Stereotactic Ablative Radiotherapy Versus Surgery in Early Lung Cancer: A Meta-Analysis of Propensity Score-Adjusted Comparative Effectiveness Studies

Corresponding author: Hanbo Chen

1. Radiation Oncology, London Regional Cancer Program, Western University 2. Radiation Oncology, VU University Medical Center, Amsterdam, The Netherlands 3. Department of Radiation Oncology, London Health Sciences Centre 4. London Health Sciences Centre 5. Department of Radiation Oncology, London Health Sciences Centre 6. Department of Radiation Oncology, London Regional Cancer Program, Western University, London, Ontario, CA

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Abstract

Objectives: Stereotactic ablative radiotherapy (SABR) represents an alternate modality to surgery in early-stage non-small cell lung cancer (ES-NSCLC). No completed randomized controlled trial (RCT) comparing these treatments in operable patients is available. Propensity score (PS)-adjusted studies attempt to minimize inherent biases of confounding by indication in retrospective data. The objective of this study is to perform a meta-analysis of PS-adjusted studies comparing SABR and surgery for ES-NSCLC.

Methods: A systematic review was carried out according to PRISMA guidelines by querying the MEDLINE and Embase databases from inception until December 2016. Peer-reviewed journal articles in the English language comparing SABR versus surgery in patients with ES-NSCLC were eligible. Guidelines, meta-analyses, reviews and studies not using PS-adjustment were excluded. Two reviewers independently reviewed records, with discrepancies settled by a third. Hazard ratios (HR) with confidence intervals (CI) for overall survival (OS) and disease-specific survival (DSS) were directly extracted, if available, or estimated from Kaplan-Meier survival curves. Meta-analysis was carried out with inverse variance-weighted random-effects models (‘metafor’ package, v1.9-9 within the R statistical platform, v3.3.2).

Results: After reviewing 1,038 records, 16 PS-adjusted studies with a total of 19,999 patients were included in the final analysis. HR for OS was available from all studies, and for DSS from 8 studies (3,985 patients). Eight studies reported data specifically for SABR vs. lobectomy, and 6 for SABR vs. sublobar resection. Seven studies used data from national population-level databases. Overall SABR vs. surgery summary HR for OS was 1.50 [95% CI: 1.30-1.72] with high statistical significance (p < 0.0001). However, the HR for DSS did not show statistical significance (HR = 1.17 [95% CI: 0.86-1.58], p = 0.32). Between-study heterogeneity was high for the OS meta-analysis (I² = 71.2%) while the heterogeneity was low for the DSS meta-analysis (I² = 35.5%). Publication bias was not detected (Egger’s test: p = 0.38). On subgroup analysis, OS was superior for both lobectomy (HR = 1.55 [95% CI: 1.20-2.02], p = 0.0009) and sublobar resection (HR = 1.33 [95% CI: 1.15-1.54], p = 0.0001) vs. SABR while the HR for DSS again did not show statistical significance (HR = 1.57 [95% CI: 0.62-3.95] and HR = 1.18 [95% CI: 0.84-1.67], respectively). On sensitivity analysis, censoring results from national population-level databases (to reduce multiple counting of patients) and including other balanced studies not using a PS-adjusted technique resulted in no changes to the conclusions of the primary
analysis. On secondary analysis, meta-analysis of proportions revealed a lymph node upstaging rate of 15.3% [95% CI: 13.0%-17.6%] and chemotherapy usage rate of 10.0% [95% CI: 8.2%-12.0%] in all patients who received surgery.

Conclusions: Patients receiving surgery for ES-NSCLC showed superior OS to SABR in this meta-analysis of PS-adjusted comparative effectiveness studies. However, the effectiveness of SABR was reflected in a similar DSS to surgery, which is further observed over a range of sensitivity analyses. A relatively small percentage of patients undergoing surgery received adjuvant chemotherapy. Whether this observed benefit in OS is real or due to residual confounders requires confirmation in currently-recruiting RCTs.