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RESULTS IN PATIENTS UNDERGOING REOPERATIVE RESECTION?

To the Editor:

I enjoyed the recent article by Smeltzer and colleagues,¹ “Survival Impact of Postoperative Therapy Modalities According to Margin Status in Non–Small Cell Lung Cancer Patients in the United States” in the August 2017 issue of *The Journal of Thoracic and Cardiovascular Surgery*. The article raised several questions.

Patients reported on in this study had positive margins and were treated with postoperative radiation therapy, chemotherapy, or both. Was the decision to leave a positive surgical margin always a result of poor pulmonary function precluding further resection, or were other factors involved (eg, negative margin according to frozen section determined to be positive on permanent section)?

The question of further treatment for those patients who have positive resection margins is often a subject at institutional tumor boards. Radiation is usually favored, because most patients refuse reoperation. Are data available for patients with incompletely resected early-stage non–small cell cancer who underwent reoperative resection? What was the interval between operations, was there any evidence of increased local recurrence, and what was long-term survival in this cohort?

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THE IMPORTANCE OF R0 Reply to the Editor:

In their original article, Smeltzer and colleagues¹ used the National Cancer Database to validate our current National Comprehensive Cancer Network guidelines on adjuvant modalities for incompletely resected non–small cell lung cancer (NSCLC). In contrast to what might be expected from these current guidelines, Smeltzer and colleagues¹ demonstrated that postoperative radiotherapy was associated with a significantly worse survival outcome for patients with incompletely resected early-stage NSCLC than for those not treated. Two critical considerations were raised in a subsequent Letter to the Editor: (1) the reason for positive margins and (2) the outcomes of patients undergoing reresection for a positive margin. Whereas neither of these considerations may be sufficiently addressed by the current data set of the National Cancer Database, several points deserve mention.

Incomplete resection for NSCLC is estimated to occur in 5% to 15% of pulmonary resections, and this event is associated with a significant detriment to overall survival of these patients.² In general, a variety of biologic (grade/stage), anatomic (tumor location), physiologic (pulmonary reserve), and technical (pathologic evaluation) factors can be responsible for the occurrence of a positive margin. In an earlier analysis of 5335 positive margins (4.7%) among 112,998 pulmonary resection in the National Cancer Database by the same group, factors associated with incomplete resection included squamous histologic type, high tumor grade, advanced pathologic stage, and tumors overlapping more than a single lobe.³ Whereas it is also possible that noncongruence between frozen and final pathologic section analyses underlies some of the positive margins, false-negative rates of frozen section are generally less than 5%.⁴ It is therefore likely that a variety of etiologies for incomplete resection are present in this data set.

In their original article, Smeltzer and colleagues¹ excluded patients undergoing repeated resection for positive margins to investigate adjuvant treatments for those with positive margins. They also cite the relatively small numbers of patients in the database who underwent reresection.¹ Understanding the outcomes of patients with incompletely resected early-stage NSCLC who undergo reresection is critical to the formulation of evidence-based management guidelines. On our review of the literature, no studies directly comparing reresection with other adjuvant therapies could be identified. In the absence of these data, extrapolation of results from studies comparing R0 and R1/2 resections to patients with incompletely resected early-stage NSCLC seems fair, and each of these studies demonstrates improved long-term survival with complete resection.^{2,3} Taking these data together with the

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uncertainties of adjuvant therapies for incompletely resected early-stage NSCLC, it is appropriate to emphasize here again that repeated resection, when possible, is the preferred treatment for incompletely resected early-stage NSCLC.

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THE VALUE OF COLLABORATION BETWEEN THORACIC SURGEONS AND RADIATION ONCOLOGISTS WHILE AWAITING EVIDENCE IN

OPERABLE STAGE I NON-SMALL CELL LUNG CANCER

To the Editor:

In the closing remarks of an editorial recently published in the *Journal*, Schaheen and D'Cunha¹ highlight the challenge for thoracic surgeons to adequately compare the efficacy of surgical resection and stereotactic body radiation therapy (SBRT) for patients with operable stage I non-small cell lung cancer (NSCLC).¹ We agree with their comments that “our patients aren’t fully able to dissect the literature and the nuances of the trials”¹ that have been published in the peer-reviewed literature and then recycled in the lay media with sensationalized headlines.² It is for this reason that a multidisciplinary committee of experts across

radiation oncology and thoracic surgery recently published the ASTRO (American Society for Radiation Oncology) SBRT evidence-based guideline for early-stage NSCLC and addressed this topic as a key question: “When is SBRT appropriate for patients with T1-2, N0 NSCLC who are medically operable?”³

On the basis of a systematic review of the literature for patients in medically operable condition, our recommendation is that for “patients with ‘standard operative risk’ (ie, anticipated operative mortality of <1.5%), lobectomy with systematic mediastinal lymph node evaluation remains the recommended treatment,” whereas “discussions about SBRT as a potential alternative to surgery are encouraged” for patients with higher operative risk.³ At the same time, we also recommend that “any patient with operable stage I NSCLC being considered for SBRT should be evaluated by a thoracic surgeon, preferably in a multidisciplinary setting to reduce specialty bias.”³

Although we also agree with Schaheen and D'Cunha¹ that a nonoperative therapy for patients with early stage lung cancer who are fit enough for surgery needs to be carefully evaluated and adequately compared with the long-established standard of care of surgical resection, we have reached a point in time when surgery is not the only treatment choice,⁴ and the available data simply do not shed adequate light to help us know which treatment is optimal for any given patient. To some, such a statement may be considered heretical. Yet, recent attempts at randomized comparisons between surgery and SBRT provided only preliminary and underpowered findings,⁵ and did not provide a signal that surgery was superior.⁶ In fact, the only time that surgery was shown to be superior in a randomized trial was in 1963, when it was compared to palliative doses of radiotherapy.⁷ It is insightful to note that this was more than a decade before the introduction of computed tomography that allows 3-dimensional targeting and more than 30 years before the first patient with lung cancer was treated with SBRT.⁶

Notwithstanding, investigators continue publishing retrospective studies that compare these two treatments, such as the referenced analysis by Yerokun and colleagues.⁸ Unfortunately, evaluations of large observational data sets are inherently imperfect as a result of unavoidable confounding factors that cannot be overcome with propensity matching because of a long-standing reservation of SBRT for patients with poorer performance statuses and shorter life expectancies. Data sets such as the NCDB (National Cancer Database) and SEER (Surveillance, Epidemiology, and End Results Program) provide important insights into cancer care and ideal opportunities to use biostatistics and propensity matching to understand outcomes better. Yet, the absence of specific information on the severity of comorbidities and pulmonary function makes their applicability to this subject limited given that those are