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Impact of Consecutive Versus Non-Consecutive Fractionation on Local Control after SBRT for NSCLC: A Systematic Review and Meta-Analysis

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Abstract

Purpose: Stereotactic body radiotherapy (SBRT) is the standard treatment for medically inoperable, early-stage non-small cell lung cancer (NSCLC); however, the optimal fractionation schedule remains unclear. There is conflicting evidence regarding whether local failure (LF) rates are reduced with non-consecutive (NC) versus consecutive (C) treatment schedules.

Methods: A PROSPERO-registered systematic review was performed by querying four databases (PubMed, Embase, Web of Science, SCOPUS) for articles published from inception to April 30, 2024. Included studies reported patients with NSCLC treated with SBRT with data on fractionation schedule (daily versus non-daily). Data were extracted and reported following PRISMA guidelines. The primary outcome was the rate of LF after SBRT. Pooled outcomes were estimated using random-effects models. Differences in rates of LF in each group were assessed using a random effects meta-analysis to compare odds ratios (OR) across studies. Univariate meta-regression models were used to assess relationships between LF and histology, tumor stage, and central location. Individual reconstructed patient data (IRPD) were were used to estimate time to LF using the Kaplan-Meier method and comparisons between groups were performed using the log-rank test.

Results: From a total of 3,744 screened studies, 7 studies (1 prospective, 6 retrospective) met inclusion criteria consisting of 1,860 patients with 1,942 treated tumors. The median prescribed dose was 50 Gy; the median number of fractions was 5. Most tumors (70%) were T1. Among cases where histology was known, 31% were squamous cell carcinoma, 42% adenocarcinoma, and 15% NSCLC N.O.S. SBRT schedule was delivered consecutively in 647 (33%) and non-consecutively in 1295 (67%). Four studies (1,037 tumors) reported LF outcomes. The pooled LF rate was 15.4% (95% CI 4.7-26.2) in patients treated with C and 8.7% (95% CI 4.1-13.4) in those treated with NC schedules, respectively. Compared with C, there was no significant difference in the odds of LF in patients treated with NC SBRT (OR 0.61, 95% CI 0.18-2.04, p=0.42). On meta-regression, none of the examined factors were associated with LF. Pooled analysis of IRPD identified a significant difference in time to LF: 3-year freedom from LF was 83.1% (95% CI 79.2-87.1) in the C group versus 90.5% (95% CI 87.5-93.7) in the NC group (log-rank p=0.02).

Conclusion: The currently published literature on the impact of SBRT schedule on LF in NSCLC is limited and heterogeneous. Using pooled study level data, there was no significant difference in LF by treatment schedules. However, analysis of reconstructed individual patient time-to-event data revealed C was associated with reduced LC compared to NC treatment. compared to NC treatment. Additional studies are warranted to assess these findings.