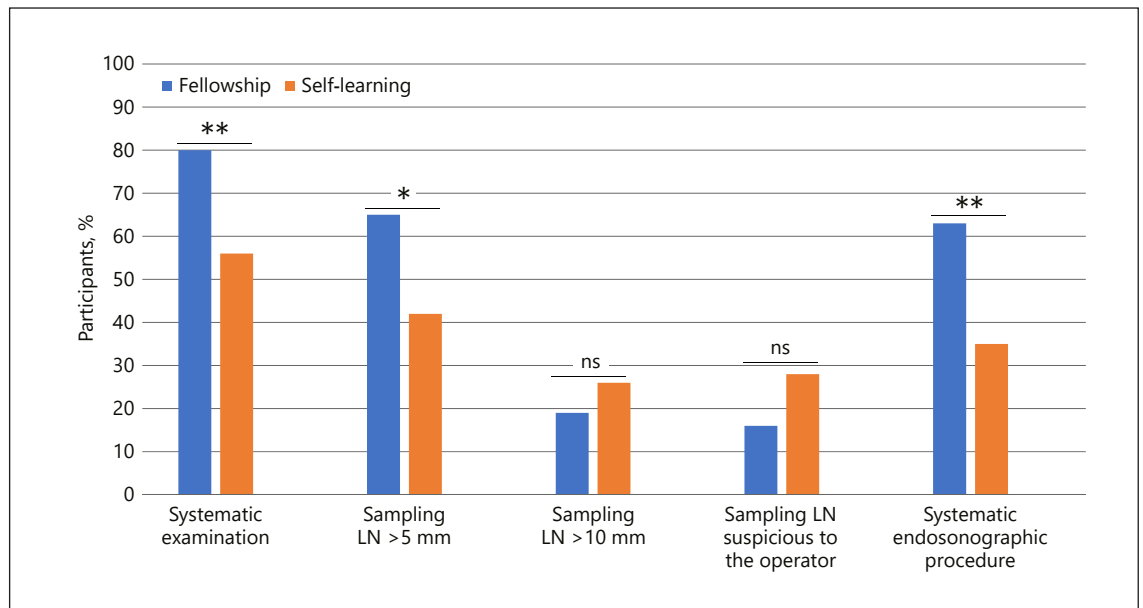
When asked whether they perform a systematic or targeted examination of mediastinal nodal stations, 69.2% responded that they perform a systematic examination (fellowship = 79.5%, SL = 56.1%) (Fig. 2). When asked about criteria used to sample an LN, 54.6% answered that they sample all LN >5 mm in short axis (fellowship = 64.4%, SL = 42.1%), 22.3% that they sample all LN >10 mm (fellowship = 19.2%, SL = 26.3%) and 23.1% that they sample all LN suspicious to them regardless of size (fellowship = 16.4%, SL = 28%). Overall, 50.8% responded that they perform a systematic endosonographic procedure (fellowship = 63%, SL = 35%).

When asked about further investigations necessary after a negative endoscopic mediastinal staging with systematic sampling and adequate samples, 47.7% recom-

