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Commentary: Spread the news: Spread through air spaces matters

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Spread through air spaces (STAS) represents an invasive pattern of lung cancer consisting of micropapillary clusters or single cells in air spaces separate from the main body of the tumor. The incidence of STAS in adenocarcinoma has been estimated to be between 15% and 50%. STAS is associated with poor prognostic factors in lung adenocarcinoma such as lymphovascular invasion, pleural invasion, tumor diameter, maximum standardized uptake value, and higher tumor consolidation/tumor ratio.¹ More recently, STAS has been shown to be a poor prognostic factor in squamous cell cancer.

A study by Kadota and colleagues² involving T1aN0 and T1bN0 lung adenocarcinoma noted that locoregional recurrence was higher after sublobar resection than lobectomy (42.6% vs 10.9%), suggesting that sublobar resection may be inadequate for STAS tumors. The current study by Jung and colleagues³ involving 506 T1b, T1c, and T2a node-negative patients undergoing lobectomy at a single institution builds on previous publications. A multivariable Cox proportional hazard regression showed that patients with STAS + T1b (hazard ratio, 7.0) and T1c (hazard ratio, 2.9) had a significantly higher risk of recurrence than STAS-negative patients. Inverse probability treatment weighting controlling for potentially confounding variables of age, many comorbidities, standardized uptake value maximum, lymphovascular, and pleural invasion suggested that STAS independently adversely affected both locoregional and distant recurrence rates.

The study shows a higher recurrence rate not only with sublobar resection, as one might expect when there is local spread through airways, but also with distant recurrence rate, suggesting a more aggressive phenotype. There are

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CENTRAL MESSAGE

Spread through air spaces is independently associated with increased locoregional and distant recurrence and worse survival in early lung adenocarcinomas.

implications for using STAS as an independent variable (similar to visceral pleural invasion) in upstaging T1b and T1c cancers. There are also implications for use of STAS as an inclusion criterion for adjuvant therapy trials. It is still not entirely clear for which tumor sizes STAS adds to the prognosis. A prior study showed that STAS affected recurrence-free or overall survival for tumors greater than 2 cm, but not in tumors 2 cm or less.⁴ This study suggests that, as in spread to nodes, lymphatics, or vessels, spread through air spaces appears to be an independent predictor of recurrence and survival.

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