Clarity and clairvoyance: Review and prediction of management guidelines for early stage lung cancer

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The National Comprehensive Cancer Network (NCCN) clinical practice guidelines in oncology are a set of recommendations designed to support health care professionals in the diagnosis, treatment, and management of patients with cancer. In the United States, this document is referred to by physicians in academic, community, and private practices, and by residents and students caring for patients and preparing for board examinations. This document defines expectations of care for many patients with cancer and is the scripture routinely referred to in tumor boards around our country. It is a primary component of the “standard of care” in oncology.

Recommendations issued in the NCCN guidelines are established on the basis of available evidence and expert opinion, and it has been shown that adherence to these guidelines correlates favorably with survival outcomes^{1,2}. Even though these guidelines are frequently updated, the accumulation of reproducible evidence necessary to amend them may take years to amass. In this issue of the *Journal*, Eguchi and Adusumilli³ present a clear and clairvoyant account of published work that identifies and stratifies patients with early stage lung cancer who are at high risk of recurrence or death, and they provide a glimpse of future management standards.

A central theme of this article is the influence of lung adenocarcinoma histologic subtype on patient care, including implications for invasive mediastinal staging, extent of resection, and adjuvant systemic therapy. For example, we have become increasingly aware that micropapillary and solid predominant histologic variants of lung adenocarcinoma are associated with increased of occult N2 disease,⁴ suggesting that patients with these histologic types may benefit from preoperative invasive mediastinal staging. Currently, NCCN guidelines⁵ recommend invasive mediastinal staging for clinical stage IB-IIIa non-small cell lung cancer, and “consideration” of invasive mediastinal staging for clinical stage IA disease. However, a recent multi-institutional prospective trial has called this practice into question.⁶ Among 90 patients

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Central Message

Lung adenocarcinoma histologic subtype will become increasingly important in preoperative and postoperative decision making for patients with lung adenocarcinoma.

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with clinical stage I NSCLC who were considered at risk for occult N2 disease (T2N0 or T1N0 with standardized uptake value >10 by positron emission tomography), mediastinoscopy detected occult N2 disease in only 1.1% of patients. Mean tumor size was substantial at 4.3 cm, ranging from 1.3 to 12 cm. Taken together, we may expect to see a refinement of national guidelines in upcoming years regarding recommendations for invasive mediastinal staging that may very well incorporate tumor histologic subtype.

In their review, Eguchi and Adusumilli³ highlight recent evidence supporting an elevated risk of recurrence for patients undergoing sublobar resection of adenocarcinoma tumors with micropapillary and solid predominant histology compared with lobectomy.⁷ In contrast, sublobar resection is associated with excellent long-term survival outcomes for preinvasive adenocarcinoma in situ and minimally invasive adenocarcinoma lesions, which are well represented radiographically as predominantly ground glass nodules.^{8,9} Currently, the NCCN guidelines have begun to consider such elements in their recommendation of sublobar resection as an alternative treatment for patients with peripheral nodules no larger than 2 cm with pure adenocarcinoma in situ pattern or at least 50% ground glass appearance.⁵ As our collective experience of preoperative determination of lung adenocarcinoma histologic subtype improves, whether through core needle biopsy or

radiographic-pathologic correlation, we may anticipate that preoperative adenocarcinoma histologic subtype will play an increasing role in the decision making underlying the choice of lobar versus sublobar resection.

Finally, Eguchi and Adusumilli³ undertake a timely discussion of a variety of postresection pathologic variables that are associated with prognosis, highlighting the increased recurrence after resection of any adenocarcinoma tumor that contains some degree of high-grade histologic type, such as micropapillary or solid predominant.^{7,10} Currently, the NCCN recommends *consideration* of adjuvant chemotherapy for patients with pathologic stage 1b (T2aN0) and node-negative stage II cancers in the presence of certain high-risk features, including vascular invasion, wedge resection, size greater than 4 cm, and visceral pleural involvement. In addition to important roles in preoperative decision making, we can anticipate that adenocarcinoma histologic subtype may become a high-risk feature that will influence recommendations for adjuvant systemic therapy.

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