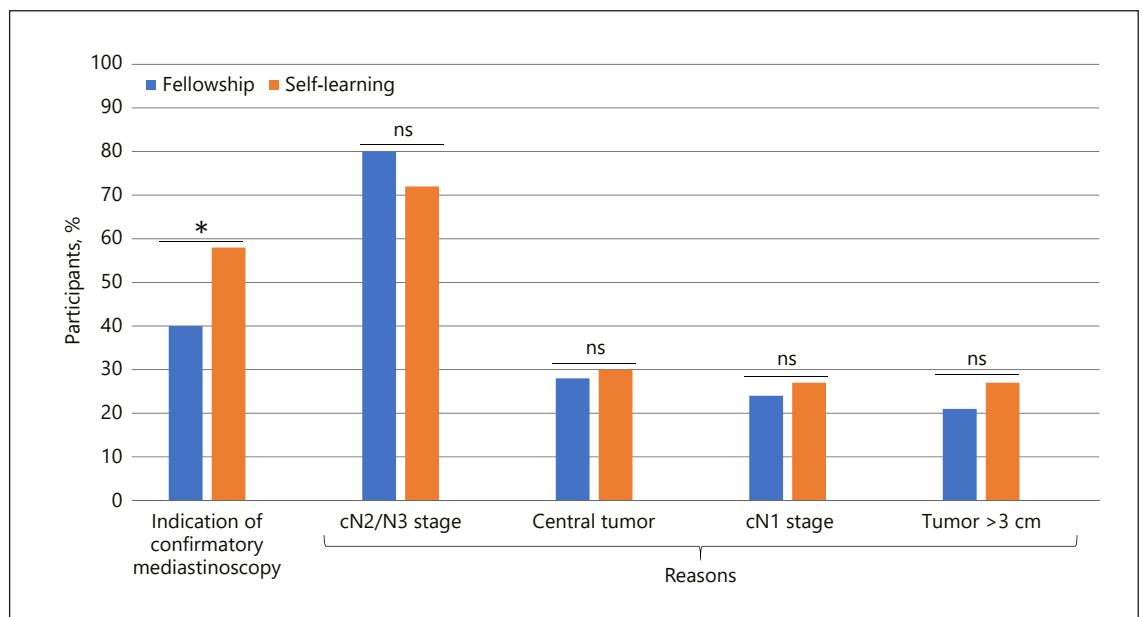
mended a confirmatory mediastinoscopy (fellowship = 39.7%, SL = 57.8%) (Fig. 3). The most frequent indications for confirmatory mediastinoscopy reported were hypermetabolic mediastinal LN (75.8%), enlarged mediastinal LN (37.0%), central tumor (29.0%), hypermetabolic or enlarged N1 LN (25.8%) and tumor >3 cm (24.2%).

## Discussion

This survey allows us to obtain a contemporary picture of mediastinal staging practices amongst interventional bronchoscopists around the world. It demonstrates areas of divergence between published guidelines and current



**Fig. 2.** Sampling criteria and use of systematic examination according to learning method. LN, lymph node. \*  $p < 0.05$ ; \*\*  $p < 0.01$ ; ns, nonsignificant.



**Fig. 3.** Indication for confirmatory mediastinoscopy after a negative endosonographic procedure according to learning method. \*  $p < 0.05$ ; ns, nonsignificant.

practices in endoscopic non-small-cell lung cancer mediastinal staging. Despite current guidelines recommending invasive mediastinal staging in patients with a radiologically normal mediastinum and a central tumor, a tumor >3 cm or a cN1 stage, only about half of the respon-

dents reported performing invasive mediastinal staging in this population. ESTS and ESGS guidelines also recommend a systematic examination of all mediastinal LN and sampling of the largest LN >5 mm in the short axis at each station. Despite these recommendations, only 69.2% of

respondents reported performing a systematic examination of which 54.6% sample all LN >5 mm. These findings highlight the insufficient knowledge of guidelines and evidence amongst interventional bronchoscopists.

The latest staging guidelines by the ERS-ESTS-ESGE published in 2015 favor a combined endosonographic procedure as the first test of choice. EUS or EUS-B is known to be complimentary to EBUS, allowing access to unreachable stations by EBUS such as stations 5, 6, 8 and 9 as well as a portion of the left lobe of the liver and the left adrenal gland. Since publication of this guideline, additional evidence on this topic has been published. A meta-analysis reported a significant increase in sensitivity (12%) for the combined use of EBUS and EUS compared with either test alone [8]. More recently, the SCORE study found a 9% higher sensitivity in detection of mediastinal LN metastases with use of a systematic combined endosonographic approach with the same EBUS scope (EBUS + EUS-B) than with a targeted EBUS strategy alone [7]. Moreover, additional clinically relevant staging information was found in 10% of patients. In this survey, half of the respondents reported having the skills to perform EUS-B, but only a minority used CEP systematically in staging procedures. These results are inconsistent with the fact that most respondents think that combined EBUS/EUS or EUS-B has a better negative predictive value than EBUS alone. Appropriate training in esophageal endoscopic techniques is certainly a barrier to guideline consistent care but access to the equipment may also play a role as even physicians with appropriate training were not performing these techniques frequently.

