



Mediastinal staging by thoracic surgeons: are we close to a paradigm shift?

Aimée J. P. M. Franssen^{1^}, Juliette H. R. J. Degens^{2^}, Jean H. T. Daemen^{1^}, Iris E. W. G. Laven^{1^}, Karel W. E. Hulsewé^{1^}, Yvonne L. J. Vissers^{1^}, Erik R. de Loos^{1^}

¹Division of General Thoracic Surgery, Department of Surgery, Zuyderland Medical Center, Heerlen, The Netherlands; ²Department of Respiratory Medicine, Zuyderland Medical Center, Heerlen, The Netherlands

Correspondence to: Erik R. de Loos, MD, PhD. Division of General Thoracic Surgery, Department of Surgery, Zuyderland Medical Center, Henri Dunantstraat 5, 6419 Heerlen, The Netherlands. Email: e.delooos@zuyderland.nl

Comment on: Wiesel O, Kaufman D, Caplan-Shaw C, *et al.* Perspective and practice patterns of mediastinal staging among thoracic surgeons. *J Thorac Dis* 2022;14:3727-36.

Keywords: Mediastinal staging; endobronchial ultrasonography (EBUS); mediastinoscopy

Submitted Oct 11, 2022. Accepted for publication Dec 05, 2022. Published online Jan 06 2023.

doi: 10.21037/jtd-22-1420

View this article at: <https://dx.doi.org/10.21037/jtd-22-1420>

Mediastinal lymph node assessment plays a pivotal role in staging patients with potentially resectable non-small cell lung cancer (NSCLC). Current American (1) and European (2) clinical practice guidelines for preoperative mediastinal lymph node staging recommend minimally invasive procedures, such as endobronchial ultrasonography (EBUS) and endoscopic ultrasonography (EUS), as the method of choice. If E(B)US is negative, but with suspected N2 disease on positron emission tomography/computed tomography (PET/CT), confirmatory surgical video-assisted mediastinoscopy or video-assisted mediastinoscopic lymphadenectomy (VAMLA) is advised. While multiple reports exist on the use and diagnostic accuracy of E(B)US compared to mediastinoscopy as the gold standard (3-5), limited data is available on training and experience of both techniques by thoracic surgeons.

The article by Wiesel *et al.* (6), published in this issue, reports training and practice trends of EBUS and mediastinoscopy among thoracic surgeons in the United States. The authors also aimed to determine whether there is a paradigm shift in mediastinal staging after the introduction of EBUS. While 87% of 97 responding

thoracic surgeons received training in EBUS, either during their residency/fellowship or practice years, only 69% of the thoracic surgeons who were trained in EBUS actually perform EBUS in their current practice. Of those who perform EBUS in their current practice, 84% reported to perform mediastinoscopy less frequently since EBUS has become available as a good alternative in the early 2000's. Furthermore, 48% of the responding thoracic surgeons prefer EBUS over mediastinoscopy, with most of these surgeons (78%) stating that EBUS is safer than mediastinoscopy. Regardless of preference, it must be recognized that in clinical practice, indications for invasive mediastinal staging vary according to clinical stage as determined by PET/CT. Furthermore, the choice between endoscopic staging or surgical staging often also depends on local expertise.

Strikingly, only 22% of the responding thoracic surgeons performs EUS in their daily practice, as reported by Wiesel and colleagues (6). This suggests that complete (systematic) preoperative mediastinal staging, including paraoesophageal and inferior ligament nodes, is rarely performed by thoracic surgeons. Furthermore, it is worth

[^] ORCID: Aimée J. P. M. Franssen, 0000-0001-6399-1663; Juliette H. R. J. Degens, 0000-0003-0279-9656; Jean H. T. Daemen, 0000-0002-4878-3951; Iris E. W. G. Laven, 0000-0001-8976-5293; Karel W. E. Hulsewé, 0000-0001-8131-1895; Yvonne L. J. Vissers, 0000-0002-2890-8390; Erik R. de Loos, 0000-0001-6313-2658.

noticing that the survey by Wiesel and colleagues (6) did not include any data on VAMLA or transcervical extended mediastinal lymphadenectomy (TEMLA), where complete resection of targeted mediastinal nodes with surrounding adipose tissue is achieved. Compared to nodal biopsy with EBUS and mediastinoscopy, accuracy of both VAMLA (7) and TEMLA (8) are higher, although at the cost of higher morbidity and mortality rates.

