Editorial

Editorial response: "Stereotactic Ablative Radiotherapy *vs.* Sublobar Resection for Non-Small Cell Lung Cancer: Choosing the Right Patients (an editorial)"

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Comment on: Paul S, Lee PC, Mao J, *et al.* Long term survival with stereotactic ablative radiotherapy (SABR) versus thoracoscopic sublobar lung resection in elderly people: national population based study with propensity matched comparative analysis. BMJ 2016;354:i3570.

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The authors do a commendable job of attempting to determine whether SABR and sublobar resection (SLR) are comparable in treatment for early-stage NSCLC disease (1). Using the primary endpoint of lung-cancer specific survival (LCSS), and thoroughly evaluating the Surveillance, Epidemiology and End Result (SEER) data using propensity matching, the authors show that, based on their primary analysis, SABR and SLR were equivalent in producing cancer-related survival. On secondary analysis, they suggest that patients with larger tumors (≤5 cm but >2 cm) may do better with SLR than SABR. Those conclusions are thought-provoking and provide rationale for future studies investigating these two techniques, which theoretically should have equivalent disease-related outcomes since neither address regional nodes and both have a highly comparable and focused local approach (2). Yet, as the authors note, even after their thorough evaluation, definitive conclusions cannot be drawn from the results, and more investigation is needed.

While there have been improvements in capture with the SEER database, significant endpoints that are important for determining cancer-specific and treatment-related outcomes, including patterns of failure, quality of treatment, and functional status (e.g., FEV1, DLCO), among many others, are missing, making reporting and propensity matching a challenge (3). Further, SEER data only captures a fraction of the patients treated and it relies upon patients utilizing Medicare insurance (4). Additionally, the authors recognize that overall survival (OS) is often a difficult end-point for reasonable comparison between SABR and surgical patients since inoperable SABR patients have an inherently worse co-morbidity. That fact is reflected even in this study by the demonstration that, despite best-matching and equivalent LCSS in patients with tumors ≤2 cm, OS is still different and lower in SABR patients. Still, the authors chose to evaluate LCSS as an effectiveness endpoint. While we agree with this approach generally, as the authors acknowledge, utilizing LCSS as the appropriate measure can be misleading for a number of reasons. First, as the authors point out, from a practical, real-world care perspective, accurate recording and subsequent reporting of cause of death and other factors can be significantly inaccurate, including in the SEER database (5,6). In fact, the NCI warns against use of SEER data for cancer-specific survival reporting (3). Further, and equally important, many reported causes of death are ultimately reported as "unknown" and, as such, make the true LCSS impossible to correctly calculate. Thus, it may have been helpful for this study to report the proportions of deaths recorded as "lung cancer", "cause other than lung cancer," and "unknown". Indeed, this distinction is where local, regional, and distant control and progression-free survival data become pivotal in drawing more solid conclusions regarding cancer-related effectiveness outcomes between treatments. An important notable difference between the two groups, even after matching, is that SABR patients had better follow-up with

imaging than did the surgical cohort (1) (Table 3). While it is not entirely clear, differences in imaging follow-up for two groups may highly impact the accuracy of disease assessment and reporting on LCSS, with higher rates in the SABR group that had more vigilant surveillance for disease status, and is a practical concern that deserves consideration.

Another question raised on both ends of the study is the quality of treatment, a factor which, again, is not captured by SEER data. As shown in the report, SABR was more commonly and increasingly performed as time progressed from 2007–2012. This increase may reflect the improvements in SABR technique and a growing confidence in its effectiveness as a treatment, as reported in studies demonstrating its efficacy (7-13). Historically, larger tumors may have been more difficult to cover with SABR since they often more closely abut critical structures, making it more difficult to safely deliver an effective radiotherapeutic dose (14). That may be one reason SLR may have been shown to be more effective than SABR and, in fact, may eventually be proven to be more appropriate in patients with larger tumors. However, we now know that being able to deliver dose to the full planning treatment volume (PTV) in SABR treatment is crucial for local control (15), and we are able to effectively treat larger and central tumors than was possible before (see: how to fly in a no-fly zone) (16,17).

Despite these criticisms and concerns, the results here are highly valuable and draw attention to an important topic that will pave the way for determining appropriate surgical and SABR approaches for patients. Theoretically, SLR and SABR should have similar outcomes given their nearly identical approaches. If, in fact, the two techniques show comparable patient outcomes, as has been suggested, it would be conceivable to choose the technique that is less-invasive and has lower morbidity (i.e., SABR). However, it is important to resolve whether one technique is more appropriate than the other for select patients (e.g., SLR for larger tumors). This report demonstrates the necessity of phase III randomized studies. It also highlights the need for single and multi-institution data that can capture and provide more comprehensive and revealing cancer-specific outcomes, treatment quality, adverse effects, and survival data in order to help determine which patients unsuited for lobectomy, but able to undergo less comprehensive surgery, should be treated with SLR or SABR.

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Footnote

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