

RESEARCH ARTICLE

Radical Oncological Surgery and Adjuvan Therapy in Non-Small Cell Lung Cancer Patients over 70 years of Age

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Abstract

Background: The incidence of lung cancer increases with age. Approximately 50% of non-small cell lung cancer (NSCLC) patients are over 70 years old. Because of the increasing elderly population, treatment approaches in this age group continue to be studied similar to groups of young people. **Materials and Methods:** In the current study, 26 patients who underwent radical surgery and adjuvan chemoradiation at Ataturk Chest Diseases and Chest Surgery Training and Research Hospital were evaluated retrospectively. **Results:** Of 21 patients (81%) were male and the average age was 74.4. Lobectomy was performed in 18 cases, pneumonectomy in 3, sleeve lobectomy in 3 and bilobectomy in 2. There was no perioperative or early period mortality. Overall survival was 24.5 months. **Conclusions:** From our study, lung cancer surgery and adjuvant therapy can be performed safely with low morbidity in the elderly.

Keywords: Elderly -lung cancer -radical surgery -chemotherapy -radiotherapy

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Introduction

Lung cancer is the most lethal cancer type. The incidence of lung cancer increases worldwide. Despite advances in technology and medicine, prognosis of lung cancer is still poor. Additionally 85% of patients are diagnosed at advanced stages. Lung cancer incidence increases with age and peaks at the age of 60s-70s (Jemal et al., 2010). Life expectancy is increasing with progress in medicine and the world's population is growing older. Due to the co-morbidities, physical and mental indulging, the elderly population is undergoing fewer and milder treatment approaches compared with younger ones. Still, we are not able to determine the true biological age. Therefore, chronological age is used to define the older age. In studies conducted recently, different chronological ages and cut-off values are used to identify the elderly population such as 65, 70 and 75. However, the most widely accepted limit has been 70. Physiological changes associated with aging increases after this age. In the treatment of early stage lung cancer, surgery is the best chance for cure so in appropriate patients surgical treatment should be performed. Five year survival of non-small cell lung cancer (NSCLC) is 75% in stage IA, 25% in stage IIIA (Le Chevalier et al., 2010; Ulger et al., 2015).

In recent years, 50% of lung cancer patients diagnosed over the age of 65 and up to 30% is above the age of

70 (Maione et al., 2010). Due to the increasing age of the population, in this age group treatment approaches continue to be studied as similar group of young people. For this purpose, we aimed to present our radically operated and adjuvant treated cases older or equal to 70 years of age.

Materials and Methods

Patients older or equal to 70 years of age who underwent radical pulmonary resection for NSCLC between 2008-2012 in the Ataturk Chest Diseases and Chest Surgery Training and Research Hospital were included to study. Patient age, gender, smoking history, comorbidities, invasive staging procedures before thoracotomy, the operation, tumor histology, postoperative stage, postoperative complications were recorded retrospectively.

Survival time of patients was defined as the time from the date of diagnosis to date of death or the last date of arrival to hospital. Surgical mortality included all deaths during the first 30 days after operation.

The statistical software SPSS 21.0 (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, United States) was used for all analyses. Results were evaluated with descriptive statistical methods. Study was approved by the local ethics committee.

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Results

There were 21 (81%) males and 5 (19%) females, ranging in age from 70 to 84 years (median age of 77.4). 19 cases were between the ages of 70-75 and 7 cases were between the ages of 75-84. 21 (81%) cases were smokers or ex-smokers and 7 cases had co-morbid disease (4 hypertension and 3 diabetes mellitus). The tumor was located at the right lung in 16 (61.5%) cases and at the left lung in 10 (38.5%) cases. Three cases were staged with mediastinoscopy and 1 case with endobronchial ultrasound. The rest of the cases were staged with radiologic procedures. Preoperative stages were 8 (30.7 %) cases Stage IB, 7 (26.9 %) cases Stage IIA and 11 (42.3 %) cases Stage IIB. The types of pulmonary resections were performed are; lobectomies (69%), bilobectomies (7.7%), sleeve upper lobectomies (11.5%), and pneumonectomies (2 right sided, 1 left sided) (11.5 %)(Table 1). Postoperative stages were 5 (19.2%) cases Stage IB, 2 (7.7%) cases Stage IIA, 10 (38.5%) cases Stage IIB and 9 (34.6%) cases Stage IIIA (Table 2). Squamous cell carcinoma was the most common histologic type of cancer (50%), followed by adenocarcinoma (15.4%) and non-otherwise-specified (NOS)(15.4%) (Table 3). There was no mortality in the per-operative period or in the early period. Minor complications occurred in 4 cases (3 supraventricular arrhythmia and 1 respiratory failure does not require mechanical ventilation). Four cycles of vinorelbine and cisplatin chemotherapy were performed to twenty-four patients and only vinorelbine chemotherapy was performed to 2 patients because of renal toxicity. Seven patients (26.9%) who had positive mediastinal lymph nodes underwent adjuvant mediastinal radiation therapy with a daily 2 Gy fractionated radiation dose to a total dose of 46-50 Gy. Severe toxicity was not observed except Grade 1 neutropenia and Grade 1-2 nausea. In 7 patients who received mediastinal radiotherapy, 5 patients experienced Grade 1-2 esophagitis. None of the patients experienced Grade 3 or higher toxicities. All of them completed the planned irradiation course. The median

Table 1. Operation Characteristics

Resection type	Number of patients (Percentage)
Lobectomy	18 (69)
Bilobectomy	2 (7.7)
Sleeve lobectomy	3 (11.5)
Pneumonectomy	3 (11.5)

Table 2. Postoperative Stages

Postoperative stage	Number of patients (Percentage)
Stage IB	5 (19.2)
Stage IIA	2 (7.7)
Stage IIB	10 (38.5)
Stage IIIA	9 (34.6)

Table 3. Histopathologic Characteristics

Histologic type	Number of patients (Percentage)
Squamous cell carcinoma	13 (50)
Adenocarcinoma	9 (34.6)
Non-otherwise-specified (NOS)	4 (15.4)

overall survival was 24.5 months for all stages, 21.8 months for Stage IB, 35.4 months for Stage IIA, 27.6 months for Stage IIB and 21.8 months for Stage IIIA.

