Lung Cancer in the Very Young: Treatment and Survival in the National Cancer Data Base

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ABSTRACT

Introduction: Young patients with lung cancer represent a distinct subset of patients with this disease. The National Cancer Data Base includes patients of all ages and contains detailed staging, treatment, and survival information. The objective of this study was to examine treatment patterns and outcomes in young patients with non–small cell lung cancer (NSCLC).

Methods: The National Cancer Data Base was queried for NSCLC cases from 2003 to 2009. Younger patients were defined as those aged 20 to 46 years. Older patients were defined as those aged 47 to 89 years. Patient demographics, tumor characteristics, treatment, and survival were analyzed. The primary outcomes were 5-year overall and relative survival.

Results: The study included 173,856 patients; 5657 were 20 to 46 years of age. Younger patients were treated differently and received more aggressive therapy at each stage. At stage I, 64% of younger patients received surgery only versus 55% of the older patients ($p < 0.0001$). Younger patients had improved survival at all stages. This effect was more pronounced at earlier stages (the hazard ratios for the older group were 1.84, 1.62, 1.18, and 1.14 for stages I through IV, respectively [all $p < 0.0001$]). The absolute differences in 5-year overall survival between the younger and older groups were 25% for stages I and II but only 9% and 2% for stages III and IV, respectively.

Conclusions: Overall and relative survival in younger patients with NSCLC is better than in older patients, with greater benefit seen in earlier stages. Despite having fewer comorbidities and undergoing more aggressive treatment, younger patients with advanced-stage NSCLC have only marginally better overall and relative survival than older patients.

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Introduction

Lung cancer is the leading cause of cancer mortality in the United States.[1] Although lung cancer classically remains a disease of older patients, there is a distinct and significant subset of patients in whom lung cancer is diagnosed at a young age. Some studies have concluded that outcomes between older and younger patients are similar,[2–5] whereas other studies have shown improved survival in younger patients.[6–10] These studies have shown that younger patients with lung cancer are more likely to be female, be non-smokers, and present at more advanced stages of disease. Most of the studies are either single-institution studies or use the Surveillance, Epidemiology, and End Results (SEER) database, which does not provide detailed treatment data unless paired with the Medicare-linked database. The Medicare data do not have much information on young patients. The National Cancer Data Base (NCDB) has an inherent benefit over other databases because of the inclusion of patients of all ages with a wealth of cancer-related information, making it well suited for examining the care of younger patients with non–small cell lung cancer (NSCLC). We studied differences in patient, tumor, and treatment characteristics between younger and older

patients to better understand the factors that affect survival in this unique set of patients.

Materials and Methods

Data Source

The NCDB is a hospital-based tumor registry run by the American College of Surgeons and the American Cancer Society. Currently there are approximately 1500 Commission on Cancer–accredited facilities that are mandated to report all new cancer cases to the NCDB. These hospitals represent approximately 30% of all hospitals in the United States and are estimated to capture approximately 70% of all newly diagnosed lung cancer cases.[11] The SEER database captures only approximately 28% of all cancer cases.[11] The NCDB captures detailed staging information as well as information on initial treatment and survival. The data used in this study are derived from a de-identified NCDB file, and thus, this study is exempt from Institutional Review Board approval.

Patient Selection

The NCDB participant user file for lung cancer was queried for all patients between the ages of 20 and 89 years inclusively in whom NSCLC was diagnosed from 2003 through 2009. Patients were excluded if their lung cancer was not their first primary cancer, if they were missing clinical stage information or tumor size, if they received nonstandard of care therapy (e.g., clinical trial, immunologic, hormonal, or ablative therapy and wedge resections), if their first course of treatment was unknown, and if they had positive margins or received postoperative radiation therapy alone without postoperative chemotherapy (Fig. 1). The NCDB began capturing comorbidity data in the form of a modified Charlson-Deyo score in 2003, and the seventh edition of the American Joint Committee on Cancer (AJCC) cancer staging manual came out in 2010, so patients in whom cancer was diagnosed before 2003 and after 2009 were excluded to ensure complete comorbidity data and to avoid the changes to the staging system. Patients were also excluded if there was no information on survival and if there was a mismatch between the clinical tumor, node, and metastasis indicators and overall clinical stage. This mismatch occurred if the combination of the clinical tumor, node, and metastasis indicators for a particular patient were not consistent with the resultant clinical stage. These mismatches were likely to due to coding errors or other nuances and were eliminated to avoid any confounding data. Patients were defined as young if their age at diagnosis was greater than two standard deviations less than the mean age of diagnosis. Therefore, patients aged 46 years or younger at the time of

diagnosis were considered young. The older group comprised patients aged 47 to 89 years.

Data Elements

The primary outcomes were 5-year overall and relative survival. Independent variables included sex, race, ethnicity, facility location, proximity to an urban area, insurance type, income level, education level, modified Charlson-Deyo score, facility type, tumor size, histologic diagnosis, primary tumor site, tumor grade, laterality, AJCC sixth-edition clinical stage, initial treatment, and presence or absence of palliative care. The NCDB uses a modified Charlson-Deyo score, with patients with two or more comorbidities grouped together. Tumor size was treated as a categorical variable. Although there is significant overlap, tumor size was chosen instead of clinical tumor stage to separate the effects of tumor size from other tumor characteristics that are encompassed in the tumor stage. Furthermore, with the transition from sixth-edition AJCC staging to seventh-edition staging, many of the definitions for tumor stage changed and most of these changes were related to tumor size.[12,13] Additionally, in the upcoming eighth edition of the lung cancer staging system, it appears that there will be further modifications based on tumor size.[14] Therefore, tumor size was thought to be more applicable to the current AJCC seventh-edition staging definitions than to the AJCC sixth-edition tumor stage.[12,13] Initial treatment was determined using specific data fields in the NCDB to determine the individual therapies received as well as the time after diagnosis at which each therapy was initiated. Patients who had therapy that began more than 180 days from initial diagnosis were excluded. The use of adjuvant and neoadjuvant therapy was calculated by comparing the therapy start dates for surgery and the additional therapy. Chemotherapy was defined as having received multiagent chemotherapy. Radiation therapy was defined as having received at least 4500 cGy combined between the initial and boost dose, and only patients who received radiation to the lung and chest wall were included. Missing data for each variable were coded as unknown and included in the multivariable models.

Statistical Analysis

Bivariate analysis of the independent variables was done using the chi-square test to compare characteristics between the two age groups. Differences in treatment between the groups were analyzed at different stages using the chi-square test. Survival analysis was performed using the Kaplan-Meier product-limit technique and compared by the log-rank test. Patients were stratified by clinical stage. Relative survival analysis was