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COMMENTARY

The best that surgery has to offer

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The treatment of patients with stage I lung cancer continues to be examined through decades of controversy:

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lobectomy versus sublobar resection, minimally invasive strategies versus open approaches, and most recently the use of nonsurgical interventions versus resection. Each of these debates pivots on the competing principles of optimizing oncologic efficacy while minimizing invasiveness and complications. Although the Lung Cancer Study Group established lobectomy as the standard of care for clinical stage I lung cancer,¹ those findings are being challenged by trials demonstrating equivalent results with segmentectomy in selected patients² and currently being tested again in a prospective, randomized trial (Cancer and Leukemia Group B 140503).³ More clearly established is the

superiority of thoracoscopic lobectomy compared with open approaches.^{4,5}

The role of surgery in the management of patients with clinical stage I lung cancer is now being challenged by the emergence of 2 nonsurgical interventions: radiofrequency ablation (RFA) and stereotactic body radiation therapy (SBRT). RFA has been demonstrated to be safe and effective in selected patients with lung cancer in several studies and is under evaluation now in a recently completed multi-institutional prospective phase II study: American College of Surgeons Oncology Group [ACOSOG] Z4033.⁶ In addition, SBRT has been used with success in the management of clinical stage I lung cancer, most notably in a prospective phase II study (Radiation Therapy Oncology Group 0236),⁷ and it is currently being compared with sublobar resection in a prospective, randomized trial: ACOSOG Z4099.⁸

As all practitioners involved in the multidisciplinary management of lung cancer await the results of this study, a recent comparative analysis of completed clinical trials of RFA, SBRT, and sublobar resection may improve our understanding of these 3 competing techniques.⁹ The stated purposes of this analysis were to compare selection criteria and to assess the short-term outcomes of the 3 studies. The power of this analysis is limited by several factors, including the size of the RFA study (ACOSOG Z4033; n = 51)⁶ and the size of the SBRT study (Radiation Therapy Oncology Group 0236; n = 55).⁷ The complications that may have arisen from the biopsy procedures in the nonsurgical trials was not assessed. Another important limiting factor is the allowance of wedge resections (more than two thirds of patients) and thoracotomy (more than one third of patients) in the sublobar resection trial (ACOSOG Z4032),¹⁰ strategies that proved to be inferior to anatomic and thoracoscopic approaches in this patient population.^{2,4,5} In addition, comparisons between nonsurgical techniques and resection are limited by the use of clinical, as opposed to pathologic, staging. It is also difficult to assess patient selection in the nonsurgical trials—why patients were turned down for surgery. Pulmonary function tests are relatively objective, but measuring frailty and other comorbid conditions is more complex. Finally, although the assessment of short-term outcomes is important, the absence of long-term oncologic outcomes does limit the conclusions of any comparative analysis.

Although there were some statistically significant differences among the 3 trials in pretreatment clinical parameters (age and pulmonary function), there are 4 important results that are elucidated in this analysis.⁹ First, 29.3% of patients in the sublobar resection trial were upstaged (clinical stage vs pathologic stage) after surgery. Although there were some differences in the baseline characteristics of the 3 trials, one must assume that the assignment of clinical stage underestimates the pathologic stage in 25% to 30% of patients treated by RFA and SBRT. Although the ongoing prospective randomized trial comparing SBRT and sublobar resection

will more definitively address this question when the incidences of local and regional recurrences between the 2 techniques can be compared, the issue of clinical understaging and assignment of interventional therapy remains of concern.

Second, the propensity-matched analysis demonstrates no difference in the development of significant adverse events (3+) after SBRT and sublobar resection. Although the complication profile after resection of lung is well understood,^{4,5} it may be erroneously assumed that SBRT—described as noninvasive—is associated with a lower procedural risk. Although the number of post-therapy deaths was higher in the sublobar resection group, the rate of 3+ adverse events was not significantly different. Accurate risk assessment will certainly be important in the selection of therapy for patients with marginal pulmonary function or other comorbid conditions.

Also of note, the post-treatment decline in pulmonary function was not significantly different in patients treated with SBRT or sublobar resection. Although it may be difficult to draw conclusions in an analysis of patients treated with 2 different modalities in 2 separate clinical trials, the possible assumption by clinicians evaluating patients with clinical stage I lung cancer and marginal pulmonary function that SBRT is associated with higher preservation of pulmonary function may be incorrect. Again, this question will be better addressed in the ongoing prospective trial.

Finally, it must also be pointed out that approximately 13% of patients in the sublobar resection trial had no documented lymph node staging.⁹ I believe it is safe to assume that a significant fraction of patients in this trial also did not have the minimum of 3 mediastinal lymph nodes assessed, as is recommended by current clinical guidelines.¹¹ That, in conjunction with the fact that approximately two thirds of the patients underwent wedge resection as opposed to segmentectomy and approximately one third of patients underwent resection via thoracotomy as opposed to thoracoscopy,⁶ describes a therapeutic surgical strategy that is suboptimal and may prove to be inferior to SBRT in the randomized trial. This ongoing trial may define how patients with clinical stage IA cancers will be treated in the future, a population that is likely to grow as lung cancer screening becomes more prevalent. These patients may not be receiving the ideal therapy in the future if surgeons do not recognize and practice the best that surgery has to offer in optimizing oncologic efficacy while minimizing invasiveness and complications.

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