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Commentary: Stereotactic body radiation therapy versus surgery for stage I non–small cell lung cancer in healthy patients: Not quite there yet

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In this issue of the *Journal*, Littau and colleagues¹ performed an instrumental variable analysis of the National Cancer Database (NCDB) to examine the outcomes of otherwise-healthy patients with stage I non–small cell lung cancer (NSCLC) who underwent either surgical resection or stereotactic body radiation therapy (SBRT). The 20,498 patients who underwent surgical resection demonstrated a significantly improved long-term overall survival regardless of the extent of resection (15,822 lobectomy patients, 4676 sublobar resections) compared with the 5465 patients who underwent SBRT. After propensity matching and employing an instrumental variable analysis using facility SBRT rate as the instrument, the authors found that overall survival for surgical resection remained significantly longer compared with SBRT, as lobectomy had a hazard ratio of 0.32 and sublobar resection a hazard ratio of 0.52.

This study builds on previous analyses of the NCDB indicating an improved survival for surgical resection compared with SBRT.^{2–4} As with all previous analyses, there are significant weaknesses inherent to the use of the NCDB



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CENTRAL MESSAGE

Advanced analysis of the NCDB suggests that resection prolongs overall survival in healthy stage I NSCLC patients compared to SBRT. Randomized studies still needed to answer this question definitively.

(lack of granularity, incomplete staging information) and the retrospective nature of this study, limitations that the authors acknowledge appropriately. The present report furthers the effort to account for some of the weaknesses by including sublobar resections, although it does not discriminate between outcomes of segmentectomy versus wedge resection. The major novelty of this study rests in the use of the instrumental variable analysis statistical technique, which strengthens the conclusion by accounting for the variability of use of SBRT between different facilities. Intuitively, it makes sense that patients being treated in facilities with high SBRT use and expertise would potentially be offered that option more readily than patients treated in facilities where such expertise or infrastructure is lacking. The authors validate this intuitive conclusion by showing that facility SBRT rate predicts the chance of receiving that therapeutic modality while it is not independently associated with overall survival.

The authors correctly declare that the issue at hand is how to advise healthy patients with early NSCLC who would be candidates for both modalities on the best therapeutic strategy. Undoubtedly, both modalities achieve excellent local control with low morbidity in experienced hands. Two incomplete phase III trials have failed to answer the question, and a pooled analysis⁵ of the results yielded opposing

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Disclosures: The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

Received for publication Nov 3, 2021; revisions received Nov 3, 2021; accepted for publication Nov 5, 2021; available ahead of print March 11, 2022.

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JTCVS Open 2022;9:262-3

2666-2736

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<https://doi.org/10.1016/j.jxjon.2021.11.011>

results to multiple retrospective studies. The Achilles heel of this debate remains the relative uncertainty with regards to the lymph node status of the patients undergoing SBRT. In the present report, only a minuscule fraction of surgical patients had occult lymph node metastases, while the true number of SBRT patients is unknown. The challenge is to design a randomized trial that will accrue truly node-negative healthy patients with true equipoise toward each treatment modality. Littau and colleagues¹ should be congratulated for a great job of adding to the discussion, given our current available resources and data. Ultimately, until studies like the VALOR (Veterans Affairs Lung Cancer or Stereotactic Radiotherapy) trial become available, an unbiased, multidisciplinary discussion will continue to make all the difference in order to provide our patients with early NSCLC with the best chance for cure.

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