

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

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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 ($I^2 = 71.2\%$) while the heterogeneity was low for the DSS meta-analysis ($I^2 = 35.5\%$). 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-

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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.