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Commentary: Resection of clinical early-stage lung cancer with unexpected nodal disease—can less really be the same?

Chi-Fu Jeffrey Yang, MD, and Mark F. Berry, MD

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Surgical management of lung cancer has been driven for more than 2 decades by the landmark Lung Cancer Study Group randomized trial that was published in 1995. This trial demonstrated a significant 3-fold increase in the locoregional recurrence rate and a 30% increase in overall death rate ($P = .08$, one-sided) for sublobar resection when compared with lobectomy for cT1 N0 M0 non-small cell lung cancer (NSCLC).¹ This study had considered wedge resections and segmentectomies in the sublobar group, and these lesser resections have subsequently generally been reserved for patients who might not tolerate lobectomy due to impaired pulmonary function or other medical comorbidities. However, during the past 25 years, imaging and staging modalities have clearly evolved such that cancers are being detected more commonly at small sizes. Many retrospective studies²⁻⁴ have explored and found that a sublobar resection may not compromise oncologic outcomes for small or part-solid tumors compared with lobectomy, and 2 randomized controlled trials designed to further improve our understanding of lobectomy and limited resection for cT1a (peripheral tumors < 2 cm) N0 M0 NSCLC are ongoing: CALGB 140503⁵ and JCOG0802/WJOG4607L.⁶ The primary endpoint for both of these trials has not matured yet, although short-term outcomes have been reported.^{5,6}

The use of segmentectomy for early-stage lung cancer for certain clinical situations will likely increase if these randomized trials confirm no significant difference in survival

CENTRAL MESSAGE

The uncommon scenario of unsuspected N1 and N2 disease during a segmentectomy for cT1 No Mo non-small cell lung cancer may occur more frequently in the future and deserves further investigation.

compared with lobectomy. If so, surgeons will likely increasingly encounter the clinical scenario investigated by Razi and colleagues⁷ in this issue of the *Journal*—unexpected nodal involvement (pathologic N1 or N2) found following resection with segmentectomy or lobectomy of small tumors (cT1) that were clinically staged as node negative.

Currently, evidence to guide patient care for this clinical scenario is limited. There are no randomized data to help guide our decision making, and there may never will be. Should a planned segmentectomy for cT1 N0 M0 NSCLC be extended to a lobectomy at the time of surgery if nodes are found on frozen section to be involved? If the nodal disease is not known until the time of the pathology report, when the patient is likely well on their way to recovery, should surgeons recommend that they return to the operating room to complete the lobectomy? This study by Razi and colleagues tried to answer these questions by assembling and analyzing a relatively large cohort of patients from 2004 to 2015 in the National Cancer Data Base who underwent segmentectomy ($n = 452$) and lobectomy ($n = 14,107$) for cT1 N0 M0 NSCLC who were discovered to have “unsuspected” pathologic N1 or N2 disease. Using propensity-score matching and multivariable Cox proportional hazards modeling to minimize confounding and bias, the authors had 3 main findings with potentially important clinical implications: (1) positive N1 or N2 disease was found in 4.9% and 10.6% of patients who underwent segmentectomy and lobectomy for

From the Department of Cardiothoracic Surgery, Stanford University Medical Center, Stanford, Calif.

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Address for reprints: Chi-Fu Jeffrey Yang, MD, Falk Cardiovascular Research Center, 300 Pasteur Dr, Stanford, CA 94305 (E-mail: cjyang@post.harvard.edu).

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cT1aN0M0 NSCLC, respectively, (2) adjuvant chemotherapy given after unsuspected disease was found to be associated with a significant improvement in survival, and (3) survival was not significantly different between lobectomy and segmentectomy when nodal disease was unexpectedly found.

Any surgeon who has already been in this scenario probably will feel at least a little bit of gratitude at having some data to help guide what can be a challenging decision for both the surgeon and the patient. Although this study has all of the inherent limitations of a retrospective registry study, with the authors properly acknowledging specific limitations of their study (including the lack of detailed information as to specific location and character of nodal disease [eg, microscopic vs macroscopic, single vs multistation]), there is now some published data on this uncommon situation. The study should not replace surgical judgment and multidisciplinary evaluation that consider the specific details of particular patients, but it can be used as an important component of that evaluation process. The patients themselves will also probably be appreciative to know that there is some science behind the recommendations being made for their care.

The study results suggest that there should be equipoise with regard to whether segmentectomy is worse than lobectomy for small peripheral tumors with N1 disease (suspected or unsuspected) and unsuspected N2 disease. In the setting of unsuspected nodal disease found on permanent pathology following a planned segmentectomy for cT1 N0 M0, we think the study data preliminarily support proceeding with adjuvant chemotherapy as opposed to a completion lobectomy, although we would not criticize surgeons who continue to perform a completion lobectomy in this setting until randomized data direct them to do otherwise.

However, the most important take-home point of this study may not necessarily be what type of resection is performed for a small lung tumor, but that resection should follow the proper oncologic principle of performing a thorough lymph node

dissection and evaluation. In many cases and particularly early in a surgeon's experience, a segmentectomy is probably technically more challenging than a lobectomy and it may be tempting to simply perform an easy wedge resection of a small peripheral tumor and not take the time and effort to dissect out the anatomic structures so that the specific lymph nodes that drain the location of the cancer can be removed and assessed. However, this study suggests such a practice could lead to 5% to 10% of patients being understaged and by extension undertreated, and would eliminate what is one of the primary advantages of resection over treatment with nonsurgical ablative therapies. Whether this current study would change a surgeon's practice in their management of unexpected nodal disease, all surgeons should not forget that a practice of performing "less" of a parenchymal resection does not also allow the performance of "less" of a pathologic lymph node evaluation.

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