Risk stratification for distant recurrence of resected early stage non–small cell lung cancer is under construction

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In our efforts to offer curative pulmonary resection for patients who harbor stage I non–small cell lung cancer (NSCLC), we fall short in identifying patients who should be deemed high risk for distant recurrence and offering them adjuvant treatment. Independent prognostic histopathologic factors have been published and include tumor size,1 visceral pleural invasion,2 lymphovascular invasion,3 large cell neuroendocrine phenotype,4 and micropapillary adenocarcinoma subtype.5 Some investigators have moved to tumor molecular profiling and validated gene expression assays to risk stratify patients.6 Others have assessed the predictive role of common driver mutations in resected early stage NSCLC.7 Despite this knowledge (albeit limited), the enthusiasm to further the understanding and implementation of adjuvant strategies to mitigate risk in stage I NSCLC is lackluster.

In their retrospective series in this issue of the Journal, Brandt and colleagues8 reviewed a large number of patients (n = 893) in a 16-year period (2000-2016) who underwent lobectomy with curative intent for T1-3N0 adenocarcinoma (which included stages IA, IB, IIA, and IIB). All patients with non-adenocarcinoma histology, sublobar resection, and death within 90 days were excluded. Tumor genomic data were collected for a fraction of the patients. Primary outcomes were distant recurrence, disease-free survival, and overall survival. Recurrence was defined as distant, locoregional, or both. Median follow-up was short, just under 3 years. Of the patients, 13% (115/893) developed recurrence, with 86% of these distant recurrences (99/115) and 14% of these isolated local recurrences (16/115). The overall recurrence rate of 13% in this cohort was astonishingly low compared with what is understood to be usual for stage I and II disease in the seventh edition lung cancer TNM staging system. This speaks to a highly selected patient population, or is a consequence of excluding non-adenocarcinoma histologic type. The analysis is vulnerable to changes in treatment over time as adjuvant therapy became more accepted for stage IB (tumors >4 cm), stage IIA, and IIB disease.9 The study cohort was enriched for less aggressive disease by excluding patients who may have received adjuvant therapy from 2006 on. Finally, the 1.8% observed rate of local recurrence in this cohort (16/893) was also impressively low, in contrast to the 6% local recurrence reported in the Lung Cancer Study Group, in which the tumors were smaller than 5 cm. Brandt and colleagues8 conclude that tumor size and lymphovascular invasion are independent predictors of recurrence.

The observations reported in this study are not novel, but they further corroborate the importance of these specific histopathologic parameters when assessing recurrence risk in completely resected, node-negative NSCLC. Brandt and colleagues8 are to be congratulated on analyzing a large cohort and including only patients undergoing lobectomy, which is the most potent oncologic modality to treat node-negative NSCLC. Prediction of recurrence in early stage NSCLC is in its infancy and should be further refined by enhanced molecular profiling, circulating tumor cells, and perhaps circulating tumor DNA. As “molecular fingerprinting” of NSCLC expands, it is my strong conviction that thoracic surgeons have a leadership role in the development of adjuvant therapy trials, because we have the most impact on early stage NSCLC.

References


