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ORIGINAL ARTICLE

Surgical results and prognosis of lung cancer in elderly Japanese patients aged over 85 years: comparison with patients aged 80–84 years

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Abstract
Objective With the increase in lung cancer patients over 80 years of age, lobectomy with mediastinal lymph node dissection is often performed in patients in a good general condition. However, the age limit for this procedure has not yet been determined. In this study, we examined the safety, therapeutic results, and prognosis of surgical treatment for lung cancer patients over 85 years of age.
Methods Among the 4446 lung cancer patients who underwent surgery at our hospital from January 1997 to March 2019, we assessed 320 patients (7.2%, Group A, aged 80–84 years) and 74 patients (1.7%, Group B, aged over 85 years).
Results The median age of the patients in Group B was 86 years. Compared to Group A, Group B had significantly more patients with a history of ischemic heart disease, lower pack-year smoking, and lobectomy and lobectomy less resection (reduced surgery), and a shorter operation time ($P<0.05$). There was no significant difference between the two groups in terms of postoperative complications. There was no significant difference in survival rate and prognosis between the two groups, and the 2-, 3-, and 5-year survival rates were 79.0%, 74.7%, and 53.6%, respectively, in Group B. In Group B sex (female) and early stage of cancer were independent prognostic factors of non-small cell lung cancer (stage I).
Conclusions In a limited number of patients, surgical resection in patients aged over 85 years was safely performed, and the survival of these patients was comparable to those aged 80–84 years.

Keywords Lung cancer · Elderly patient · The oldest old · Reduction surgery · Prognostic predictor

Introduction

Today, there is a steady increase in the proportion of aging population in developed countries [1], and currently, Japan has the highest global percentage of elderly (aged ≥ 80 years) adults, comprising 27.7% of the Japanese population. By 2065, the average age of Japanese men and women is expected to be 84.95 years and 91.35 years, respectively [1]. The changes associated with a chronologic age of 85 years can be divided into several domains: normal aging, common diseases, functional, cognitive/psychiatric, and social changes. Individuals older than 85 years have decreased visual acuity [2], hearing loss [3], slowed reaction time [4], and decline in balance [5]. Moreover, by the age of 85 years, approximately 20% of people meet the criteria for sarcopenia (meaningful loss of muscle mass and strength) [6]. Adults aged 85 years and older, sometimes referred to as the "oldest old", are the fastest-growing age group in the United States.

Lung cancer is the leading cause of cancer death in Japan, and predominantly affects the elderly. Given the increase in the aging population, it is important to consider the consequences of surgery for adults aged over 85 years. Lung resection is established as a treatment for early-stage lung cancer [7]; however, postoperative complications after pulmonary resection are inevitable, with a reported incidence of 9.0–53.4% [8–10]. Short-term mortality is closely linked to the severity of postoperative complications [7, 8], which are well documented as poor prognostic factors [11]. Age

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is an important risk factor of morbidity and mortality after lung resection, and therefore curative lung cancer surgery is less commonly proposed to older patients [12].

The purpose of this study was to clarify the safety, therapeutic results, and prognosis of surgical treatment for lung cancer patients aged ≥ 85 years.

Subjects and methods

Study population

This protocol was approved by the ethics committee of our institute (2015015). All patients provided written informed consent prior to their enrollment.

From January 1997 to March 2019, surgery in 4446 cases of pulmonary malignancies was performed at our institution. Among them, we extracted 394 patients (8.9%) who were over 80 years old at the first operation and divided them into two groups as follows: 80–84 years at the time of surgery (Group A, $n = 320$) and over 85 years at the time of surgery (Group B, $n = 74$). In total, 4052 patients were aged ≤ 79 years.