Discussion

Ageing is a process that should be considered with physical, psychological and social dimensions. There are different opinions about the ageing limit. Studies usually use 70 years as ageing limit but some other studies use 65, 75 or 80 years as ageing limit. In the European Respiratory Society and the European Society of Thoracic Surgeons clinical lung cancer guidelines, patients over 70 years of age are considered as “elderly” and patients over the age of 80 are considered as “too old” (Brunelli et al., 2009). In the elderly population co-morbidities such as diabetes mellitus, renal failure, ischemic heart disease, congestive heart failure and peripheral vascular disease are common. More than 50% of NSCLC patients are older than 65 years while over 30% are at least 70 years old at diagnosis but studies in this age group do not contain enough. Therefore treatment in this age group is going to be a question mark (Langer et al., 2011). Elderly NSCLC cases are diagnosed at early stages (Jaklitsch et al., 2003). In a study, while 69% of patients older than 75 years who underwent surgery were Stage 1, 53% of patients under the age of 70, were found in same stage (Gonzalez-Aragoneses et al., 2009). This situation increases the chance of elderly NSCLC patients to benefit from surgery. In parallel with the normal cell biology of aging, tumor cells may show less aggressive behavior according to young people. This condition may increase incidence of early-stage disease in this group. Besides the differences in cell biology, histopathologic differences is also available. Squamous cell cancer in the elderly is more frequent compared to younger population (Maione et al., 2010). In our study, 50% of our patients had squamous cell cancer.

Elderly patients should be evaluated for all treatment options applied to the general population. All patients should have equal chance for surgery regardless of age. Besides in a study compiled from different age groups of patients <69 years, 70 to 79 years and > 80 years of age operative mortality did not differ (respectively 1.6%, 4.2% and 2.8%). However, mortality in the elderly population has been associated with pneumonectomy. Cardiac and pulmonary function test abnormalities was not associated with specific risk increase (Pagni et al., 1998). As result of multivariate analysis in different studies; age was found a nonspecific factor on overall survival (Thomas et al., 1998; Bouchardy et al., 1999; Oliaro et al., 1999; Jazieh et al., 2000). In previous studies, surgical treatment of elderly NSCLC population has been reported not suitable with high mortality and morbidity, in new studies with the advancement of surgical techniques and medical treatment contrary opinions have been reported. Many publications showed that perioperative mortality of lobectomy or segmentectomy in patients greater than or equal to 80 years of age was same as normal population (Matsuoka et al., 2005; Dominguez-Ventura et al., 2007; Okami et al., 2009). In our study, 3 patients underwent pneumonectomy because lesions were centrally located

and in these cases 3-year survival was found 25%, but the number of cases is few. Important issue in the surgical treatment of elderly patients is, the size of surgery. This age group is likely to encounter in the early stages of cancer as well as complications and increased mortality due to wider resection; so limited resection as possible should be preferred. Mery et al. (2005) showed that when lobectomy or more limited surgery performed; survival of young population and ≥ 75 years was similar. Also Burfeind et al. (2008) found quality of life and survival similar between young and elderly population when lobectomy performed.

Mun and Kohno et al. (2008) showed operative mortality of resection by video-assisted thoracic surgery 3.6%, 3 year survival 76.4 % and 5 year survival 65.9 % in Stage I cases >70 years. In our study, overall survival was 30.4 months in those who had lobectomy and 31.2 months in those who had pneumonectomy and the difference was not statistically significant ($p>0.05$). Mizushima et al. (1997) found operative mortality 22% in >70 years patients and 3.2% in young patients. In our study we haven't seen operative mortality or serious complication. Only medically treatable cardiac arrhythmia and respiratory failure have developed. This may be associated with low comorbidity of our patients and small number of cases.

Adjuvant chemotherapy in the elderly population is another controversial case. Most physicians are acting abstention at administration of chemotherapy due to toxicities and the lack of chemotherapy studies in this age group. In Lacey meta-analysis various adjuvant chemotherapy regimens were evaluated in all three different age groups (<65 , $65-69$, >70 years), although all three groups differed in efficacy, the total number of cycles-side effects profile were similar in all three groups (Fruh et al., 2008). In our study, all patients had four cycles of single-agent or platinum-based chemotherapy and we didn't observe severe toxicity except Grade 1 neutropenia and Grade 1-2 nausea.

There is limited data regarding the effectiveness of postoperative radiation therapy for elderly patients. Kang et al. (2012) concluded that the treatment-related toxicity with radiotherapy was noticeably lower. In our study 7 patients who received mediastinal radiotherapy, 5 patients experienced Grade 1-2 esophagitis. None of the patients experienced Grade 3 or higher toxicities. All of them completed the planned irradiation course.

Our study has several drawbacks related to its retrospective nature and inclusion of a relatively small number of cases from only one tertiary hospital.

In conclusion if elderly patients are suitable for radical oncological surgery and there is no obstacle in the preoperative evaluation, they should be considered for aggressive anti-cancer treatment regardless of age.

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