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INVITED COMMENTARY

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Lung cancer: is it node number or node station? Pardon me, but what is the question?

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The title's choice refers to Dr F.C. Detterbeck's editorial to Saji *et al.* back in 2013 [1, 2] in which both the number of involved lymph node and their location were analysed for their prognostic value in patients with surgically completely resected NSCLC.

Whereas the current guidelines (IASLC, European Society of Thoracic Surgeons, American Joint Committee on Cancer and Union for International Cancer Control) [3–5] recommend that at least 3 mediastinal LN stations, including station 7, be sampled (or dissected) for surgically resected NSCLC, Kamigaichi *et al.* raised an additionnal question in their current study, as to which is the minimal (or optimal) number of mediastinal lymph node (mLN) to be analysed by the pathologist in surgically completely resected early stage (Clinical N0) NSCLC patients independently of nodal station location [6].

From a cohort of 1420 patients, the authors have demonstrated that 3 mLNs is the optimal number of mediastinal lymph nodes to be analysed, conveying a survival advantage in the pN1 subgroup, which represented only 107 patients of their cohort. The effect was neutral in cN0–pN0 and cN0–pN2 patients. Unexpectedly, the subgroup of 24 patients with cN0, but pathological N1 disease who had minimal mediastinal staging (2 mLNs or less examined) had a dismal 5-year survival of 28%, which is lower that one would have expected [7].

While the authors suggest that stage migration could be one of the potential explanations for their findings, unfortunately many other co-variables were not included in their study.

First, lymph node sampling/dissection was not evenly matched between subgroups: in the group with ≤2 mLNs examined, 81.5% was lobe specific and 18.5% systematic compared to 48.7% lobe specific and 51.3% systematic in the group with ≥3 mLNs examined. It has been shown that systematic LN sampling/dissection was superior to lobe-specific lymph node sampling/dissection in the assessment of lymph node status [8].

Second, the authors did not provide information on additional pathological details (e.g. presence of vascular permeation at the nodal site, lymph node fragmentation on the pathological specimen or if extra-capsular spread at the LN level was noticed). Finally, the information on the expression of tumour biomarkers (EGFR mutations, ALK rearrangement, KRAS mutation) was not available.

This study will add on many other reports supporting the need for comprehensive lymph node staging at the time of resection. The question will remain open. To further expand on the role of pathological examination in clinical research on NSCLC prognosis, Zhu *et al.* (on behalf of AME Lung Cancer Collaborative Group) recently reported their results on 3002 patients with resected pathological T1-T3N0M0 NSCLC, where they compared patients with at least 10 examined lymph nodes, including at least 1 station 10, 11 LN and 1 station 12, 13, 14 LN to those with who did not match the above-mentioned criteria. When they combined the 2 criteria (>1200 patients), they demonstrated a survival advantage across all T stages in the group where both station 10/11 and stations 12–13–14 lymph nodes were examined, resulting in 5-year survival rates of 83% vs 77%, respectively ($P < 0.001$) [9].

Nonetheless, Kamigaichi *et al.* have to be complimented in trying to better refine the multimodal treatment approach of patients with surgically resected NCSLC, where the knife of the pathologist becomes another important key player along with the oncologist and the surgeon!

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