The IASLC Lung Cancer Staging Project: “The Nodal Zone”

Katherine M. W. Pisters, MD, and Gail Darling, MD

The paper by Rusch et al.1 represents a Herculean effort by the staging committee of the International Association for the Study of Lung Cancer (IASLC) to determine whether the current nodal descriptors for non-small cell lung cancer2 should be maintained or revised. A retrospective international lung cancer database was developed with staging and outcome data on 100,869 lung cancer cases managed between 1990 and 2000. From this, 67,725 met initial screening, 38,265 were clinically without metastases, and 28,371 had pathological staging (defined at thoracotomy). Further survival analyses in relation to pN1 and pN2 subsets could be performed on only 2876 patients.

The authors analyzed survival by anatomic location (or “zone”) of involved nodes (Table 2b), presence of skip metastases (Table 2c), and number of involved nodal stations (Table 2a and Figure 5). “Zone analysis” was done after analyses by station failed to identify significant differences. Zones were defined as peripheral (levels 12–14), hilar (levels 10 and 11), upper (levels 1–4), aortopulmonary window (levels 5 and 6), subcarinal (level 7), or lower (levels 8 and 9). Although significant differences were not seen, right-sided tumors with single-zone N1 had median survival rates of 56 to 63 months versus 34 to 37 months for single-zone N2. Left-sided tumors with single-zone peripheral involvement had a median survival of 52 months versus 40 months for hilar and 39 to 44 months for mediastinal.

Patients with left upper-lobe tumors and skip metastases (N2 involvement in the absence of N1) had improved survival (44 versus 24 months), whereas this difference was not significant for right upper-lobe primaries (37 versus 28 months). Improved survival for left upper-lobe/aortopulmonary window disease confirms previous reports and supports surgical therapy for these “better” N2 patients. Sentinel node mapping may play a role in the identification and further evaluation of “skip” metastases.

Survival analysis by number of involved lymph node zones was significant, with three separate prognostic groups emerging: patients with single-zone N1 disease, multiple-zone N1 or single-zone N2, and multiple-zone N2 (Figure 5). It is unfortunate that only 1992 cases had sufficient data for this analysis and that further exploration of these prognostic nodal groups in conjunction with T stage could not be performed. Anatomic location by zone did affect survival, with single-zone N2 faring worse than single-zone N1, although the authors did not conclude this.

Increasingly smaller T1N0M0 lung cancers are being identified by computed tomography screening, leading to the reevaluation of sublobar resection. To determine the appropriateness of sublobar resection and accurate prognostication, meticulous intraoperative staging with dissection of level 10, 11, 12, 13, and 14 nodes will be required, as eloquently demonstrated by Mr. P. Goldstraw (personal communication, Toronto Refresher course, June 2006). Previously, most surgeons did not conduct such meticulous staging; rather, they concentrated only on identifying N2 disease before proceeding with resection. More recently, adjuvant chemotherapy has been shown to improve survival in resected non-small cell lung cancer patients,3–5 and accurate lymph node staging is critical for selection of patients most likely to benefit.
Tumor, node, metastasis (TNM) staging has been the basic classification for all solid tumors for decades. The use of this system has assisted health care providers in the selection of appropriate therapies for individual patients and has defined appropriate populations for clinical research strategies. Obvious issues with the current nodal station maps are complexity (fewer than 5% of cases who met initial screening criteria had sufficient nodal labeling/sampling for the final analysis) and clinical heterogeneity within the N1, N2, and N3 categories. Appropriate selection of radiation or surgery for locally advanced patients cannot be made on the basis of the current nodal descriptors.

The IASLC staging committee has validated the current lung cancer lymph node staging descriptors and has proposed a three-tiered zone system within the current N1 and N2 patient subsets for further evaluation. The authors did not evaluate potential N3 subsets (contralateral mediastinal, unilateral, or bilateral supraclavicular zones spring to mind), nor did they address how future lung cancer databases should be constructed to facilitate collaboration and research. Reconciliation of the Naruke and ATS lymph node maps is being addressed by the IASLC staging committee and should facilitate these efforts. The use of lymph node zones as suggested in this paper may enhance data collection and analysis as a simplification over the current 14-station system.

The IASLC is to be congratulated for tackling the huge task of validating the current staging system and for embarking on future collaboration for its revision. The staging systems for lung cancer and, indeed, for all solid tumors represent a work in progress. We look forward to the day when accurate surgical and molecular staging will accurately predict prognosis.

REFERENCES