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Mediastinoscopy after negative endoscopic mediastinal nodal staging: can it be omitted?



To the Editor:

We read with great interest the study by VILMANN *et al.* [1], proposing new guidelines for diagnosis and staging of lung cancer, particularly discussing the role of combined endobronchial ultrasound (EBUS) and endoscopic oesophageal ultrasound (EUS) in mediastinal nodal staging. We have several comments on this paper.

Various other guidelines have recently already been published on this matter, from the American College of Chest Physicians (ACCP) in 2013 [2] and the European Society of Thoracic Surgeons (ESTS) in 2014 [3]. When comparing these three guidelines, specifically on invasive mediastinal nodal staging, notable differences are few. However, it is interesting to see the fluctuating role of mediastinoscopy after negative endoscopic staging through EBUS and/or EUS. The ESTS guidelines have stated that mediastinoscopy is indicated after negative endoscopic staging. Then again, mediastinoscopy has a much more optional character in the ACCP guidelines [2], emphasising the thoroughness with which the procedure is performed rather than which test is used. It would seem that, the fewer surgeons are involved in the development of the guideline, the more non-committal mediastinoscopy becomes in the diagnostic algorithm of the mediastinum. In the new guidelines by VILMANN *et al.* [1], a combined effort between surgeons, respiratory physicians and endoscopists, mediastinoscopy after negative endoscopic staging is

recommended when imaging studies demonstrate abnormal mediastinal/hilar nodes, and can be considered when imaging studies show no mediastinal involvement. Only for mediastinal nodal restaging, mediastinoscopy is said to be indicated after negative endoscopic staging [1].

All can agree that the combination of endoscopic and surgical techniques results in the highest accuracy of mediastinal nodal staging [3]. Therefore, we are surprised to notice this trend of omitting mediastinoscopy in the recent guidelines [1, 2] in favour of performing endoscopic staging alone. Is mediastinoscopy such a feared procedure that should be avoided at all costs? VILMANN *et al.* [1] stated that mediastinoscopy is associated with morbidity and significant costs. However, in a contemporary series with 1970 patients undergoing mediastinoscopy [4], mortality and recurrent laryngeal nerve injury was 0%, and bleeding complications requiring sternotomy 0.1%. Additionally, most procedures can be performed in an outpatient setting in 20 min, sampling three nodal stations medianly. These numbers underscore the safety of the procedure, rivalling data from endoscopic techniques.

However, the surgical community also acknowledges the value of endoscopic staging of the mediastinum, certainly as the first-line invasive diagnostic tool. Moreover, EUS has the ability to access station 8 and 9 [1], unreachable by mediastinoscopy and EBUS. Even the surgical guidelines by the ESTS consider the omission of mediastinoscopy after a negative EBUS/EUS, but only if the number of nodes explored and the number of needle passes in each node meet the established requirements [3]. In this regard, we find it appropriate that VILMANN *et al.* [1] have stated that “complete mediastinal staging” by endoscopic techniques should include the sampling of at least three mediastinal nodal stations, similar to the requirements set by the ESTS [3]. As shown in a recent multicentre study, false-negative results after EBUS was 2.4% when sampling of at least three mediastinal stations were performed, but rose to 15% when two or fewer were sampled [5]. However, VILMANN *et al.* [1] do not offer further quality definitions or recommendations regarding specimen acquisition and handling techniques [6] like a minimal number of aspirations per target lymph node station, or the use of rapid on-site cytology evaluation. Furthermore, learning curves of individual practitioners show substantial variability, affecting diagnostic yield [1]. With varying operator experiences and differing clinical practices, the wide range of FN results reported after endoscopic staging is not unexpected. Reported FN rates range from 2–15% for EBUS, 1–20% for EUS and 0–13% for EBUS/EUS combined [7]. We expect the real-world practice to be even more variable. Then again, completeness of mediastinoscopy in daily practice may be similarly inconsistent, meeting guideline standards in only 40% [8]. Therefore, we would like to emphasise the need for continued outcomes-based measures of quality, individually and institutionally, reviewing the negative predictive value and diagnostic accuracy of EBUS/EUS procedures and preoperative mediastinal nodal staging in general on a regularly basis. In our own institution, we found 8.8 mediastinoscopies have to be performed to prevent one futile thoracotomy after negative endoscopic staging [9], a number which is lowered to 6.1 when patients have suspicious mediastinal lymph nodes on fluorodeoxyglucose-positron emission tomography. Specifically for cN1-patients, 10 mediastinoscopies are needed to detect one false-negative N2 on endosonography [10]. As such, in our centre, all patients will undergo mediastinoscopy after negative endoscopic staging.

