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Commentary: Can big data effectively answer important clinical questions?

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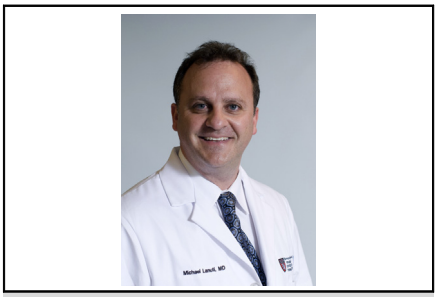

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CENTRAL MESSAGE

Comparisons of sublobar resection, SBRT, or percutaneous thermal ablation for treatment of early stage NSCLC are difficult in a nonrandomized setting.

Wu and colleagues[1] have submitted an analysis from a large national cohort to examine overall survival differences of sublobar resection versus stereotactic body radiation therapy (SBRT) or percutaneous thermal ablation in the treatment of early stage non–small cell lung cancer (NSCLC). The authors queried the National Cancer Database (NCDB) for patients harboring clinical stage I (T1abc-T2a N0) NSCLC from 2004 to 2014 treated with either sublobar resection (wedge or segmentectomy), versus nonsurgical modalities such as SBRT or percutaneous thermal ablation. The primary outcome measure was overall survival (and not disease-free survival), which is nonspecific for treatment effect, particularly in patients with multiple comorbidities that may have been carefully selected for these treatment modalities. This study includes just more than 30,000 patients treated with sublobar resection; nearly 22,000 patients treated with SBRT, and approximately 1400 patients treated with thermal ablation. Median follow-up was just <3 years. Of note, SBRT and percutaneous thermal ablation for stage I NSCLC were evolving as curative strategies during this study period. Adoption of SBRT for inoperable stage I NSCLC was not widely implemented until after 2010 when results from the Radiation Thoracic Oncology Group 0236 trial were published.[2] In addition, the NCDB lacks granularity for critically evaluating thermal ablation because ablation methods, tumor location (central vs peripheral), and methods of surveillance are not available. Radiofrequency was the workhorse of percutaneous ablation during this time interval.[3] Microwave ablation was just being explored and has now become the preferred thermal ablation modality when treating medically inoperable stage I NSCLC. Not surprisingly, patients treated with SBRT or ablation in this study were older than those treated with surgery. Unadjusted Kaplan-Meier curves show improved overall survival in those treated with sublobar resection compared with SBRT or percutaneous ablation. After propensity matching, percutaneous thermal ablation was associated with shorter overall survival compared with sublobar resection or SBRT even with tumor size $\leq$2 cm. This is an important distinction because thermal ablation techniques are often associated with increased recurrence in tumors $\geq$2 cm. Sublobar resection was still associated with improved overall survival when matched to SBRT patients with smaller tumors ($\leq$2 cm).

The large number of patients is clearly a strength of this study when comparing SBRT to limited lung resection. Despite the large number of patients derived from the NCDB, the authors acknowledge inherent selection bias when studying these specific treatments, which clearly limits conclusions. Presumably, many patients in this analysis harbored comorbidities or limitations to cardiopulmonary function that precluded standard of care treatment such as lobectomy for stage I NSCLC. It is reassuring that the authors show that segmentectomy had superior overall survival compared with wedge and SBRT after propensity matching.

In the absence of randomized controlled trials that can address survival outcomes in patients treated with SBRT versus sublobar resection for operable early stage NSCLC, this large retrospective study can provide some guidance to

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treatment comparisons, albeit with clear limitations. Conclusions regarding thermal ablation comparisons in this study should be interpreted with caution given the small number of thermal ablations and the ambiguous coding derived from the NCDB. Comparing SBRT to sublobar resection is a topic of great interest among surgeons and the authors should be congratulated. This study suggests improved overall survival of sublobar resection compared to SBRT for stage I NSCLC; however, further validation will still be necessary.

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