4 Wei B, Bryant AS, Minnich DJ, *et al.* The safety and efficacy of mediastinoscopy when performed by general thoracic surgeons. *Ann Thorac Surg* 2014; 97: 1878–1883.
5 Sanz-Santos J, Serra M, Gallego M, *et al.* Determinants of false-negative results in non-small-cell lung cancer staging by endobronchial ultrasound-guided needle aspiration. *Eur J Cardiothorac Surg* 2015; 47: 642–647.
6 van der Heijden EH, Casal RF, Trisolini R, *et al.* Guideline for the acquisition and preparation of conventional and endobronchial ultrasound-guided transbronchial needle aspiration specimens for the diagnosis and molecular testing of patients with known or suspected lung cancer. *Respiration* 2014; 88: 500–517.
7 Zhang R, Ying K, Shi L, *et al.* Combined endobronchial and endoscopic ultrasound-guided fine needle aspiration for mediastinal lymph node staging of lung cancer: a meta-analysis. *Eur J Cancer* 2013; 49: 1860–1867.
8 Smulders SA, Smeenk FW, Janssen-Heijnen ML, *et al.* Surgical mediastinal staging in daily practice. *Lung Cancer* 2005; 47: 243–251.
9 Verhagen AF, Schuurbiers OC, Looijen-Salamon MG, *et al.* Mediastinal staging in daily practice: endosonography, followed by cervical mediastinoscopy. Do we really need both? *Interact Cardiovasc Thorac Surg* 2013; 17: 823–828.
10 Dooms C, Tournoy KG, Schuurbiers O, *et al.* Endosonography for mediastinal nodal staging of clinical N1 non-small cell lung cancer: a prospective multicenter study. *Chest* 2015; 147: 209–215.

Eur Respir J 2015; 46: 1846–1848 | DOI: 10.1183/13993003.01166-2015 | Copyright ©ERS 2015

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 recourses.

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.

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

Jouke T. Annema[1], Paul De Leyn[2], Paul Clementsen[3], Mette Siemsen[4] and Peter Vilmann[5]
[1]Academic Medical Center Amsterdam, Dept of Respiratory Medicine, Amsterdam, The Netherlands. [2]Thoracic Surgery, University Hospital Gasthuisberg, Leuven, Belgium. [3]Dept of Pulmonology, Gentofte Hospital, University of Copenhagen, Copenhagen, Denmark. [4]Thoracic Surgery, Copenhagen, Denmark. [5]Hospital Herlev, Copenhagen University, Copenhagen, Denmark.

Correspondence: Jouke T. Annema, Academic Medical Center Amsterdam, Dept of Respiratory Medicine, Meibergdreef 9, P.O. Box 22660, 1100 DD Amsterdam, The Netherlands. E-mail: j.t.annema@amc.nl

Received: Sept 03 2015 | Accepted: Sept 26 2015

Conflict of interest: Disclosures can be found alongside the online version of this article at erj.ersjournals.com

References

1 Verhagen AF, Schuurbiers OC, Looijen-Salamon MG, *et al.* Mediastinal staging in daily practice: endosonography, followed by cervical mediastinoscopy. Do we really need both? *Interact Cardiovasc Thorac Surg* 2013; 17: 823–828.
2 Annema JT, van Meerbeeck JP, Rintoul RC, *et al.* Mediastinoscopy *vs* endosonography for mediastinal nodal staging of lung cancer: a randomized trial. *JAMA* 2010; 304: 2245–2252.
3 Vilmann P, Clementsen PF, Colella S, *et al.* Combined endobronchial and oesophageal endosonography for the diagnosis and staging of lung cancer. *Eur Respir J* 2015; 46: 40–60.
4 Talebian Yazdi M, Egberts J, Schinkelshoek MS, *et al.* Endosonography for lung cancer staging: predictors for false-negative outcomes. *Lung Cancer* 2015 [in press; DOI: 10.1016/j.lungcan.2015.09.020].

Eur Respir J 2015; 46: 1848–1849 | DOI: 10.1183/13993003.01472-2015

Pulmonary arterial hypertension in patients treated with interferon

To the Editor:

We read with interest the article by Savale *et al.* [1] reporting pulmonary arterial hypertension (PAH) associated with treatment with interferon (IFN) in 53 patients from the French PAH registry. As noted by the authors, patients receiving IFN-α have confounding factors such as portal hypertension or HIV infection that may classify them in group 1.4.3 or 1.4.2, respectively, according to the 2013 updated pulmonary hypertension classification [2]. Therefore, "pure" cases, such as those treated with IFN-β for multiple sclerosis are important to identify in order to strengthen the causal relationship between the suspected drug and PAH.

We briefly report here the case of a 72 year-old woman who was diagnosed with multiple sclerosis back in 1992. Starting from 1999, she was treated regularly with IFN-β subcutaneously every other day (Bayer AG, Zurich, Switzerland) without significant interruption. Additional diagnoses included cigarette-induced chronic obstructive pulmonary disease (COPD) with a post-bronchodilator forced expiratory volume in 1 s of 79% predicted, together with a type 2 diabetes mellitus. During the previous 2 weeks her dyspnoea had rapidly increased from New York Heart Association (NYHA) class 2 to 4 and she was admitted to the intensive care unit (ICU) with mild hypoxaemia (arterial oxygen tension of 59 mmHg) and clinical signs of right heart failure. A transthoracic echocardiography revealed a dilated right ventricle with severe systolic dysfunction (tricuspid annular plane systolic excursion (TAPSE)=11 mm), a small pericardial effusion (4 mm) along the right cavities, and a three-quarters tricuspid regurgitation with maximal jet velocity of 3.77 $m \cdot s^{-1}$ (maximal right ventricular/right atrial gradient of 57 mmHg). There was a D-shape deformation of the interventricular septum but the left ventricular systolic function was otherwise normal. Haemodynamic measurements collected at the ICU confirmed a precapillary pulmonary hypertension with a pulmonary pressure of 72/34–48 mmHg (systolic/diastolic–mean) and a pulmonary wedge pressure of 13 mmHg (table 1). The cardiac index was measured at 2.3 $L \cdot min^{-1} \cdot m^{-2}$, and the pulmonary resistance was calculated at 14.5 Wood Units. No vasoreactivity was observed after inhalation of 20 ppm nitrous oxide. A ventilation/perfusion ratio (V'/Q') scan and a computed tomography (CT) scan angiography ruled out thromboembolic disease and lung interstitial disorder. Emphysematous alteration of the lung parenchyma was minimal. In the work up for PAH group 1, HIV serology returned negative, there was no clinical or biological sign for liver cirrhosis or connective tissue disorder, and the history for familial PAH was negative. The severity score according to the REVEAL registry was 12 out of 22, corresponding to a very high risk [3]. We concluded that this patient had PAH associated with chronic intake of IFN-β (group 1.3, 2013 classification [2]) and this medication was stopped. She was treated with an upfront dual oral regimen including a phosphodiesterase-5 inhibitor (sildenafil) and an endothelin receptor antagonist (macitentan), allowing regression of the dyspnoea from NYHA class 4 to 3 after 3 weeks. Follow-up at