

Pneumonectomy for Clinical Stage I Non-Small Cell Lung Cancer in Elderly Patients over 70 Years of Age

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Background: Lobectomy is the generally accepted standard treatment for early-stage non-small cell lung cancer (NSCLC). However, especially in elderly patients, it is often necessary to perform pneumonectomy in order to maximize the likelihood of curative treatment, although pneumonectomy is a challenging procedure. **Methods:** We analysed patients who were clinically diagnosed with stage I NSCLC and underwent pneumonectomy with curative intent from 2004 to 2011. The patients were divided into an elderly group (≥ 70 years) and a younger group (< 70 years). We retrospectively analysed the outcomes of these groups of patients in order to characterize the role of pneumonectomy as a treatment for elderly patients with clinical stage I NSCLC. **Results:** Thirty patients younger than 70 years of age (younger group) and fourteen patients 70 years of age or older (elderly group) who underwent pneumonectomy were enrolled in the present study. The median follow-up period was 35 months (range, 0 to 125 months). The perioperative mortality rate (within 90 days after the operation) was 7.1% in the elderly group and 6.7% in the younger group ($p=0.73$). No significant differences between the two groups were observed regarding the occurrence of pneumonia, acute respiratory distress syndrome, cardiac arrhythmia, bronchopleural fistula, and vocal cord paralysis. The overall five-year survival rate was 79.4% in the younger group and 35.7% in the elderly group, which was a significant difference ($p=0.018$). The five-year disease-free survival rate was 66.7% in the younger group and 35.7% in the elderly group, but this difference was not statistically significant ($p=0.23$). **Conclusion:** Although elderly patients with early stage lung cancer showed a worse long-term survival rate after pneumonectomy than younger patients, the outcomes of elderly patients were similar to those of younger patients in terms of perioperative mortality and postoperative complications. Patients should not be denied pneumonectomy solely due to old age.

Key words: 1. Non-small-cell lung carcinoma
2. Geriatrics
3. Surgery
4. Aged

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INTRODUCTION

Non-small cell lung cancer is the leading cause of cancer-related death in both men and women older than 65 years in Western countries [1], and an increasing number of patients suffer from this disease. Surgical resection is the most effective treatment for early-stage non-small cell lung cancer (NSCLC), and lobectomy is the standard surgical technique for treating NSCLC. Nonetheless, in some instances pneumonectomy is the only surgical option for curative resection in patients who require the removal of more than one lobe in order to accomplish a complete resection. However, pneumonectomy itself is associated with higher rates of morbidity and mortality than other standard procedures [2-5]. Most surgeons try to avoid pneumonectomy as much as possible due to these potential adverse outcomes, especially among elderly patients. Moreover, NSCLC is often diagnosed in elderly patients [6]. Thus, an older population is expected to have an increasing risk of lung cancer, and elderly patients must often undergo pneumonectomy for the treatment of lung cancer. However, it is not clear whether elderly patients obtain the same benefits from major surgical procedures, especially pneumonectomy, as younger patients. Recent evidence shows that pneumonectomy in elderly patients with lung cancer appears to be justified because its outcomes are comparable to those observed in younger patients [7,8]. In this study, we retrospectively evaluated the clinical outcomes of patients at least 70 years of age who underwent pneumonectomy for clinical stage I NSCLC.

METHODS

1) Patients and data collection

We performed a retrospective review of all patients who underwent pneumonectomy for NSCLC at Samsung Medical Center between 2004 and 2011. Clinical data were obtained from the patients' medical records. A total of 44 patients who underwent pneumonectomy for clinical stage I NSCLC were enrolled in the present study. These patients were divided in two groups according to age: an elderly group (≥ 70 years) and a younger group (< 70 years).

The two groups were compared with regard to demographic,

clinical, and histopathological factors, as well as perioperative mortality, postoperative complications, recurrence, and overall survival. The clinical presentation of these patients was evaluated using brain magnetic resonance imaging, chest computed tomography (CT), and 18F-fluorodeoxy-D-glucose positron emission tomography CT (FDG-PET CT). Pathological typing and staging were performed according to the current International System for Staging Lung Cancer (seventh edition).

2) Operational procedure and follow-up surveillance

Patients were considered to be candidates for lung resection if there was no evidence of extensive mediastinal involvement of the tumour and if they were deemed to have an adequate cardiac reserve and adequate predicted postoperative lung function, as assessed by preoperative spirometry. Pneumonectomy was only performed in patients with lung cancer that could not be completely resected via a sleeve lobectomy or bilobectomy. After resection of the main tumour, all patients underwent a complete mediastinal lymph node dissection. A complete resection (R0) was defined as the absence of any residual gross or microscopic disease detected at the bronchial or vascular margins and the absence of residual disease in the mediastinum after nodal dissection. Incomplete resection (R1 and R2) was defined as the presence of microscopic residual tumour fragments at the resected bronchial or vascular margins or residual unresectable nodal disease. Adjuvant chemotherapy was administered when postoperative stage II or III disease was evident on the pathological report. Postoperative radiation therapy was administered in cases of histologically positive N2 lymph nodes, positive multi-N1 lymph nodes, or a positive resection margin at the time of surgery.

