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Advanced non-small cell lung cancer in the elderly: The impact of age and comorbidities on treatment modalities and patient prognosis

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ABSTRACT

Objectives: Data on the treatment modalities and prognostic factors for elderly patients with advanced non-small cell lung cancer (NSCLC) remain limited. This study investigates the impact of age and comorbidities on treatment modalities and patient prognosis.
Materials and Methods: From January 2004 to December 2008, patients aged ≥70 years old and diagnosed with stage IIIB or IV NSCLC were included retrospectively. Their clinical characteristics were reviewed and analyzed. Comorbidity status was evaluated using Charlson comorbidity index (CCI) and simplified comorbidity score (SCS).
Results: A total of 576 patients were included in this analysis. Four hundred and nineteen patients (72.7%) received systemic therapy, including 182 (31.6%) patients who received chemotherapy, and 237 (41.1%) patients who received epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) as initial treatment. Patients aged ≥80 were less likely to receive chemotherapy as initial treatment than those aged 70–79 (12.3% vs. 40.9%, $p < 0.001$). There was no significant difference in proportion of chemotherapy between patients with high and low comorbidity score. Receipt of systemic therapy, male gender, PS ≥ 2, and histologic type were associated with a poorer prognosis. In the multivariate analysis, which included the comorbidity items of SCS, cigarette smoking (HR: 1.73, 95% CI: 1.36–2.21), age ≥80 (HR: 1.30, 95% CI: 1.01–1.67), and PS ≥2 (HR: 3.07, 95% CI: 2.37–3.98) were associated with a shorter survival period.
Conclusion: Age may limit chemotherapy use for elderly patients with NSCLC. Cigarette smoking is an important independent prognostic factor for this particular population.

1. Introduction

Lung cancer is the leading cause of cancer death in most countries.[1] Approximately 85% of patients with lung cancer have non-small cell lung cancer (NSCLC) and more than two-thirds are older than 65 years.[2] According to the Surveillance, Epidemiology, and End Results (SEER) data in the United States, the median age of patients with lung cancer was 71 years (70 in

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males and 71 in females).[3] In Taiwan, the median age of patients with lung cancer was 72 in males and 67 in females.[4] Lung cancer has always been a disease of the elderly.

In most clinical trials on lung cancer, there was a significant under-representation of elderly patients.[5–7] Previous studies demonstrated that selected elderly patients with local and locally advanced lung cancer could tolerate surgery, radiotherapy, and chemo-radiation.[8] Elderly patients could tolerate and benefit from chemotherapy if they were carefully selected.[9–12] Quoix et al. showed that platinum-based doublet chemotherapy had survival benefits compared with vinorelbine or gemcitabine monotherapy in elderly patients.[13] Nonetheless, there was limited data regarding treatment modalities and outcomes of patients aged ≥70 years old, especially among those who did not participate in clinical trials.[14]

The number and severity of comorbidities often increased with age and might limit the treatment options of elderly patients with NSCLC.[15,16] Among patients aged ≥65 years, only 35% of patients with regional disease and 27% with metastatic disease received guideline-recommended treatment.[16] The decline of drug metabolizing capability, reduction in bone marrow, liver, and renal function reserves in elderly patients might influence the decision for chemotherapy.[17] The optimal treatment for NSCLC in elderly patients might be different from that in younger patients.

Comorbidities were demonstrated as prognostic factors in several types of cancer.[18–23] However, the prognostic value of comorbidities for patients with NSCLC remained controversial. Cardiovascular diseases and chronic obstructive pulmonary disease (COPD) were related to postoperative morbidity and mortality.[24] Okami et al. also demonstrated that comorbidity (including any one of the following 11 items: active smoking history, obesity, cerebrovascular or neurologic diseases, COPD, interstitial pneumonitis, ischemic heart disease, renal dysfunction, liver cirrhosis, diabetes mellitus, anemia, and autoimmune disease) was associated with poorer survival and higher operative risk in octogenarians with stage I NSCLC.[25] In contrast, Takenaka et al. reported that cardiovascular comorbidities did not influence the long-term outcomes of patients with NSCLC after pulmonary resection.[26]

A number of comorbidity scoring systems were used for predicting prognosis of patients with NSCLC. The higher comorbidity score evaluated by the Cumulative Illness Rating Scale for Geriatrics (CIRS-G) and Charlson comorbidity index (CCI) was related to worse overall survival in stage I and III NSCLC.[21,22] In two randomized trials, chemotherapy in advanced NSCLC and adjuvant chemotherapy in stage I-II NSCLC, high CCI score was related to poor overall survival.[27] The simplified comorbidity score (SCS), a recently developed scoring system, demonstrated better prognostic prediction than CCI in NSCLC and small cell lung cancer (SCLC).[28–30] Read et al. reported that comorbidities evaluated by the Adult Comorbidity Evaluation (ACE-27) had greater prognostic impact in patients with early stage disease than patients with late stage disease.[31]

Because of the scarcity of data on the treatment modalities and prognosis in elderly patients with NSCLC, this retrospective cohort study was conducted to investigate the relationship among age, comorbidities, treatment modalities, and outcomes, and to explore the prognostic factors in elderly patients with advanced NSCLC.

2. Methods

2.1. Study Population

From January 2004 to December 2008, patients diagnosed with NSCLC at the National Taiwan University Hospital were identified retrospectively via computer registration database according to the International Classification of Diseases, version 9 coding system. Patients aged ≥70 years old with advanced stage (stage IIIB or IV) NSCLC were included. The diagnosis was based on pathologic examination of surgical or biopsy specimens, or on cytology examination of lung or lymph node aspiration or pleural effusion. The exclusion criteria included clinical diagnosis of lung cancer without pathologic or cytologic confirmation, or lack of comorbidity data. The Research Ethics Committee of National Taiwan University Hospital approved this study.

2.2. Data Collection

Clinical characteristics, including age, sex, comorbidities, smoking history, performance status (PS), tumor histology, cancer stage, initial treatment modalities, and overall survival (OS) were recorded from chart review. The Eastern Cooperative Oncology Group (ECOG) PS was determined retrospectively from the medical records based on evaluation from the attending physician, nurses, and physical therapist for the patients' extent of dependence in activities of daily living, including oxygen demand, caregiver needs, and oral intake. Clinical staging was performed according to the patients' computed tomography (CT) scan of the thorax, including the upper part of the abdomen, brain CT scan, and radionuclide scanning of the bone. Cancer stages were determined according to the TNM classification system.[32] Histological analysis was based on the World Health Organization (WHO) classification.[33]

The comorbidity scores were calculated using CCI and SCS systems, as described in the previous studies.[28,34] Systemic therapy was defined as patients who received chemotherapy or epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) therapy. If the patients did not receive any systemic treatment, they were defined as patients who received supportive care, including palliative radiotherapy only.

2.3. Statistics Analyses

Categorical variables were compared by chi-square test. Continuous variables were analyzed using independent *t*-test. OS was defined as the period from the date of diagnosis established to the date of death or last visit, and was analyzed by the Kaplan–Meier method with log-rank test. Patients were followed until January 31, 2012.

Univariate analysis was conducted to examine the unadjusted associations between each variable and overall survival, including age, sex, performance status, cancer stage, SCS, CCI, and individual items of SCS (smoking, diabetes mellitus, renal insufficiency, alcoholism, respiratory, cardiovascular, and neoplastic comorbidity). Multivariate analysis with a Cox proportional hazard model was applied to calculate the hazard ratio (HR) and its 95% confidence interval (CI). Age, sex, and factors with a p-value < 0.10 in the univariate analysis were selected for