The question remains whether endoscopic techniques like EBUS and EUS are meant to substitute the place of mediastinoscopy in the algorithm for mediastinal staging in lung cancer patients, or whether these techniques are complementary to each other. We believe firmly in the last.



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Mediastinoscopy should not be omitted after negative EBUS/EUS <http://ow.ly/T4Qap>

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From the authors:

We read with interest the comments of Li and colleagues on the need for a routine mediastinoscopy following a nodal negative endosonographic mediastinal evaluation. This topic is frequently a subject of discussion in multidisciplinary lung cancer teams and therefore deserves full attention.

Accurate mediastinal nodal staging is required to provide patients with the optimal treatment. Roughly speaking, about half the patients that are referred for an endosonographic mediastinal evaluation have metastatic nodal involvement. Both endobronchial ultrasound (EBUS) and endoscopic oesophageal ultrasound (EUS) are excellent techniques in confirming metastases, but have limitations in excluding them. Routine performance of mediastinoscopy in all patients that are staged negative by EBUS/EUS confirms endosonography findings in the vast majority of cases. In both the study by VERHAGEN *et al.* [1] and the ASTER study [2], mediastinoscopy did not provide any benefit in eight out of nine patients. The drawbacks for these patients are obvious: a delay in the diagnostic workup and start of treatment, performance of unnecessary surgery and anaesthesia, and use of scarce healthcare resources.

For the optimal use of subsequent surgical staging, the key question is to identify predictors for false negative EBUS/EUS outcomes. They could be related to specific imaging findings (nodal size, 2-fluoro-2-deoxy-D-glucose positron emission tomography uptake or specific sonographic characteristics) and tumour histology. Another approach is to assess the thoroughness of the endosonographic evaluation: performance of EBUS alone *versus* the EBUS–EUS combination, systematic nodal evaluation of the mediastinum *versus* the “hit and run” approach, the number of nodal stations sampled and adequacy of nodal tissue obtained. Currently, more data are urgently needed to shed light on this issue in order to create a predictive model for false negative EBUS/EUS findings [4].

The European Society of Gastrointestinal Endoscopy/European Respiratory Society/European Society of Thoracic Surgeons guideline on combined EBUS–EUS lung cancer staging [3] provides room for the local tumour board to proceed directly to thoracoscopy (video-assisted thoracic surgery) or thoracotomy following a tumour negative endosonography, and omit a confirmatory mediastinoscopy. This is only allowed after careful consideration and in combination with meticulous monitoring and evaluation of endosonography outcomes. On this point we fully agree with Li and colleagues.

It should be clear that in the opinion of the guideline authors, endosonographic needle-based techniques are complementary to surgical staging and are not completely substituting it. However, mediastinoscopy should preferably be performed only in those patients with a high risk of false negative EBUS/EUS results as routine performance results in too many unnecessary surgical staging procedures. Identification of predictors of false negative EBUS/EUS outcomes is therefore important, and this is exactly the research topic on which both pulmonologists and surgeons should focus.



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NSCLC staging: mediastinoscopy can be omitted in selected cases following a nodal negative EBUS/EUS examination <http://ow.ly/TKKkf>

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