Postoperatively, the follow-up schedule involved visits to the clinic every three to four months during the first two years, and every four to six months from the third to the fifth years. The usual follow-up procedures included a physical examination and a chest CT scan. FDG-PET CT imaging was performed annually.

3) Statistical analysis

For comparisons of continuous and categorical variables, the Mann-Whitney U-test, the chi-square test, or the Fisher's exact test were used, depending on which as appropriate.

Table 1. Patients' characteristics

Parameter	Younger (< 70 yr) (n=30)	Elderly (> 70 yr) (n=14)	p-value
Gender			0.38
Male	29 (96.7)	14 (100.0)	
Female	1 (3.3)	0	
Age (yr)	60.1±5.9	73.3±2.3	<0.001
% Predicted forced expiratory volume 1 second (%)	85.1±14.7	86.5±14.5	0.78
% Predicted diffusing capacity of the lung for carbon monoxide (%)	87.4±17.7	97.5±16.4	0.07
Co-morbidities			
Chronic obstructive pulmonary disease	9 (30.0)	3 (21.4)	0.72
Stroke	1 (3.3)	0	1.00
Cardiac disease	1 (3.3)	2 (14.3)	0.23
Other disease (renal or hepatic)	0	0	NS

Values are presented as number (%) or mean±standard deviation.

Survival was calculated from the time of pneumonectomy to the last date of follow-up by means of Kaplan-Meier curves and the log-rank test. Perioperative mortality included death within 90 days after the operation and in-hospital deaths.

Disease-free survival was measured from the date of pneumonectomy to the date of recurrence or death from any cause. All p-values <0.05 were considered to indicate statistical significance. All statistical analyses were performed using JMP ver. 11.0.1 (SAS Institute Inc., Cary, NC, USA).

RESULTS

A total of 44 patients were analysed, and their characteristics are summarized in Table 1. The median follow-up period was 35 months (range, 0 to 125 months). The median age of the patients at the time of pneumonectomy was 64.5 years (range, 49 to 79 years), and 43 patients (97.8%) were male. The mean predicted forced expiratory volume in one second was 85.1%±14.7% in the younger group and 86.5%±14.5% in the elderly group, and the mean diffusing capacity of the lung for carbon monoxide was 87.4%±17.7% in the younger group and 97.5%±16.4% in the elderly group. Data regarding the tumour histology and postoperative pathological data are summarized in Table 2. The percentage of patients under-

Table 2. Tumor histologic and surgical outcomes after pneumonectomy

Parameter	Younger (< 70 yr) (n=30)	Elderly (> 70 yr) (n=14)	p-value
Cell type			0.35
Squamous cell carcinoma	26	11	
Adenocarcinoma	2	3	
Large cell carcinoma	1	0	
Adenoid cystic carcinoma	1	0	
Pathologic stage			0.80
Stage I	10 (33.3)	6 (42.9)	
Stage II	14 (46.7)	6 (42.9)	
Stage III	6 (20.0)	2 (14.2)	
Sideneess			0.64
Right pneumonectomy	6 (20.0)	2 (14.3)	
Indications for pneumonectomy			0.84
Main bronchus involvement	16	6	
Pulmonary vessel involvement	10	6	
Trans-fissural invasion	1	1	
Non-functioning remaining lung	3	1	
Resection			0.14
Complete resection (R0)	30 (100.0)	13 (97.7)	
Adjuvant therapy			
Chemotherapy	17 (56.7)	5 (35.7)	0.19
Radiotherapy	1 (3.3)	1 (7.1)	0.37

Values are presented as number or number (%).

going a right pneumonectomy was 20% in the younger group and 14.3% in the elderly group (p=0.64). Squamous cell carcinoma was the most common histological type in both groups (p=0.35). In the younger group, 10 patients were in postoperative stage I, 14 patients were in postoperative stage II, and six patients were in postoperative stage III. In the elderly group, six patients were in postoperative stage I, six patients were in postoperative stage II, and two patients were in postoperative stage III. The perioperative mortality rate (death within 90 days after surgery) was 7.1% (one patient) in the elderly group, and 6.7% (two patients) in the younger group (p=0.73). The causes of perioperative death in the younger group were pneumonia (one patient) and acute respiratory distress syndrome (ARDS) (one patient). The cause of perioperative death in the elderly group was pneumonia (one patient). No significant differences between the two groups were found regarding the occurrence of postoperative complications (pneumonia, ARDS, cardiac arrhythmia, bronchopleural fistu-

Table 3. Postoperative complications

Postoperative complication	Younger (<70 yr) (n=30)	Elderly (>70 yr) (n=14)	p-value
Pneumonia	4	2	0.93
Acute lung injury/acute respiratory distress syndrome	1	0	0.38
Bronchopleural fistula	1	0	0.65
Arrhythmia (atrial fibrillation)	1	0	0.38
Empyema	3	1	0.25
Vocal cord palsy	2	2	0.43
Total	12	5	0.66

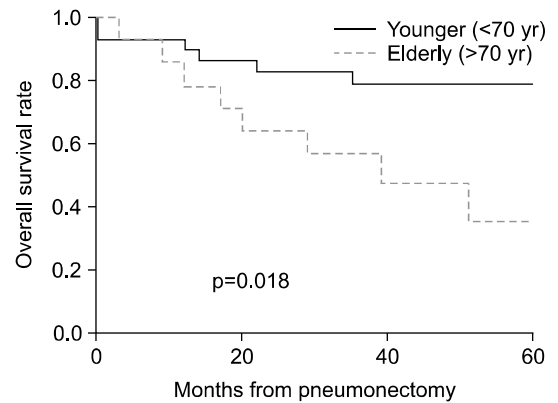
la, and vocal cord paralysis) (Table 3).

