Adding an invasive procedure will not necessarily change treatment or outcome of NSCLC patients with preoperative clinical N1 disease

To the Editor:

We have read with great interest and welcome the publication of a prospective multicentre study regarding the role of mediastinal staging by video-assisted mediastinoscopy (VAM) in patients with clinical N1 (cN1) nonsmall cell lung cancer (NSCLC) [1]. The objective of the study was to assess the sensitivity, negative predictive value and accuracy of VAM in a well-defined group of patients with cN1.

This nonrandomised prospective study planned to recruit 250 NSCLC patients with stage cT1-3N1M0 deemed operable based on integrated fluorodeoxyglucose-positron-emission tomography/computed tomography. The surgical resection with systemic nodal dissection was the reference standard. The primary end-point was sensitivity, defined as the proportion of patients with positive mediastinal staging by VAM or VAM-lymphadenectomy (VAMLA) out of all the patients with mediastinal nodal disease.

The authors concluded that 25% of the patients within the study eventually had unsuspected N2 disease with a 73% sensitivity by VAM and proposed the procedure as a possible standard of care in this setting.

As conceived by the authors, there are several limitations in this study, two particularly important and worth mentioning further. The first regards the slow and inadequate recruitment leading to only 105 patients being enrolled into the study instead of the pre-planned 250 patients. The second point is the fact that in nearly one-third (31%) of cases the nodal dissection was performed by VAMLA and not only by VAM. Although similar, the two procedures are different: during VAMLA a systematic lymphadenectomy is performed bi-manually through the video mediastinoscope and the number of lymph nodes removed is doubled compared to standard mediastinoscopy [2].

Although these two issues do not allow us to conclude that VAM(LA) could be a new standard in cN1 NSCLC patients, another point regards the real implication of routinely performing VAM(LA) in this setting. Even if this is recommended within the guidelines of the European Society of Thoracic Surgeons [3], the level of evidence is certainly not that strong (level IIB) and unlikely to change the outcome or treatment of such patients. There is also evidence that patients with unsuspected N2 disease have a better overall survival than those with standard N2 nodal disease [4] and that those with single-station N2 involvement have similar overall survival than those with multiple N1 disease, as established recently [5].

In conclusion, we should certainly praise the authors for making such an effort to design and conduct a multicentre prospective study; however, we believe that there is not adequate evidence to justify VAM(LA) as a standard tool to adopt in all cN1 NSCLC patients preoperatively.

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From the authors:

We would like to thank A. Addeo and G. Banna for their correspondence with comments on our article entitled "Mediastinal staging by videomediastinoscopy in clinical N1 non-small cell lung cancer: a prospective multicentre study" [1]. In this prospective multicentre study, we found a 25% rate of unforeseen N2 disease after staging and resection, confirming the result of a previous prospective study, similar in size and design, investigating the performance of endosonography in the mediastinal staging of clinical N1 (cN1) patients [2]. However, the sensitivity and negative predictive value of videomediastinoscopy *versus* endosonography was 0.73 (95% CI 0.54–0.86) *versus* 0.38 (95% CI 0.18–0.57) and 0.92 (95% CI 0.83–0.97) *versus* 0.81 (95% CI 0.71–0.91), respectively. We acknowledge the lower accrual than initially projected, which resulted in wider width of confidence interval than aimed for. Nonetheless, with these results we argue that videomediastinoscopy could be the preferred technique of invasive mediastinal staging in patients with cN1 disease, outperforming endosonography in this patient group.

Whether invasive staging should be performed at all in patients with cN1 disease is a different point of discussion that was not part of this study. Correct staging prior to the start of therapy is not only responsible for an apparent better survival due to stage migration, but also leads to diverse surgical and non-surgical treatment strategies in individual patients, and is of paramount importance for comparative purposes. Furthermore, invasive staging in patients with cN1 is indeed recommended by the current guidelines of the European Society of Thoracic Surgeons and the European Society for Medical Oncology [3, 4].

We acknowledge that one third of the videomediastinoscopy procedures were video-assisted mediastinoscopic lymphadenectomies (VAMLA), although not all authors use a bi-manual instrumentation as suggested in the correspondence by A. Addeo and G. Banna. We want to stress to the readers that videomediastinoscopy and VAMLA are performed through the same small incision with similar instruments. While VAMLA goes beyond a pure diagnostic procedure and might be a first step in a complete lymphadenectomy, VAMLA should not be confused with transcervical extended mediastinal lymphadenectomy (TEMLA), which is performed through a cervical incision of 5–8 cm and includes elevation of the sternal manubrium and complete mediastinal lymphadenectomy except for stations 9 and most distal 4L [5]. In our study, the VAMLA results showed no false negatives and no complications [1]. The numbers were too small to compare standard videomediastinoscopy with VAMLA, but in our opinion a pre-resection VAMLA can help to perform a complete mediastinal lymphadenectomy in these cN1 patients with clearly significant clinical risk of mediastinal nodal disease.

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