An interesting finding by Wiesel *et al.* (6) was that all responding thoracic surgeons believe that EBUS should be formally incorporated into (cardio-)thoracic surgery training, and 89% feels that less exposure to EBUS during their training program could negatively affect the future of (cardio-)thoracic surgery trainees. Thoracic surgeons with EBUS training who prefer mediastinoscopy or do not perform EBUS at all have stated that EBUS is primarily performed by pulmonologists at their institution. Indeed, the upcoming of interventional pulmonologists and the emergence of EBUS has been shown to reduce the need for surgical lymph node/lung biopsies performed by thoracic surgeons (4). Hence, it's not unusual for thoracic surgeons to also gain experience and proficiency in interventional bronchoscopies, considering their extensive knowledge of the mediastinum through operative experience. Even so, when thoracic surgeons are proficient in both EBUS and mediastinoscopy, they can increase multidisciplinary team discussions on which procedure to use best per patient.

Integrating intraoperative EBUS with frozen-section analysis (9) or molecular detection techniques such as rapid-on-site evaluation (ROSE) (10) and one-step nucleic acid amplification (OSNA) (11) enables intraoperative surgical decision-making. ROSE and OSNA are not only considered superior to histopathological approaches for the detection of micrometastases (12), more importantly, patients do not need to undergo multiple separate staging procedures if applied intraoperatively. Unfortunately, these techniques are only available in a small number of diagnostic centers and is therefore not widely applicable for the whole patient population where mediastinal staging is required. As Wiesel and colleagues (6) pointed out rightly, same setting diagnosis and treatment could become routine in the modern-day toolbox of a thoracic surgeon. However, with an alarming decreasing number of fellowship applications under thoracic surgeons in the last 10 years and a growing population in the United States, resulting in a higher workload for surgeons (13), one could argue if EBUS expertise of both thoracic surgeons and intervention pulmonologists is necessary or even desirable.

Even though guidelines recommend invasive mediastinal staging upon abnormal PET/CT to determine whether patients are not denied a potentially curative resection, it is still debated whether N2 disease is an argument against surgery. Over the years, immunotherapy has taken the field of oncology by storm. While several hurdles remain to be overcome to be applied in a broad patient population, neoadjuvant immunotherapy has readily demonstrated to have a potent pathological response on the primary tumor, especially in combination with neoadjuvant chemotherapy (14-16). A recent study has also shown a good pathological response rate in metastatic lymph nodes, potentially leading to nodal downstaging (17). Indeed, it has been suggested that a multimodality treatment may be reasonably offered to selected NSCLC patients with N2 disease in whom a radical anatomic and lymph node dissection may be anticipated (18). Considering this, one could wonder whether pathological (re-)staging of N2 disease will continue to play a pivotal role in determining treatment options, and whether (re-)staging could rely on only PET/CT. Consequently, a future paradigm shift on N2 nodal staging is perhaps waiting for us.

Overall, the study by Wiesel *et al.* (6) has shed interesting light on whether EBUS could be relevant to thoracic surgeons and the authors are to be commended for bringing this issue to everyone's attention. Whether their argument, that EBUS training should be incorporated into all thoracic training programs in addition to mediastinoscopy, holds true for each country or region is open to debate. It may be more important that every thoracic center features the full array of mediastinal staging techniques, regardless by which type of physician, surgeon or interventional pulmonologist, the procedure is performed. Furthermore, with the technical evolution over the past decades one cannot overcome integration between different specialties.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Journal of Thoracic Disease*. The article did not undergo external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-22-1420/coif>). ERdL reports

consulting fees from Johnson & Johnson for training in uniportal VATS lobectomy. YLJV reports consulting fees for training in uniportal VATS lobectomy, honorarium for teaching lectures in thoracic oncology, and payments for testimony on reducing complication in lung surgery from Johnson & Johnson; payments for testimony on the use of OSNA in breast surgery from Sysmex. YLJV is a board member of the Dutch Society for Lung Surgery. KWEH reports consulting fees from Johnson & Johnson for training in uniportal VATS lobectomy. KWEH is a board member of Dutch Federation of Medical Specialists. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

