

therapy. Alternatively, perhaps some of the patients who were not known to have received chemotherapy actually did receive chemotherapy at centers that are not as high quality as those included in the current study. Also, because of the long time frame of the study, positron-emission tomography was only performed on 17% of the study population making accurate staging problematic. Next, a substantial percentage of patients in this study had tumors that were node positive or greater than T2. Presumably, these patients had resection of lesions without initial biopsy with surprise histology and nodal upstaging were found on pathologic analysis. In the modern era, preoperative histologic analysis of mediastinal and hilar lymph nodes for larger and central tumors would allow for purer stages for analysis.

Aside from adjuvant therapy, the natural history of nonhilar small cell tumors is unclear. We generally accept that non-small cell carcinoma spreads centripetally to segmental, hilar, and then mediastinal nodes. Anatomic resection with hilar and mediastinal lymph node dissection is effective because all disease is resected.⁴ Whether or not small cell lung cancer is similar in pattern of spread is less clear. Although hematologic spread seems more common, the current study demonstrates survival improvement of lobectomy

over sublobar resection. Although confounding may again be an issue, this is an important finding for surgeons. Complete resection of all disease may be possible in some patients with anatomic resection.

As imaging and the ability to use navigational bronchoscopy and liquid biopsy to diagnose patients continue to improve, surgeons will see more limited-stage small cell lung cancer that is resectable. Clearly, anatomic resection with adjuvant chemotherapy provides reasonable survival and should be the procedure of choice at present. As the number of these patients increases, opportunities to analyze the condition in more granular ways will exist.

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Commentary: Find, resect, and treat: The evolving early-stage small cell lung cancer story

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The paper by Zhou and colleagues¹ in this issue of the *Journal* analyzes a cohort of 169 patients who had surgery for limited-stage small cell lung cancer over a 30-year period at 5 excellent institutions in North America. Their

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CENTRAL MESSAGE

Patients with early-stage small cell lung cancer should be offered surgical resection followed by systemic chemotherapy.

surgical results were superb, and the careful analysis demonstrated a survival benefit for adjuvant chemotherapy regardless of nodal status. Adjuvant radiation therapy,

either to the head or chest, did not show any benefit. Most striking is the incredibly rare nature of surgery as the first treatment for small cell lung cancer. Given the long time period and the involvement of 5 institutions, the accrual rate is about 1 patient per center per year. As with any retrospective study, it is difficult to know exactly how the patients were chosen for surgery and who was excluded. The take-home message is that we should be on the constant lookout for these patients with early-stage small cell lung cancer and offer them surgical resection followed by systemic chemotherapy. What is very difficult to know is whether patients treated with chemoradiation and then offered surgery would do better or worse than upfront surgery followed by chemotherapy. Since small cell lung cancer is rare to begin with and patients with potentially resectable disease are even rarer, it is unlikely a randomized study will ever be done. Thus, we need to do our best to determine the optimal course of treatment based on available data. Zhou and colleagues' paper provides more information by which we can make better decisions. When patients present with small cell lung cancer or indeterminate cancer and they do not have central tumors whereby resection is challenging, then nodal staging should

be done as per the National Comprehensive Cancer Network guideline.² If negative, appropriate anatomic surgical resection and nodal dissection should be carried out and adjuvant chemotherapy should be given to all patients with resected small cell lung cancer. If, at initial presentation, mediastinal nodes are positive or the tumor is T3 or T4 and marginally resectable, chemotherapy and radiation therapy should be administered. Depending on the outcome, surgical resection might be considered after that.

Hunting for that rare surgical animal, early-stage small cell lung cancer, is a lonely but important mission. When rounded up, the surgeon must resect and then treat all of these patients. With the advent of improved radiology and pathologic testing, we may be able to ferret out more of these cases until such time that the entity becomes extinct due to the decline in smoking.

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