

## Micrometastasis and skip metastasis as predictive factors in non-small-cell lung cancer staging

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We have read with interest the article by Anami *et al.* [1], which focused on skip micrometastasis in left lung cancer. The authors report their retrospective experience with 19 patients who underwent bilateral thoracoscopic mediastinal nodal dissection (BMD) compared with 25 unilateral dissection (UMD).

Considering that the unsatisfactory survival observed in Stage I, left-sided, non-small-cell lung cancer (NSCLC) is most likely related to a higher incidence of occult contralateral nodal involvement (N3), many authors have suggested complete clinical staging with right nodal biopsies. We routinely sample right paratracheal nodes in left upper NSCLC with mediastinoscopy since this allows us to turn the patient just once intraoperatively, avoiding the need for bilateral chest tubes. However, we congratulate the authors because there were no significant differences between the groups regardless of the bilateral approach used.

The authors have reported on two topics already separately investigated, namely micrometastases and skip metastases, although uniquely focusing on the selective population with both N3 skip nodal involvement and micrometastases.

We would like to highlight some points concerning their findings.

First, only 1 of the 19 patients was upstaged at pathological examination, but molecular studies revealed that 11 of the 19 were affected by micrometastases, determining a further upstaging. The possibility of contralateral nodal involvement has been already demonstrated, with an incidence of 21–44%, concurring with the 8 of 19 cases. However, it is remarkable that in 7, there were skip micrometastases.

This suggests that contralateral nodal involvement is rarely predicted by pN1/N2 and that its evaluation based on routine pathological investigation may lead to downstaging.

Consequently, contralateral nodal biopsies should always be performed, and in particular molecular studies encouraged, leading to the result that bilateral surgical staging and resection should always be done at two different times.

The other topic is the relevance of N3 skip metastasis to prognosis. There are contrasting opinions on the significance of N2 skip metastases on survival and no data on N3 skip micrometastases. However, it has been reported that patients staged as

pN0/N1 with micrometastases have the same survival as pN2 [2, 3] and that micrometastases strongly correlate with prognosis [4].

Patients with BMD had better overall and disease-free survival than UMD, although not statistically significant. Nevertheless, patients with skip N3 micrometastases are all alive without disease recurrence, while 5 of 25 UMD died due to cancer relapse (pTNM of this last group is not reported). This suggests that BMD correlates with a better survival and that N3 skip micrometastases do not contraindicate surgery. Unfortunately, the authors did not report if N3 skip micrometastases involved one or multiple nodes [5] and if patients underwent adjuvant chemotherapy. These limitations and the small population of the study do not allow for conclusions to be drawn, however, their data encourage better investigation of some topics. Does N3 skip micrometastases detection guarantee a more efficient pre-operative prognostic staging? Does an N3 micrometastatic finding contraindicate surgery or should nodal dissection be considered therapeutic? We congratulate the authors for this interesting paper giving the cue for further studies.

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