The overall five-year survival rates were 79.4% for the younger group and 35.7% for the elderly group. The overall survival rate was significantly higher in the younger group than in the elderly group ($p=0.018$) (Fig. 1). The five-year disease-free survival rate was 66.7% for the younger group and 35.7% for the elderly group. The disease-free survival rate was not significantly different between the younger and elderly group ($p=0.23$) (Fig. 2).

DISCUSSION

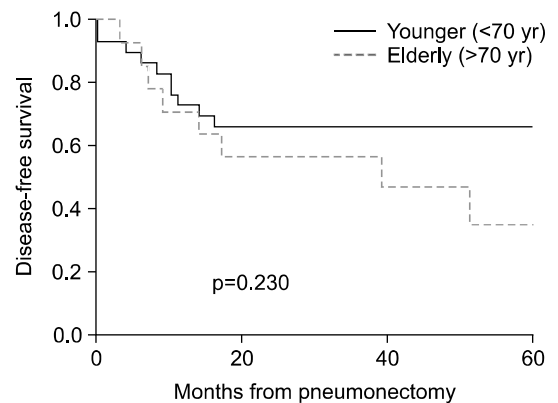
Non-small cell lung cancer is the leading cause of cancer-related death in both men and women older than 65 years in Western countries [1]. Despite recent developments in chemotherapy and radiotherapy, surgical resection for stage I or II disease remains the only reliably curative treatment [9]. The Korean population is increasing in age, and elderly age is still regarded as a major risk factor for surgery. Elderly patients tend to be denied surgery or are urged to undergo palliative treatment. It has been found that 92.3% of patients younger than 75 years of age received curative surgery for stage I NSCLC, compared to only 69.6% of patients over 75 years of age [10].

Questions remain about the real risks of lung resection surgery, especially in elderly patients. Some studies have assessed the role of surgery in elderly patients with NSCLC. Cerfolio and Bryant [11], in a nested case-control study published in 2006, reported that the overall five-year survival in elderly patients (≥ 70 years of age) was 78%, which was sig-



	Month						
	0	10	20	30	40	50	60
Younger	30	30	27	23	21	17	17
Elderly	14	13	10	9	6	5	4

Fig. 1. Overall survival curve for patients with clinical stage I lung cancer.



	Month						
	0	10	20	30	40	50	60
Younger	30	25	21	20	19	15	15
Elderly	14	11	9	9	6	5	4

Fig. 2. Disease-free survival curve for patients with clinical stage I lung cancer.

nificantly higher than the rate in the younger group (69%, $p=0.01$), and concluded that elderly patients with early NSCLC should not be denied pulmonary resection. In contrast, another study found a higher postoperative death rate among elderly patients undergoing pneumonectomy [12]. The results of our study showed no significant differences between the two groups (younger vs. elderly) regarding perioperative mortality and morbidity. However, the overall five-year survival rate was significantly higher in the younger

group than in the elderly group, while disease-free survival was not significantly different between the two groups. Goodgame et al. [13] conducted a retrospective study of stage I NSCLC and found that elderly patients have similar recurrence-free survival rate, but worse overall survival than younger patients (five-year survival, 52% vs. 67%; $p < 0.0001$), which was similar to our results. Birim et al. [14] found that increasing age was a significant prognostic factor affecting long-term outcomes, along with other metrics such as the Charlson comorbidity index. We consider it likely that the lower five-year survival rate in the elderly group reflected the natural life course and the presence of increased comorbidities towards the end of the lifespan. The average life expectancy of Koreans is 81.4 years, as reported by the National Statistical Office [15].

This study has several limitations, including its retrospective single-centre design and a small number of patients, and therefore it should not be interpreted as presenting strong conclusions, especially regarding overall survival. Nonetheless, old age alone should no longer be considered a factor that excludes the possibility of surgical treatment for stage I NSCLC. A recent study has shown that the proportion of elderly patients (> 75 years) with stage I NSCLC who undergo surgery has increased from 35% to 49% over the period from 1989 and 2009 [15]. Our study found no significant differences in perioperative mortality and morbidity between the elderly group and the younger group. Therefore, pneumonectomy should not be avoided in elderly patients, assuming the careful selection of patients based on preoperative evaluations. Nonetheless, attention should be paid to the relatively poor long-term outcomes of elderly patients who undergo pneumonectomy, and further studies are needed to assess the prognosis associated with pneumonectomy in various populations.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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