Current guidelines of the ACCP recommend a confirmatory mediastinoscopy when the clinical suspicion of mediastinal LN involvement remains high after endoscopic staging and those of the ESTS in cases of a clinically abnormal mediastinum only. Several studies have demonstrated the low sensitivity of EBUS in the radiologically normal mediastinum [9–13] including a recent meta-analysis [14]. The Leuven Lung Cancer Group published an interesting study reporting the need for confirmatory mediastinoscopy in cN1 patients, a subgroup of patients at high risk of radiologically occult mediastinal LN involvement. Indeed, sensitivity of EBUS alone to detect occult mediastinal disease was 38% and increased to 73% by adding a mediastinoscopy after a negative EBUS staging procedure [9]. In this survey, half of the respondents recommended a confirmatory mediastinoscopy after negative endosonography, mainly in patients with a radiologically abnormal mediastinum. Only one quarter of respondents felt a confirmatory mediastinoscopy was

necessary in certain patients with a radiologically normal mediastinum. Central tumor, cN1 and tumor >3 cm were the most reported indications for confirmatory mediastinoscopy in patients with a radiologically normal mediastinum. Again, these findings highlight the insufficient knowledge of current evidence amongst interventional bronchoscopists.

Half of the respondents reported performing endoscopic procedures under GA. The most frequently cited reason for this practice was that it “allows a better staging.” Casal et al. [15] have previously published a randomized controlled trial demonstrating no difference in diagnostic yield, major complication rate and tolerance between EBUS-transbronchial needle aspiration performed under GA or CS, but this study did not focus on staging procedures which can be longer and more complex than diagnostic procedures.

Differences were also noted between answers of bronchoscopists who trained through a fellowship program and those who trained through self-learning methods. Bronchoscopists who trained through a fellowship program were more likely to perform a systematic endoscopic staging procedure. An interesting finding is that only 40% of respondents who learned through a fellowship program recommended a confirmatory mediastinoscopy after a negative EBUS mediastinal staging while 58% of respondents who learned through SL did. This may reflect a lower degree of confidence in the quality of the mediastinal staging performed in respondents who learned through SL. Rates of mediastinal staging indications consistent with current guidelines were higher in respondents who learned through a fellowship program but remained low. We expected training through a fellowship to be associated with a more significant difference in practice pattern. This may be explained by the heterogeneity among fellowship programs. Fellowship programs are only accredited by a national association with well-defined objectives and procedural requirements with a board examination after completion in the USA to our knowledge.

This survey also demonstrates differences between European and North American respondents. European respondents were more experienced as physicians but less experienced with endoscopic mediastinal staging techniques which may reflect that they learned these techniques while they were already in practice. They also learned these techniques through SL more frequently than North Americans, consequently the above comparisons between bronchoscopists who trained through a fellowship versus self-learning apply when evaluating differences

between European and North American respondents. More North American respondents felt EBUS alone was the procedure with the best negative predictive value while European respondents favored CEP and videome-diastinoscopy.

One of the limitations of this survey is the limited and nonrandom sample. Only a minority of members of the different associations responded to our survey. Certain areas of the world are not well represented such as Asia despite representation in the World Association for Bronchology and Interventional Pulmonology, perhaps due to language barriers in completing an English language survey. Certain countries also carry a disproportionate weight such as France amongst Europe (26/84, 31.3%) and Canada amongst NA (19/52, 36.5%). Thus, the results presented should not be generalized to Europe or NA and are presented as “European respondents” or “North American respondents.” It is also

important to note that most respondents work at academic centers hence we may not obtain an accurate picture of mediastinal staging practices in all types of practices, although we can speculate that our main finding of guideline discordant mediastinal staging practices would have been more pronounced in nonacademic environments.

## Conclusion

This international survey reports several areas of divergence between practice guidelines and current practices reported by interventional bronchoscopists. There is a need to standardize training through fellowship programs and certification exams to ensure interventional bronchoscopists possess adequate knowledge and technical skills prior to entering practice.

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