

4L Lymph Node Involvement in Left-Sided Lung Cancer: Unique or Not?

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See accompanying article on page [2935](#)

In the article that accompanies this editorial, Wang and colleagues¹ report on the prognostic impact of dissecting the station 4L mediastinal lymph node (LN) in left-sided lung cancer. Using propensity score weighting, two retrospective patient groups who received surgery between 2005 and 2009 were compared: one with 4L dissection (n = 139) and one without (n = 518). No chemotherapy was given, and staging with [¹⁸F]fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) scanning, brain imaging, or invasive mediastinal staging (if indicated) was not systematically performed. Therefore, the results cannot be extrapolated to centers where these procedures are common practice. The overall rate of involvement of station 4L was nearly 21%, and the 5-year overall survival (OS) and disease-free survival were significantly superior for the group that had a 4L LN dissection (disease-free survival: 54.8% v 42.7%; $P = .04$; OS: 58.9% v 47.2%; $P = .02$). The conclusion is that 4L involvement is not rare, especially when station 10L is involved, and that the station 4L LN should be systematically dissected at the time of surgery. These findings are intuitively attractive.

It should be stressed that the definition of what exactly station 4L is differs according to surgical or nonsurgical literature.² Wang et al¹ used the surgical definition in their study. Complete resection of station 4L may be technically challenging because of its anatomic relation with the aortic arch, the thoracic duct, and the recurrent nerve. Operative complications are therefore more frequent, and station 4L may not be resected adequately.³ Nevertheless, when radical surgery is being considered, a systematic LN dissection is frequently advocated.³ Given the technical challenges of performing a station 4L dissection, some have questioned whether the rate of incomplete resection is higher for 4L dissection compared with other LN stations. An indirect way to assess the rate of incomplete resections is to look at the patterns of recurrence after surgery for stage III non-small-cell lung cancer. If the rate of incomplete resection of station 4L is higher than the rates for other LN stations, it can reasonably be expected that the local recurrence rate will be higher as well. However, this has not been observed.⁴⁻⁶ The majority of local recurrences after surgery for left-sided lung cancer do not occur in station 4L; instead, they occur in stations 4R and 7. Station 4L can be resected completely with video-assisted mediastinal lymphadenectomy, which results in optimal staging and local treatment at the same time in many patients.⁷ The complete surgical removal of station 4L, as recommended in most

guidelines, is therefore feasible and appropriate.⁸ From a surgical point of view, 4L should therefore be regarded as an LN station that should be resected in left-sided lung cancers with a success rate comparable to that of other LN stations.

The question of whether removal of station 4L will lead to a survival gain is more difficult to prove. Indeed, randomized phase III trials failed to show that systematic versus lobe-specific nodal dissection had any impact on OS, although more patients were upstaged to N2 disease and therefore had an indication for adjuvant chemotherapy.^{9,10} The findings in the Wang et al¹ study, that surgical removal of station 4L might improve OS, should therefore be viewed as hypothesis generating only. As the authors note, their study is retrospective with significant known imbalances in the prognostic factors between the group treated with 4L dissection and the other group. Propensity techniques are an attempt to deal with the imbalance of confounders, but they are by no means as strong as randomization.¹¹ The reason why the majority of patients did not undergo a dissection of 4L in the same time period is unknown and adds to bias, which is difficult to correct for. In addition, pathologic TNM staging was used as confounder for the propensity weighting instead of clinical TNM, adding possible bias and suggesting incomplete preoperative staging. Conversely, not removing 4L in a left-sided cancer would not comply with current recommendations and would qualify the resection as being incomplete.¹² In these cases, postoperative radiotherapy is recommended, although improvements in local tumor control rates have been reported without a proven benefit on OS.^{13,14} Obviously, this is the case only when 4L is not FDG-avid or not enlarged on CT scan. In the case of macroscopic involvement, an attempt should be made to obtain pathology from station 4L, and postoperative chemoradiotherapy is recommended in the case of involvement and incomplete resection.

The article by Wang et al¹ thus provides us with useful data that underscore the recommendation to dissect station 4L, although the effect on OS remains unproven. In the case of nonremoval of station 4L that is not involved on FDG-PET/CT, and in the absence of 10L involvement, postoperative radiotherapy may be omitted. If 10L is involved, irradiating 4L is of uncertain value. Clear involvement of 4L qualifies for postoperative chemotherapy and radiotherapy.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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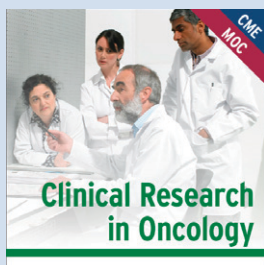
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