The following clinical backgrounds and peri- and postoperative results were analyzed: age, sex, preoperative comorbidities, smoking history, pack-year smoking, respiratory function (VC, %VC, FEV1, FEV1%, $\%DL_{CO}$), clinical stage, lymph node dissection, operative time, intraoperative blood loss, pathological stage, drain insertion, length of hospital stay, postoperative complications, which were defined based on the Clavien–Dindo classification grade 2 or more; and the home oxygen therapy (HOT) introduction rate. With regard to the tumor and lymph node, metastasis staging, chest radiograph, computed tomography (CT) of the chest, CT or ultrasound of the upper abdomen, whole-brain CT or magnetic resonance imaging (MRI), and positron emission tomography PET–CT were performed. All CT findings were reviewed anew by the authors (two radiologists: Kazuhiro Suzuki and Akihiro Hotta), one pulmonary medicine physician (Kazuhiro Ando), and two thoracic surgeons (Mariko Fukui and Kazuya Takamochi). Diagnoses of idiopathic interstitial pneumonias (IIPs) were based on reported criteria and classified into three groups: UIP pattern, possible UIP pattern, and inconsistent with UIP pattern based on the official ATS/ERS/JRS/ALAT statement [13]. For the purpose of the discussion, only the complication rate and the mortality rate within 30 and 90 days were examined for patients aged ≤ 79 years and compared to patients aged ≥ 80 years. The ECG (electrocardiogram) master test and heart sonography were performed in all cases as routine preoperative physical examinations for elderly patients. Cervical echo and dementia check were not performed in all cases.

Surgical procedure and postoperative follow-up

All operations were performed under the observation and guidance of the thoracic surgery supervisor. The absolute indication criterion for limited lung resection at our institute is limited predictive forced expiratory volume in 1 s of less than 600 ml/m^2. The surgical approach was divided into open thoracotomy (skin incision 8 cm or more) and video-assisted thoracoscopic surgery (VATS) (skin incision 8 cm or less). The surgical approach was chosen taking the oncological aspects and patients' background into consideration. Mediastinal lymph node dissection was conducted routinely during lobectomy and more. Limited surgery was considered for patients with a Performance State (PS) of ≥ 1 that had heart disease and/or chronic kidney disease that required hemodialysis with the objection of preoperative comorbidity. By considering the average life expectancy, we selected limited surgery for patients in their late 80 s or older since these patients do not always strive to achieve a 5-year survival.

We divided the surgical procedure into four groups as follows: (1) wide wedge resection; (2) segmentectomy; (3) lobectomy, and (4) surgery larger than lobectomy (bilobectomy, pneumonectomy, chest wall combined resection, bronchoplasty). Lymph node dissection was divided into three groups: ND0, without lymph node dissection or lymph node sampling; ND1, intrapulmonary and hilar lymph node dissection and ND2, and ND1 plus mediastinal lymph node dissection.

The surgical morbidity and mortality occurring within 30 and 90 days of operation was evaluated, and the following pathological backgrounds were examined: tumor size, pathology, pathological stage, and outcome (causes of death). The tumor stage was determined according to the 7th edition of the TNM staging system of the International Union against Cancer [14]. The histologic tumor type was determined according to the 3rd edition of the World Health Organization classification [15].

Comorbidities and postoperative complications

Comorbidities and postoperative complications were diagnosed and recorded during daily clinical practice by laboratory, radiologic, and physiological examinations. Comorbidities comprised 13 items: hypertension (history of internal use), ischemic heart disease, arrhythmia, active smoking history within 1 month before surgery, obesity (body mass index > 30 kg/m^2), cerebrovascular or neurologic diseases, chronic obstructive pulmonary disease (FEV1% < 70%), interstitial pneumonitis (apparent interstitial shadow detected by chest CT), renal dysfunction (serum creatinine > 2.0 mg/dl), liver cirrhosis, diabetes mellitus (HbA1c > 8.0%), anemia (Hb < 8.0 g/dl), and autoimmune disease.

The postoperative complications were as follows: arrhythmia, HOT, delirium, pneumonia (presenting as abnormal shadow on chest radiograph), wound infection (accompanying wound failure), empyema, postoperative hemorrhage (500 mL/h or more), prolonged air leakage (1 week or longer), chylothorax (1000 mL/d or more), bronchopleural fistula, bronchovascular fistula, pulmonary embolism, respiratory failure (required mechanical ventilation for 3 days or longer), myocardial infarction, and cerebral infarction.