1. Silvestri GA, Gonzalez AV, Jantz MA, et al. Methods for staging non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2013;143:e211S-50S.
2. De Leyn P, Dooms C, Kuzdzal J, et al. Revised ESTS guidelines for preoperative mediastinal lymph node staging for non-small-cell lung cancer. *Eur J Cardiothorac Surg* 2014;45:787-98.
3. Annema JT, De Leyn P, Clementsen P, et al. Mediastinoscopy after negative endoscopic mediastinal nodal staging: can it be omitted? *Eur Respir J* 2015;46:1848-9.
4. Jackson A, Griffiths P, Waqar A, et al. P76 The rise of EBUS: the fall of mediastinoscopy? *Thorax* 2018;73:A142-3.
5. Agrawal A, Murgu S. EBUS vs. Mediastinoscopy for Initial Pathologic Mediastinal Staging in NSCLC. In: Ferguson MK, editor. *Difficult Decisions in Thoracic Surgery*. *Difficult Decisions in Thoracic Surgery: An Evidence-Based Approach*. Cham: Springer International Publishing, 2020:67-81.
6. Wiesel O, Kaufman D, Caplan-Shaw C, et al. Perspective and practice patterns of mediastinal staging among thoracic surgeons. *J Thorac Dis* 2022;14:3727-36.
7. Lozekoot PWJ, Daemen JHT, van den Broek RR, et al. Surgical mediastinal lymph node staging for non-small-cell lung carcinoma. *Transl Lung Cancer Res* 2021;10:3645-58.
8. Zielinski M, Szlubowski A, Kołodziej M, et al. Comparison of endobronchial ultrasound and/or endoesophageal ultrasound with transcervical extended mediastinal lymphadenectomy for staging and restaging of non-small-cell lung cancer. *J Thorac Oncol* 2013;8:630-6.
9. Li W, Yang XN, Liao RQ, et al. Intraoperative frozen sections of the regional lymph nodes contribute to surgical decision-making in non-small cell lung cancer patients. *J Thorac Dis* 2016;8:1974-80.
10. Chen YY, Huang HY, Lin CY, et al. High SUVmax Is an Independent Predictor of Higher Diagnostic Accuracy of ROSE in EBUS-TBNA for Patients with NSCLC. *J Pers Med* 2022;12:451.
11. Namba K, Suzawa K, Shien K, et al. One-step nucleic acid amplification for intraoperative diagnosis of lymph node metastasis in lung cancer patients: a single-center prospective study. *Sci Rep* 2022;12:7297.
12. Vodicka J, Mukensnabl P, Vejvodova S, et al. A more sensitive detection of micrometastases of NSCLC in lymph nodes using the one-step nucleic acid amplification (OSNA) method. *J Surg Oncol* 2018;117:163-70.
13. Williams TE Jr, Sun B, Ross P Jr, et al. A formidable task: Population analysis predicts a deficit of 2000 cardiothoracic surgeons by 2030. *J Thorac Cardiovasc Surg* 2010;139:835-40; discussion 840-1.
14. Shu CA, Gainor JF, Awad MM, et al. Neoadjuvant atezolizumab and chemotherapy in patients with resectable non-small-cell lung cancer: an open-label, multicentre, single-arm, phase 2 trial. *Lancet Oncol* 2020;21:786-95.
15. Rothschild SI, Zippelius A, Eboulet EI, et al. SAKK 16/14: Durvalumab in Addition to Neoadjuvant Chemotherapy in Patients With Stage IIIA(N2) Non-Small-Cell Lung Cancer-A Multicenter Single-Arm Phase II Trial. *J Clin Oncol* 2021;39:2872-80.
16. Forde PM, Spicer J, Lu S, et al. Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer. *N Engl J*

- Med 2022;386:1973-85.
17. Zhai WY, Zhao ZR, Chen S, et al. Response of primary tumor and lymph node in non-small cell lung cancer after neoadjuvant immunotherapy: a pooled analysis. *J Immunother Cancer* 2022;10:e005160.
 18. Massard G, Renaud S, Reeb J, et al. N2-IIIa non-small cell lung cancer: a plea for surgery! *J Thorac Dis* 2016;8:S849-54.

Cite this article as: Franssen AJPM, Degens JHRJ, Daemen JHT, Laven IEWG, Hulsewé KWE, Vissers YLJ, de Loos ER. Mediastinal staging by thoracic surgeons: are we close to a paradigm shift? *J Thorac Dis* 2023;15(1):10-13. doi: 10.21037/jtd-22-1420