

Outcomes of Elderly Patients Who Receive Combined Modality Therapy for Locally Advanced Non–Small-Cell Lung Cancer

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Abstract

Our objective was to determine the significance of age in patients treated with sequential or concurrent chemoradiotherapy for locally advanced non–small-cell lung cancer (LA-NSCLC). Ninety-eight patients were 70 years of age or younger and 25 were older than 70 years. In multivariable analysis, there was no difference in the progression-free survival (hazard ratio [HR], 1.15; $P = .64$) or overall survival (HR, 1.18; $P = .65$) of older versus younger patients. Chemoradiotherapy is an effective treatment in elderly patients with LA-NSCLC, with outcomes similar to that in younger patients.

Background: The objective of this study was to review our institution's experience among patients with locally advanced non–small-cell lung cancer (LA-NSCLC) treated with chemotherapy and radiation and to determine the prognostic significance of age. **Patients and Methods:** Patients were included if they underwent sequential or concurrent chemoradiotherapy from 2006 to 2014 for LA-NSCLC. Patients were stratified according to age ≤ 70 and > 70 years. Kaplan–Meier and Cox regression methods were performed to evaluate overall survival (OS) and progression-free survival (PFS). **Results:** One hundred twenty-three patients were identified. Ninety-eight patients were 70 years of age or younger and 25 patients were older than 70 years of age. The median radiotherapy dose was 6660 cGy (range, 3780–7600 cGy). A greater percentage of elderly patients were men, 72% (18 patients) versus 39% (38 patients) ($P = .006$) and received carboplatin/paclitaxel-based chemotherapy, 60% (15 patients) versus 21% (20 patients) ($P < .001$). Median follow-up for OS was 25.9 (95% confidence interval [CI], 21.3–33.9) months. There was no difference in the PFS of older patients versus younger patients (hazard ratio [HR], 1.15; $P = .64$), adjusted for significant covariates. The 1-year PFS rate for patients 70 years of age or younger was 51% (95% CI, 42%–63%) versus 45% (95% CI, 28%–71%) in patients older than 70 years. After adjusting for significant covariates, there was no difference in the OS of older patients compared with younger patients (HR, 1.18; $P = .65$). The 1-year OS rate for patients 70 years of age or younger was 77% (95% CI, 68%–86%) versus 56% (95% CI, 39%–81%) in patients younger than 70 years. **Conclusion:** Chemoradiotherapy is an effective treatment in elderly patients with LA-NSCLC, with outcomes similar to that in younger patients. Appropriately selected elderly patients should be considered for chemoradiation.

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Introduction

In the United States, lung cancer is the leading cause of cancer death and the second most common cancer in men and women. It is estimated that there will be 224,390 new cases of lung and bronchus carcinoma and 158,080 deaths from this cancer in 2016.¹ The most rapidly growing population in the United States are those aged 65 years and older.² By 2050, this age group is expected to reach 88.5 million, making up 20.2% of the population.³ Because of the increasing growth and aging of the population, as well as the prevalence of risk factors such as smoking, obesity, and sedentary

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lifestyles, the incidence of malignancy is increasing.⁴ Increasing age is directly associated with increasing rates of cancer, corresponding to an 11-fold higher incidence of cancer in persons older than the age of 65 years compared with those younger than 65 years of age.⁵ In an analysis of the Surveillance, Epidemiology, and End Results database, nearly half of lung cancer cases are diagnosed in people aged older than 70 years, and 14% of cases are diagnosed in patients older than 80 years of age.⁶

Cancer represents a significant health problem at any age, and the disease and treatments offered can affect a patient's health and quality of life. With advancing age, patients have physiologic changes resulting in reduced hepatic and renal function, increased body fat, reduced total body water, as well as added comorbidities, and decreasing social support, which might lead to decreased survival.⁷⁻⁹ The diagnosis of lung cancer in an elderly patient with the normal and pathologic changes associated with aging might introduce great complexity into the clinical decision-making process and create a difficult situation for health care providers.⁵ The risk of toxicity from aggressive cancer therapy must therefore be carefully balanced against the potential benefit in this population. Physicians must also be aware of the risk that elderly patients might be undertreated or not treated altogether, solely because of their age, despite being otherwise fit for appropriate therapy.^{10,11}

Locally advanced (LA) non-small-cell lung cancer (NSCLC) is commonly managed with multimodal therapy consisting of chemotherapy and radiation,^{12,13} yet there are limited data regarding the efficacy and safety of this approach in elderly patients.¹⁴ We therefore sought to review our institution's experience among patients with LA-NSCLC treated with chemotherapy and radiation and to determine the prognostic significance of age.

