MEDICAL OPERABILITY AND INOPERABILITY DRIVE SURVIVAL IN RETROSPECTIVE ANALYSES COMPARING SURGERY AND SBRT FOR EARLY-STAGE LUNG CANCER

To the Editor:

We read with great interest the recent article by Yerokun and colleagues¹ suggesting a dramatic survival advantage with wedge resection over stereotactic body radiation therapy (SBRT) for clinical stage IA non–small cell lung cancer (NSCLC).¹ Unfortunately, the National Cancer Database (NCDB) does not contain the requisite clinical data elements required to make appropriate comparisons between these modalities. Missing from the NCDB are the objective data that define operability, including pulmonary function, cardiac function, and performance status. Numerous studies have shown that performance status is independent of the Charlson comorbidity score,^{2–4} and no amount of propensity matching can overcome the fundamental uncertainties associated with the absence of these critical variables.

The most plausible explanation for the large survival differences observed in the NCDB by Yerokun and colleagues¹ is that patients who were medically operable by criteria not captured in the database were typically given surgery, and patients who were medically inoperable due to factors not recorded in the database were treated with SBRT. To that end, the 5-year overall survival (OS) outcomes observed by Yerokun and colleagues¹ (55% for resection vs 31% for SBRT) are strikingly similar to a Japanese analysis of 257 patients with early-stage NSCLC, all receiving SBRT, in whom the 5-year OS was 65% versus 35% for medically operable and medically inoperable patients, respectively (Figure 1)⁵—a result also demonstrated in a separate prospective study.⁶ These analyses underscore the need for randomized trials that are not subject to the biases that underlie decisions to deliver surgery or SBRT in this setting.^{7,8}

From a patterns-of-failure standpoint, it could be argued that the putative mechanism for wedge resection to outperform SBRT, if it were to do so, would be through a reduction in local failures that subsequently disseminate to life-

FIGURE 1. Survival with SBRT for medically operable versus inoperable patients with stage I NSCLC, reported by Onishi and colleagues.⁵ SBRT, Stereotactic body radiation therapy; NSCLC, non–small cell lung cancer. Reprinted with permission.⁵

threatening metastases. However, in a series of 676 patients treated with SBRT for early-stage NSCLC, local failures occurring in or adjacent to the treatment volume were observed in only 10.5% of patients at 5 years.⁹ By comparison, in the American College of Surgeons Oncology Group (ACOSOG) Z4032 trial, the comparable metric of staple line recurrences after sublobar resection occurred in 7.7% of patients at a median follow-up of 4.4 years,¹⁰ suggesting a narrow window of opportunity for surgery to improve on cancer-specific survival. In fact, dedicated patterns-of-failure analyses have shown conflicting results, with improved local and regional control after SBRT in some series and improved outcomes with sublobar resection in others.^{11,12} Nevertheless, even if wedge resection achieved 100% local control, postoperative mortality was 0%, and SBRT was poorly delivered throughout this NCDB cohort, the numbers simply would not add up to the magnitude of OS differences observed in this retrospective analysis.

At present, there are 3 multicenter prospective trials reporting SBRT outcomes for operable patients with early-stage NSCLC, including the Radiation Therapy Oncology Group 0618, the Japan Clinical Oncology Group 0403, and the STARS/ROSEL pooled analysis, in which the 3-year OSs with SBRT were 77%, 77%, and 95%, respectively.^{6,13,14} The ACOSOG Z0030 provides high-quality modern lobectomy outcomes in patients with clinical T1–2 N0 or nonhilar N1 disease, with 100% of operations performed by board-certified thoracic surgeons and a 98% rate of complete (RO) resection; the 3-year OS in this trial was approximately 76%.¹⁵ The ACOSOG Z4032 offers similar high-quality sublobar resection outcomes for stage I NSCLC less than 3 cm, for which the 3-year OS was 71%.¹⁰ Although cross-trial comparisons must be made

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cautiously, these data characterize comparable survival with SBRT and surgery in medically operable populations. To our knowledge, the only randomized data comparing SBRT and surgery come from the STARS/ROSEL pooled analysis.¹³ This study found no differences in local, regional, or distant recurrences, but the 3-year OS was superior with SBRT (95% vs 79% with lobectomy, $P = .037$). However, additional prospective studies are clearly needed.

While further randomized data are awaited, thoracic oncology physicians invested in this discussion may find comfort in the fact that they are in good company. Breast oncology was once a heated battleground for debates over mastectomy versus breast conservation, until randomized trials established the viability of both approaches.¹⁶ Likewise, urologic oncology witnessed decades of contention and untold numbers of retrospective analyses championing OS advantages with prostatectomy over radiotherapy, until randomized data showed their equivalence.¹⁷ Thoracic surgeons, like urologists and breast surgeons, are right to aspire to provide the highest quality treatment modality for their patients. Yet, at the same time, patients with cancer deserve careful interpretation of retrospective analyses influenced by selection and indication biases, as well as collegial multidisciplinary discourse promoting the completion of prospective trials. Characterizations of effective, well-tolerated treatment modalities as a “slippery slope”¹⁸ may betray a lack of perspective on historical progress in cancer management across disease sites.

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WHEN IN DOUBT, ABSTAIN

Reply to the Editor:

The contribution to the *Journal* by Rusthoven and colleagues¹ on stereotactic body radiation therapy (SBRT) focuses on several controversial issues, which are analyzed with the magnifying lens of the radiation oncologist. In fact, the conclusions are, at best, unsupported by current evidence, although they do pave the way to the design of a much-awaited randomized clinical trial of SBRT versus surgery in patients with early-stage lung cancer.

The first controversial issue is the concept of operability. The threshold for operability should be defined according to