Editor's note:

In the era of personalized medicine, a critical appraisal new developments and controversies are essential in order to derived tailored approaches. In addition to its educative aspect, we expect these discussions to help younger researchers to refine their own research strategies.

Controversies on Lung Cancer: Pros and Cons

Rebuttal from Dr. Obiols and Dr. Call

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First of all, we would like to congratulate Dr. Decaluwé and Dr. Dooms for their rigorous revision on this topic. As they have commented in their manuscript, following the recommendations of the European Society of Thoracic Surgeons (ESTS) guidelines for preoperative mediastinal nodal staging, high negative predictive values (91–95%) and low rates of unsuspected pathologic (p) N2 disease (5.1-5.5%) are achieved (1,2). The majority of patients with unsuspected pN2 have single station involvement and better survival compared with the global cohort of pN2 (2). In cIA tumours, neither endoscopic techniques nor mediastinoscopy have shown enough accuracy to certify mediastinal involvement (3,4). Therefore, these findings suggest that invasive mediastinal staging can be omitted in cIA tumours. The clinical TNM classification is based on anatomical characteristics of the tumour that are initially defined by imaging techniques. The heterogeneity of tumours included in cIA is high because several histological types and different patient's clinical parameters are included. Then, although the number of cases needed to treat in cIA to obtain a benefit from invasive staging is too high, some subgroups with an increased risk may benefit. As we commented in our previous manuscript, some authors have detected that, in cIA tumours, the combination of tumour characteristics (histological type, consolidation/tumour ratio, tumour size, SUVmax value) and other clinical parameters (serum CEA level, patient's age) have an increased risk of mediastinal involvement

(33.8%) (5,6). For this reason, invasive mediastinal staging should have a role in patients with one or a combination of the above-mentioned parameters. In these situations, invasive mediastinal staging would be omitted if only TNM classification were taken into consideration.

In agreement with Decaluwé and Dooms, videoassisted mediastinoscopic lymphadenectomy (VAMLA) in cIA tumours offers a high diagnostic accuracy to detect mediastinal nodal involvement that can not be achieved by endoscopic techniques or standard mediastinoscopy. Moreover, the main indication of VAMLA is in those cases without clinical evidence of mediastinal disease. However, to date, when this procedure detects unsuspected N2 disease, induction treatment is the accepted therapy. Regarding the role of VAMLA to select those patients with a better prognosis N2 disease (such as single station, no extracapsular involvement...) who could potentially benefit from primary surgery, prospective well-designed studies are needed.

In addition, in left sided tumours, VAMLA allows a more radical lymphadenectomy because it includes the resection of the nodes from the left inferior paratracheal station, which can not be reached at the time of pulmonary resection. The recent publication on VAMLA by Call *et al.* (7) shows that among 26 patients with mediastinal involvement diagnosed by VAMLA, 10 had left sided tumours and 40% of them had involvement of left inferior paratracheal nodes, information that would have been

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missed if VAMLA had not been performed.

In summary, the rigorous application of the ESTS guidelines on preoperative mediastinal staging achieves a low rate of unsuspected pN2 disease. In cIA tumours, the current indications to perform an invasive mediastinal staging are limited. However, the combination of tumour characteristics and clinical parameters define a subgroup of patients with an increased risk of mediastinal nodal involvement in whom an invasive mediastinal staging should be performed.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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