Statistics analysis

Descriptive statistics were used to assess patient demographic characteristics and outcomes. Normally distributed continuous data were expressed as medians, and categorical data were expressed as counts and proportions. Comparisons among all parameters were analyzed using Student's *t* test. Survival was calculated by the Kaplan–Meier method, and differences in survival were assessed by log-rank analysis. Multivariate analysis for prognostic factors was performed using Cox's proportional hazard regression model. A logistic regression model of the results of multivariate analysis was used to identify the risk factors for postoperative complications. Operative mortality was defined as mortality within 30 and 90 days of the surgery. All data were analyzed using SPSS version 23.0 (SPSS Inc., Chicago, IL). Probability values < 0.05 were considered significant.

Results

Percentage of cases during all operations every 5 years

First, we examined the percentage of all surgeries by age. Although Group B remained at approximately 1–2%, Group A has been gradually increasing in recent years (Fig. 1).

Comparison of clinical background between both groups

Next, the patients were divided into two groups based on their background (Table 1). The median age for Group B was 86 years. There was no significant difference in the sex ratio in Group B, although there was a tendency of more women. Thus, a bias may exist in Group B in the case originally selected for surgery as this was a female patient. There were 69 patients (93%) with a history of preoperative comorbidities. Among these, the most common were cardiovascular diseases, such as hypertension and ischemic heart disease. The results showed that there were significantly more cases of ischemic disease in patients aged over 85 years ($P < 0.05$). A total of 40 patients had a smoking history, but there was no significant difference between the two groups. Furthermore,

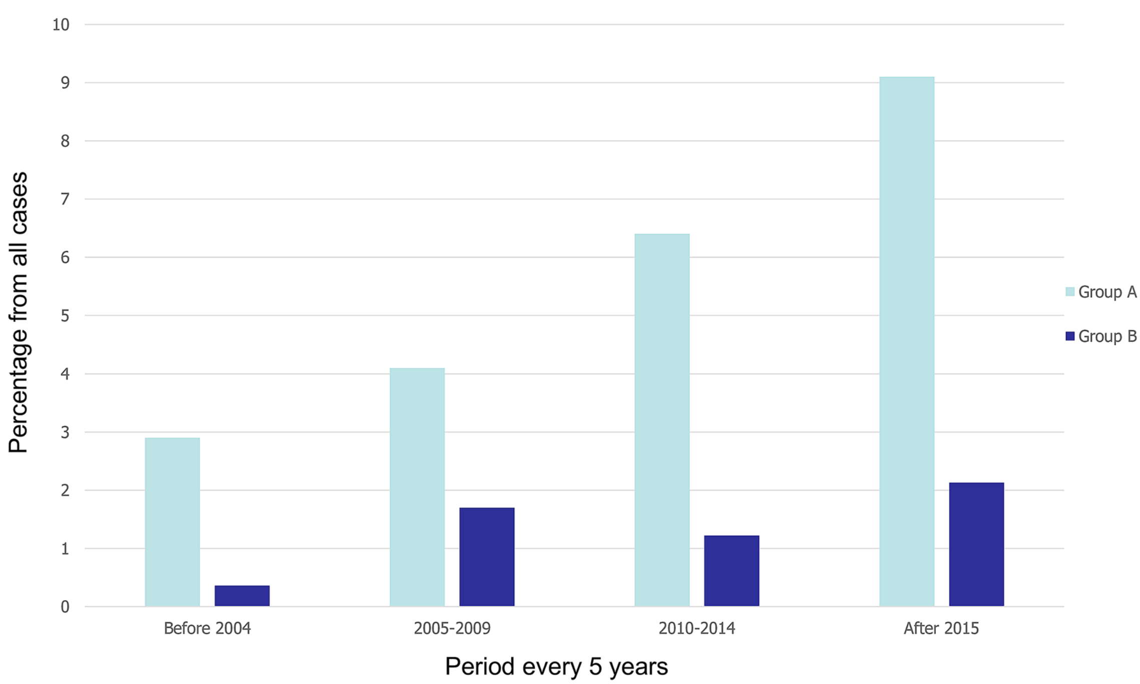

Fig. 1 Percentage of cases in all operations every 5 years

Table 1 Characteristics of the patients who underwent surgery for pulmonary malignancies

