N2 is not N2 is not N2

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The management of stage IIIA-N2 non-small cell lung carcinoma (NSCLC) is likely to remain an issue of contention among thoracic surgeons in the foreseeable future. To the understanding of many, Intergroup 0139¹ established chemotherapy and radiation as the bimodal cornerstones of treatment for this disease. Surgical resection, long considered the third modality, was found to be beneficial in the subgroup of patients who required lobectomy, but detrimental in patients who required pneumonectomy. This discrepancy embodies what most lung oncologists understand well about N2 disease: Bulky N2 is different from multistation N2, which is different from single-station N2, which is not the same as microscopic N2, which may or may not be different from occult N2.

In this issue of the *Journal*, Yang and colleagues² question the role of neoadjuvant radiation as the third modality. In a review of the National Cancer Database, 1362 surgical patients with stage T1 to T3 N2 NSCLC, treated between 2003 and 2006, were identified and stratified into a bimodality cohort (neoadjuvant chemotherapy plus surgery) and a trimodality cohort (neoadjuvant chemoradiation plus surgery). No survival difference was found between the 2 cohorts, regardless of whether the patient underwent a lobectomy or a pneumonectomy. Acknowledging some limitations, the authors conclude that the addition of induction radiation is not associated with improved survival when compared with induction chemotherapy alone.

The work by Yang and colleagues² greatly advances our knowledge of stage IIIA-N2 disease, but not in the way that the authors intended it to. It can be argued that this dataset does not allow for an answer to the question of whether neoadjuvant radiation improves survival. The absence of data on invasive mediastinal staging makes it impossible to determine the proportion of patients with true pathologic N2 disease. Similarly, it is unknown whether patients had N2 disease postoperatively because the lymph node sampling data do not distinguish between N1 and N2 stations. As such, the true incidence of N2 disease in this population is unknown, let alone the distinction between the different subtypes of N2. By virtue of those patients being surgical, a

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Central Message

In selected surgical patients with cT1-3N2 NSCLC, it is possible to achieve high survival rates with surgery after induction therapy.

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significant selection bias toward nonbulky, single-station disease is expected. In contrast, a distinction between clinical T stages was available through the database, and a significantly higher proportion of patients with T3 N2 disease was present in the induction chemoradiation cohort. This, in fact, may point to the beneficial effect of radiation in improving the survival of those patients.

More importantly, the authors² demonstrate that we have become more successful in treating clinical stage IIIA-N2 NSCLC, as demonstrated by the 5-year postoperative overall survival rate of 41%. This is dramatically higher than the survival rates of 15.7% seen in European Organization for Research and Treatment of Cancer 8941³ and 27% seen in Intergroup 0139,¹ 2 trials that accrued patients a decade previously. This is most likely due to improved staging techniques, better induction treatment regimens, and better selection of operative candidates. The study also reveals that the majority of institutions in the United States are consistent in their choice of one form of induction treatment over the other, reflecting emerging institutional philosophies derived from multidisciplinary collaborations.

N2 is not N2 is not N2. Continued efforts to understand this heterogeneity will further improve our treatment strategies for this disease. For the time being,

Yang and colleagues² demonstrate that high survival rates can be achieved in a select subset of surgical patients with stage IIIA-N2 NSCLC who receive induction treatment.

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