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Radiation therapy improves survival for unresectable postpneumonectomy lung tumors



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ABSTRACT

Background: Additional resection for cancer in the single lung is often considered a prohibitive risk. The role of radiation therapy (RT) in this patient population is less clear with very limited available data. In this study, we sought to examine patients with postpneumonectomy lung cancer not amenable to surgery, identify factors associated with receiving RT, and determine the impact of RT on survival outcomes.

Methods: The Surveillance, Epidemiology, and End Results (SEER) database (1988–2013) was queried for patients with inoperable contralateral lung cancer after pneumonectomy. Univariate and multivariate analyses were performed to identify factors associated with the receipt of RT. Survival outcomes were examined using the Kaplan–Meier method.

Results: In total, 191 patients with inoperable postpneumonectomy lung cancer were included. RT was delivered to 122 (63.9%) patients; 69 (36.1%) patients did not receive RT. On multivariate analysis, disease stage was identified as the only predictor associated with receipt of RT ($P < 0.001$). The median overall survival (OS) and disease-specific survival (DSS) for patients receiving RT were higher than those for patients who did not receive RT (25 versus 8 mo and 29 versus 10 mo, respectively; $P < 0.001$). Similarly, patients who received RT had a higher 3-y OS (34% versus 14%, $P < 0.001$) than those who did not receive RT. On subset analysis, survival benefit with RT was observed in patients with all tumor size groups, and there was a trend toward superior survival in patients with stage I/II disease, who received RT compared with those who did not. On multivariate Cox regression analysis, RT use was independently associated with decreased hazards of death after adjusting for other factors (HR, 0.539; $P < 0.001$).

Conclusions: Based on our analysis of the Surveillance, Epidemiology, and End Results (SEER) database, RT is associated with improved outcomes in inoperable patients with a contralateral lung cancer after pneumonectomy compared with observation alone.

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Introduction

Management of patients with a contralateral lung tumor after pneumonectomy poses a significant clinical challenge. Surgical resection can be offered as a curative option; however, an additional pulmonary resection is often considered as a prohibitive risk after a prior pneumonectomy because of limited pulmonary reserves, patient comorbidities, and technical difficulties associated with operating on the single lung. Limited evidence from small single-institution series demonstrates acceptable outcomes after sublobar resection in a highly selected group of patients with metachronous cancers in the solitary lung.¹⁻¹⁰ However, additional surgical resection after the previous pneumonectomy carries high risks for postoperative complications and significant morbidity. Furthermore, resection of the remaining lung can negatively impact pulmonary reserves, significantly affecting the quality of life.⁸

Radiation therapy (RT) is proposed as a useful alternative for patients in whom surgery is contraindicated. However, there is a reluctance to perform therapeutic RT in this group of patients because of concerns regarding the risk of radiation toxicity to the remaining lung.¹¹ This is evident by the limited literature on this subject, which is comprised of small series totaling approximately 70-80 cases describing the usage of different types of radiation treatments (i.e., high-dose conventional RT, hypofractionated RT [HFR], and stereotactic body radiation therapy [SBRT]) in this group of patients.¹¹⁻¹⁶ Hence, the role of RT in the treatment of postpneumonectomy lung tumors is unclear, and the subgroup of patients that might benefit from RT remains undefined. However, with advancement in delivery systems for RT, higher biologically effective doses can be delivered without increasing toxicity. Therefore, we hypothesize that RT would provide better long-term outcomes in patients with postpneumonectomy lung tumors compared with observation alone.

In this study, we sought to evaluate patients with postpneumonectomy contralateral lung cancer not amenable to surgery, identify factors associated with receiving RT, and determine the impact of RT on survival outcomes. In addition, we have summarized available evidence on the use of RT for postpneumonectomy lung cancer.

Materials and methods

Patient selection

The National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) database (www.seer.cancer.gov) was queried from 1988 to 2013. Records for all patients who underwent pneumonectomy for lung cancer (ICD-O-3 Site Codes C34.0-C34.9) were extracted, and cases with a subsequent contralateral lung cancer were identified. The SEER database provides information on cancer-directed surgery using a variable with codes corresponding to “surgery performed,” “recommended but not performed,” “surgery not recommended,” “patient refused,” and “unknown”. Using this variable, patients, for whom “surgery was not

recommended,” records were retrieved. Patients with incomplete information on tumor size, disease stage, RT, and survival were excluded. Patient selection algorithm is described in Figure 1.

Covariates

Information on patient demographics (age, gender, race), tumor characteristics (size, stage, histology, location, year of diagnosis), RT status, and survival was retrieved. Latency was calculated as the difference between the years of diagnosis of the two cancers. Tumors were staged using the American Joint Commission on Cancer (AJCC) sixth edition. For patients diagnosed after 2004, the tumor-node-metastasis (TNM) stage was directly extracted from the SEER. For cases diagnosed between 1988 and 2003, the TNM stage was manually recoded using SEER variables (EOD 10 size, EOD 10 nodes, EOD 10 extension). The tumor size was transformed into a categorical variable with three size groups based on AJCC tumor size cutoffs: ≤ 3 cm, 3.1-5.0 cm, and >5 cm.

All types of RT treatments (including external beam radiation, radioactive implants, radioactive isotopes, or a combination of either) were coded into one single radiotherapy variable (Supplementary Table S1). The additional variable “Previous RT” was defined as receipt of adjuvant RT to the mediastinum with pneumonectomy. The year of diagnosis was transformed into a categorical variable consisting of two groups. A cutoff of 2008 was chosen based on advances in the field of RT and adoption of SBRT.¹³

Statistical analysis

Univariate and multivariate binary logistic regressions were performed to identify factors associated with receiving RT. Unadjusted overall survival (OS) and disease-specific survival

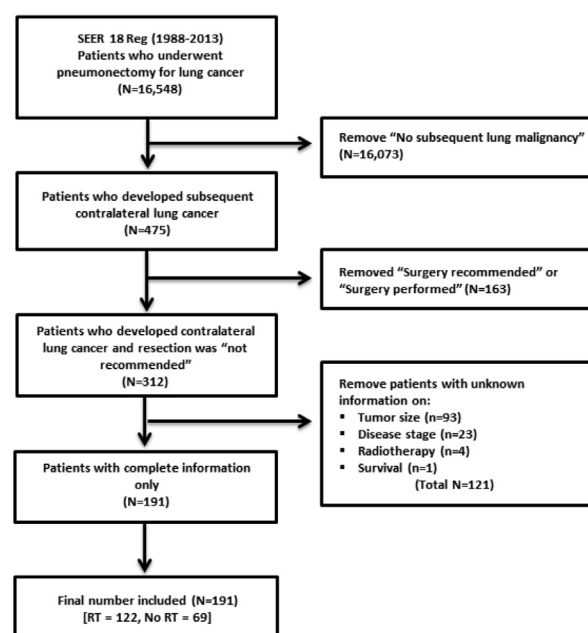


Fig. 1 – Patient selection algorithm.

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