Variables	Group A ($n=320$)	Group B ($n=74$)	*P* value
Age, median [IQR]	81 [80–83]	86 [85–87]	< 0.05
Gender male	201 (63%)	38 (51%)	0.07
Preoperative comorbidity	297 (93%)	69 (93%)	1.00
Hypertension	125 (39%)	36 (49%)	0.13
Ischemic heart disease	48 (15%)	18 (24%)	0.05
Type 2 diabetes	65 (25%)	16 (22%)	0.68
COPD	37 (12%)	9 (12%)	0.88
Arrhythmia	45 (14%)	7 (9%)	0.29
Interstitial pneumonia	39 (12%)	5 (7%)	0.18
Smoking history	206 (64%)	40(54%)	0.10
Pack-year smoking, median [IQR]	20 [0–50]	5 [0–37.5]	< 0.05
VC, L, median [IQR]	2.66 [2.23–3.20]	2.28 [1.94–2.75]	< 0.05
%VC, %, median [IQR]	97.1 [84.3–108.2]	95.3 [81.5–109.8]	0.47
FEV1, L, median [IQR]	1.74 [1.47–2.16]	1.53 [1.29–1.87]	< 0.05
FEVI%, %, median [IQR]	71.8 [65.9–76.9]	72.8 [66.3–77.7]	0.99
%DLCO, %, median [IQR]	50.9 [40.2–61.7]	50.8 [37.4–57.6]	0.55
Clinical stage IA			
IA	184 (58%)	39 (53%)	0.45
IB	75 (23%)	24 (32%)	0.11
IIA	24 (8%)	3 (5%)	0.29
IIB	14 (4%)	4 (5%)	0.7
IIIA or higher	23 (7%)	4 (5%)	0.58
Year of surgery			
1997–2010	69 (22%)	21 (28%)	
2011–2019	251 (78%)	53 (72%)	0.21
Surgical approach			
Open thoracotomy	212 (66%)	46 (62%)	
Video-assisted thoracic surgery	108 (34%)	28 (38%)	0.51
Operative			
Surgery larger than lobectomy	49 (15%)	4 (5%)	< 0.05
Lobectomy	176 (55%)	50 (68%)	< 0.05
Segmentectomy	48 (15%)	10 (13.5%)	0.75
Wide wedge resection	47 (15%)	10 (13.5%)	0.8
Lymph nodal dissection			
ND0	47 (15%)	12 (16%)	0.74
ND1	136 (42%)	31 (42%)	0.92
ND2	137 (43%)	31 (42%)	0.89
Length of operation, minutes, median [IQR]	130 [96–167]	120 [90–140]	< 0.05
Blood loss, ml, median [IQR]	15 [10–35]	15 [10–40]	0.32
Hospital stay, days, median [IQR]	9 [7–13]	9 [7–13]	0.56
Postoperative complications	147 (46%)	40 (54%)	0.25
Arrhythmia	46 (14%)	14 (19%)	0.33
Home oxygen therapy	22 (7%)	8 (11%)	0.25
Delirium	19 (6%)	5 (7%)	0.79
Pneumonia	19 (6%)	5 (7%)	0.79
30-day mortality	2 (1%)	1 (1%)	0.52
90-day mortality	9 (3%)	1 (1%)	0.47

IQR interquartile range, *COPD* chronic obstructive pulmonary disease, *VC* vital capacity, *FEV1* forced expiratory volume in one second, *DLCO* diffusing capacity for carbon monoxide, *ND* nodal dissection

Group A had a significantly higher rate of pack-year smoking than Group B ($P<0.05$), while regarding respiratory function, VC and FEV1 were significantly higher in Group A than in Group B ($P<0.05$). Perhaps due to the increased number of men in Group A, the amount of VC and FEV1 were large, and %VC and FEV1% did not change significantly. In addition, the clinical stage was not significantly different between the two groups.

