Hot nodules and histologic features: The emerging story of stage IA lung adenocarcinoma

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Lobectomy with systematic nodal dissection has been the gold standard of treatment for early-stage non-small cell lung cancer since the randomized controlled trial that demonstrated that sublobar resection resulted in higher recurrence rates than lobectomy.¹ Despite the possibility of high recurrence rates, the incidence of sublobar resection for small lung nodules within the United States is increasing.²

The prognostic significance of histopathologic subtyping of early-stage lung adenocarcinoma is now well established.³ Our group has demonstrated that the presence and increasing percentage of the micropapillary histologic subtype are associated with a higher incidence of local recurrence after sublobar resection compared with lobectomy for lung adenocarcinoma tumors 2 cm or less.⁴ We also have shown that tumor spread through air space (STAS) is a risk factor for recurrence in patients with pathologic T1aN0M0 lung adenocarcinoma who had undergone sublobar resection.⁵ Tumor STAS is now included as a form of invasion in the 2015 World Health Organization classification of lung tumors.

Histologic features are available to surgeons only after resection and intraoperative frozen sections are inadequate in identifying these features.⁶ There have been attempts to identify aggressive features of small lung nodules on preoperative scans and correlate them with pathologic non-invasiveness.⁷ We have shown that lepidic-predominant stage I lung adenocarcinomas exhibited lower maximum standardized uptake values (SUVmax).⁸

In this issue of the *Journal*, Hattori and colleagues⁹ demonstrate that, in radiologically pure solid resected clinical stage IA lung adenocarcinoma, lepidic predominance is independently associated with lower SUVmax and has better prognosis compared with other histologic subtypes.⁹ Additionally, SUVmax of 3.3 or less was an independent prognostic factor of overall survival (OS).⁹ The authors suggest that SUVmax can be useful when determining the extent of resection in radiologically pure solid tumors.

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Central Message

The recently described poor prognostic radiologic and histologic features of lung adenocarcinoma should be considered when developing treatment strategies for patients with stage I lung adenocarcinoma.

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Although it is known that lepidic predominance is a favorable prognostic factor, there is a subset of lepidic-predominant tumors that consist of a collapsed area that can present as a radiologically solid area.³ Hattori and colleagues⁹ have reported a 29% incidence of lepidic-predominant tumors within stage IA lung adenocarcinoma compared with 7% reported by our group.⁸ In addition to the difference in tumor size and ethnic backgrounds among both patient cohorts, interobserver variation among radiologists and pathologists is a potential limitation in implementing this group's recommendations. Hattori and colleagues⁹ conducted a multivariable analysis to determine OS and Kaplan-Meier curves to determine recurrence-free survival. Recurrence, rather than OS, is a valid oncologic outcome measure for T1aN0M0 lung adenocarcinoma because the majority of resected T1a lung adenocarcinoma tumors do not recur and a considerable number of patients die of other causes.¹⁰

In selecting sublobar resection for T1a lung adenocarcinoma, no studies have documented the utility of SUVmax in predicting the micropapillary histologic subtype or presence of tumor STAS. Although the growing knowledgebase of hot nodules (radiologic poor prognostic features) and histologic features (pathologic poor prognostic features) have improved our understanding of stage IA lung adenocarcinoma, they are far from ideal to be adopted as a personalized treatment strategy. The emerging knowledge can be

substantiated by implementing the assessment of radiologic and histologic features in ongoing randomized trials.

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