

# Lymph node assessment and survival: we still have work to do

Timothy Tirrell, Mark Onaitis

Department of Surgery, University of California, San Diego, CA, USA

Correspondence to: Mark Onaitis, MD. 9300 Campus Point Drive Mail Code 7892, LaJolla, CA 92037, USA. Email: monaitis@ucsd.edu.

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Thoracic surgeons generally agree that surgical resection of non-small cell lung cancer (NSCLC) should include hilar and mediastinal lymph node assessment. A quality measure of 10 or more lymph nodes have been established by the national quality forum as a target number of nodes for resection, based on work that suggested it was important for accurate staging. Adequate nodal assessment is especially important given the beneficial role for adjuvant chemotherapy in patients with nodal metastases. However, despite the consensus opinion that nodal assessment is paramount, studies have demonstrated wide variability in the number of nodes sampled (1,2) The recent paper by David and colleagues (3) confirms this variability and attempts to categorize the effects of lymph node sampling on overall and cancer-specific survival using the California Cancer Registry.

In their study, they retrospectively examined over 15,000 patients across a period of 8 years, by querying the California Cancer Registry. Disappointingly, almost 9% of patients had no lymph nodes sampled. The median number of nodes sampled was 7, and node counts ranged from 0 to greater than 12. Sublobar resections were much more likely to have no nodes sampled and more extensive resections were associated with greater node sampling. They found that in general, higher numbers of lymph nodes sampled were associated with better cancer specific and overall survival, but effects differed based on stage. For stage I NSCLC, sampling more than 10 nodes was associated with better survival than 0, 1–3 or 4–10 nodes. For stage II, sampling more than 10 was associated with better survival than 0 or 1–3 nodes, but not 4–10 nodes. For

stage III, increased survival was seen when sampling non-zero numbers of nodes, but sampling 1–3 and 4–10 nodes was not associated with improved survival over more than 10 nodes.

Strengths of this study include its large sample size and granular lymph node data. These strengths allow for well-powered analyses that make sense. In general, assessing more lymph nodes, especially in pathologically node-negative patients, is associated with improved survival due to “stage purification”. Whether removal of pathologically involved lymph nodes in patients who will receive systemic chemotherapy is additionally beneficial is unclear but makes logical sense.

However, the study also highlights work that needs to be done. First, all nodes in lung cancer are not equal, and perhaps more attention should be given to nodal stations resected rather than just numbers of nodes. Further, the study also does not allow for analysis of upstaging effects because clinical *vs.* pathological stages are not known. Frequency of upstaging may certainly be related to number of lymph nodes sampled (especially in early stage tumors) and occurs between 7–13% of the time (depending on VATS *vs.* open approach) in recent studies (4-6); thus this issue is critical to consider when determining an appropriate number of lymph nodes for sampling. Next, although the study highlights the alarming lack of lymph node assessment in sublobar resection patients, the lack of histologic detail precludes definitive conclusion. We know that lymph node assessment is much more important for a solid or micropapillary adenocarcinoma than for minimally-invasive adenocarcinoma found in a ground glass nodule (7).

In addition, surgeon specialty is not included in the analysis. Significant evidence supports improved perioperative, staging and oncologic outcomes in patients undergoing resection by a general thoracic surgical oncologist rather than a general surgeon or cardiac surgeon (8,9). It would be interesting to analyze the data controlling for this important variable. Finally, the impact of surgical approach is not analyzed. Several groups have documented decreased hilar upstaging in patients undergoing VATS resections (5,10,11), but VATS may be associated with improved long-term outcomes (12). Whether minimally-invasive resection hampers lymph node assessment in large regional databases is unanswered.

All will agree that performing as thorough a lymph node assessment as possible will improve staging and may have a direct oncologic effect in removing cancer cells. The current study adds to the literature supporting this. Importantly, increased lymph node dissection does not appear to carry associated increased mortality, so until relationship between node sampling and survival benefit is more clearly delineated, full lymph node sampling should remain a component of surgical resection of NSCLC.

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### Footnote

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

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