There was no significant difference in the operated year and surgical approach between the two groups. With regard to the surgical procedure, in Group B, there were 4 cases (5%) of extended surgery, including bilobectomy and chest wall combined resection, which was significantly less than in Group A ($P<0.05$). In Group B, 42% of patients underwent mediastinal lymph node dissection, which was not significantly different to the frequency of mediastinal lymph node dissection in Group A.

With regard to operation time, the median duration in Group B was 120 min, which was significantly less than in Group A ($P<0.05$). The median hospital stay was 9 days, and there was no significant difference between the two groups. Postoperative complications were observed in 40 (54%) patients in Group B; the breakdown of complications included 14 cases of arrhythmia, 8 cases of HOT induction due to hypoxemia, 5 cases of delirium, and 5 cases of pneumonia. With regard to 30-day mortality, two patients died in Group A and one patient died in Group B. In Group A, one patient died of respiratory failure due to pneumonia on postoperative day (POD) 27, while another patient died on POD 21 due to an acute exacerbation of interstitial pneumonia. In Group B, one patient died on POD 20 due to an acute exacerbation of interstitial pneumonia. We analyzed whether the rate of complications changed according to the surgical procedure, and found no significant difference (data not shown). We also examined the relationship between complications and length of hospital stay, and found no obvious difference (data not shown).

Comparison of pathology and prognosis between Groups A and B

Table 2 presents the pathological characteristics and outcomes (causes of death) of Groups A and B. The pathologies were examined separately for adenocarcinoma and non-adenocarcinoma, but there was no significant difference between the two groups. In Group B, the results were significantly higher only in the IB stage. Although there was no significant difference in tumor diameter, it is highly likely that this was because the tumor diameter in Group B was larger. Regarding outcomes, there were no significant differences in death from cancer, death from other diseases, or death from unknown causes between the two groups. Figure 2a shows the overall survival curve of both groups. The median length of follow-up was 787 days for the Group A patients, and the median survival time was 1214 days for all the Group A patients. The median length of follow-up was 816 days for all the Group B patients, and the median survival time was 912 days for all the Group B patients; a log-rank test was used for comparison, but no significant difference was found. In Group B, the 2-, 3-, and 5-year overall survival rates were 79.0, 74.7, and 53.6%, respectively. Figure 2b shows the recurrence-free survival curve of both groups; a log-rank test was used for comparison, but no significant difference was found. In Group B, the 2-, 3-, and 5-year overall survival rates were 74.6, 68.2, and 53.4%, respectively.

Table 2 Comparison of pathology and prognosis

Variables	Group A ($n=320$)	Group B ($n=74$)	P value
Tumor size (mm)	25	28	0.61
Pathology			
Adenocarcinoma	214 (67%)	54 (73%)	
Non-adenocarcinoma	106 (33%)	20 (27%)	0.31
Pathological stage			
IA	149 (46%)	30 (41%)	0.35
IB	70 (22%)	26 (35%)	<0.05
IIA	24 (8%)	4 (5%)	0.58
IIB	32 (10%)	6 (8%)	0.62
IIIA over	45 (14%)	8 (11%)	0.46
Outcome (causes of death)			
Lung cancer death	48 (15%)	11 (15%)	0.98
Other disease death	33 (10%)	10 (14%)	0.43
Unknown death	12 (4%)	2 (3%)	0.63

Recurrence type and secondary treatment

In Group A, 18.1% (58/320) of patients had recurrence: 19 had local recurrence, 28 had distant metastasis, and 11 had both. In Group B, 14.9% (11/74) of patients had recurrence: 2 local recurrences and 9 distant metastases. There was no significant difference in the recurrence rates between the two groups. Group A included 15 patients treated with chemotherapy, 5 treated with molecular targeted therapy, 12 on radiotherapy (RT) (palliative irradiation), and 24 treated with best supportive care (BSC) as a first-line therapy after recurrence. Group B had no patients treated with chemotherapy or molecular targeted therapy, 5 treated with RT, and 6 treated with BSC as a first-line therapy after recurrence.

