Resection of primary lung cancer with incidental pleural seeding: Seeds of change or reap what you sow?

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Central Message

Retrospective series have reported improved survival after resection of the primary lung cancer when incidental pleural disease is found intraoperatively, but this finding requires further evaluation.

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Malignant pleural disease is generally considered a contraindication to lung cancer resection and has a 5-year survival of only 2%. With modern imaging, however, incidentally found pleural disease may not be as extensive, and resection of the primary tumor may increase survival by reducing tumor burden for adjuvant chemotherapy. Studies evaluating pleural lavage have found microscopic pleural disease at the time of resection in 5.8%.¹ In this issue of the *Journal*, Li and colleagues² report improved survival after resection of the primary tumor in a retrospective study of 43 patients and argue that their results provide a seed of change for current practice.

A meta-analysis of 9 studies including 861 patients with incidental pleural disease by Xu and associates³ found a significant survival benefit with resection of the primary lung cancer. In contrast, Fiorelli and Santini⁴ evaluated 8 studies, including 4 from the meta-analysis by Xu and associates,³ and concluded the evidence was not strong enough to support resection of the primary tumor. Although Sawabata and colleagues⁵ found no benefit with resection in 43 patients, none received adjuvant chemotherapy, which could be important in treating any remaining disease.

The study of Li and colleagues² adds to knowledge in this area, but there are several limitations. The tumor resection group had a lower T stage and more limited pleural disease (13.3% vs 0%) than the group whose surgery did not include resection. These differences may have influenced the surgeon's decision making and thus may have biased the results, favoring increased survival in the resection group. There was also variability in treatment between pleurectomy and isolated resection of pleural nodules, and more patients in the resection group underwent neoadjuvant treatment (23.3% vs 7%).

Patients may have had their disease understaged, because only 50% underwent a positron emission tomographic scan, and 10 of 30 patients had their disease upstaged from N0 to N1 or N2. The pathologic staging was also incomplete. Mediastinal lymph node dissection was performed in only 9 of 16 patients (56.3%) who underwent

wedge resection, which could explain why Li and colleagues² found no difference between N0 and N1 or N2 disease. In other studies, nodal stage has been significantly associated with survival in patients undergoing resection.^{3,6}

The patient population, as in most other studies, was almost uniformly Asian. *EGFR* mutations were present in 58.1% of tumors, which is a higher prevalence than in other parts of the world, and 67.4% of patients received adjuvant therapy with tyrosine kinase inhibitors. How this affected the results and whether these findings are applicable to other patient populations must also be considered.

Although the study is thought-provoking, caution must be taken in interpreting the results because of its small sample size, Asian population, selection bias, and potential understaging. Other studies have also been limited by variability in the extent of pulmonary and pleural resection, as well as the inconsistent use of adjuvant and pleural chemotherapy, and there are not enough data to change current practice. Larger, prospective studies are needed, with standard treatment and staging protocols and clear definitions of the extent of pleural disease, before deciding that the results are seeds of change—and to ensure that you do not just reap what you sow.

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