Patients and Methods

After institutional review board approval, a retrospective study of patients treated from 2006 to 2014 for LA-NSCLC with radiation and chemotherapy was performed. Patients were included if they had biopsy-proven LA-NSCLC, defined as stages IIB to IIIB, and underwent either sequential or concurrent chemotherapy and radiotherapy. Medical records were reviewed to obtain demographic, clinical, radiographic, and pathologic data. Diagnosis was established using a bronchoscopic or computed tomography (CT)-guided biopsy and staging studies routinely included a CT scan of the thorax and abdomen, magnetic resonance imaging of the brain, and an 18-fluorodeoxyglucose positron emission tomography scan. Staging was assigned on the basis of the American Joint Committee on Cancer staging manual, seventh edition.¹⁵ Clinical radiation pneumonitis included patients with Grade ≥ 2 pneumonitis, defined according to the Common Terminology Criteria for Adverse Events version 4.0.¹⁶

All patients included in this analysis underwent a course of sequential or concurrent chemoradiotherapy. This course of therapy was determined by the treating physicians, generally after evaluation and discussion in a multidisciplinary tumor conference in which pulmonologists, thoracic surgeons, medical oncologists, radiation oncologists, radiologists, and pathologists were present. The choice of chemotherapeutic regimens, and any modifications that might have been made throughout the course of treatment, was determined by the managing medical oncologist. The dose, modality, and technique of radiation therapy were decided by the managing

radiation oncologist. For most cases, a 4-dimensional CT (4DCT) scan was typically performed at the time of simulation for assessment of tumor motion. The gross tumor volume (GTV) included the primary lung tumor and involved lymph nodes on the basis of CT and positron emission tomography imaging. The internal target volume (ITV) included GTV contoured on all 10 phases of 4DCT imaging. The ITV was typically expanded by 5 mm to generate the clinical target volume (CTV). The CTV was expanded by an additional 5 mm to generate the planning target volume (PTV) in patients for whom daily imaging was performed. In patients in whom daily imaging was not performed, a larger PTV expansion was typically used. Radiation was delivered with either a 3-D conformal technique, intensity modulated radiation therapy, or a combination of the 2 techniques. Most patients were treated to a total dose of 60 to 70 Gy in 1.8- to 2.0-Gy daily fractions. During radiotherapy, patients were evaluated at least weekly in on-treatment clinic to assess progress, manage adverse effects of treatment, and to determine whether or not a break in treatment was necessary.

Patients were stratified according to age 70 years of age or younger and age older than 70 years. Kaplan-Meier survival analysis was used to describe the data and Cox regression was performed to compare the overall survival (OS) and progression-free survival (PFS) of the 2 patient groups. Analyses were stratified according to treatment regimen received (taxane-based or nontaxane-based) to mitigate concerns about comparing survival curves in a retrospective sample. Statistically significant covariates, including age, disease stage, chemotherapy regimen and sequence, total radiation dose, and lung dosimetrics were included in the separate Cox regression models for PFS and OS.

Results

One hundred twenty-three patients were identified. The median age was 61 (range, 40-90) years for the entire cohort; 98 patients were 70 years of age or younger (median age, 59.0), whereas 25 patients were older than 70 years of age (median age, 77.7 years). In patients older than 70 years, 6 were aged 71 to 75 years and 19 were older than 75 years. Five patients were included with stage IIB, 79 with IIIA, and 39 with stage IIIB disease. The median radiotherapy dose was 6660 cGy (range, 3780-7600 cGy). Chemotherapy regimens consisted of cisplatin/etoposide ($n = 54$), carboplatin/paclitaxel ($n = 35$), carboplatin/pemetrexed ($n = 30$), gemcitabine ($n = 3$), and erlotinib ($n = 1$). Table 1 shows the patient characteristics in the 2 groups.

For patients 70 years of age and younger, 25 received sequential treatment (25%), 35 received neoadjuvant chemotherapy followed by concurrent chemoradiation (36%), and 38 received concurrent chemoradiotherapy alone (39%). For patients older than 70 years of age, 9 received sequential treatment (36%), 6 received neoadjuvant chemotherapy followed by concurrent chemoradiation (24%), and 10 received concurrent chemoradiotherapy alone (40%). Table 2 shows the treatment characteristics of the 2 groups. A higher percentage of elderly patients were men, 72% versus 39% ($P = .006$) and received taxane-based chemotherapy; 60% versus 21% ($P < .001$).

Median follow-up for OS was 25.9 (95% confidence interval [CI], 21.3-33.9) months. The median OS for patients 70 years of age and younger and those older than 70 years was 37.1 (95% CI, 26.0-not reached [NR]) months and 54.8 (95% CI, 9.5-NR) months,

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