Group A had a significantly higher proportion of patients treated with chemotherapy or molecular targeted therapy than Group B ($P<0.05$).

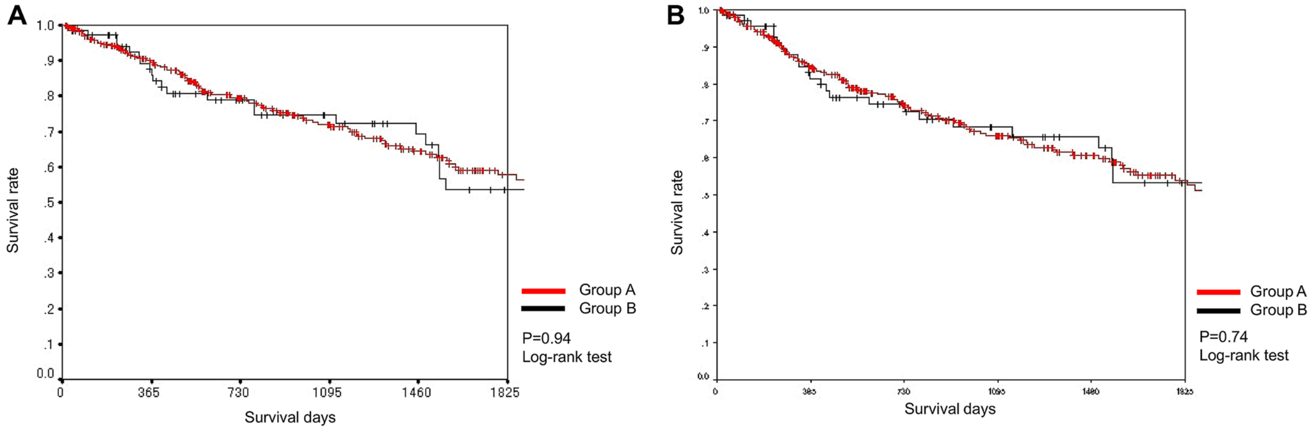

Fig. 2 A Kaplan–Meier survival curves of Groups A and B. **a** 5-year overall survival. **b** 5-year recurrence-free survival

Analysis of prognostic factors

To find predictive prognostic factors in clinical stage I, we first performed a univariate analysis of survival. In Group A, women, absence of postoperative complications, adenocarcinoma histopathological type, and pathological stage I may be good predictors of prognosis (Table 3). In Group B, the prognosis was significantly better in women and those with pathological stage I (Table 3). Multivariate analysis was subsequently performed, and in Group A it was demonstrated that women, absence of postoperative complications, and pathological stage I were independent prognostic predictors (Table 4), while in Group B women and pathological stage I were independent prognostic predictors (Table 4).

Discussion

This is the first general thoracic surgery study to primarily investigate patients over the age of 85. In our oldest old group, the 2-, 3-, and 5-year survival rates were 79.0, 74.7, and 53.6%, respectively. Other studies on patients over 80 years of age reported a 5-year survival rate of 53.1–55.7% (Table 5) [16, 17]. Therefore, patients in whom surgery was performed at the age of 85 years or older showed comparable results in terms of survival rate to cases aged 80–84 years. Karlijn reported that for the oldest old (over 85 years) receiving standard treatment, survival rates were similar to those of the elderly (71–84 years). Moreover, in the oldest old group, no survival differences were found when comparing standard or adjusted regimens for stage I and IV non-small cell lung cancer (NSCLC), while for stage III the oldest old who received standard treatment had a longer survival [18]. In our study, the rate of complications in patients ≤ 79 years was 36.8% (1491/4052), which was significantly lower in patients aged ≤ 79 years than that in patients aged ≥ 80 years. The mortality rate within 30 days for patients aged ≤ 79 years was 0.3% (12/4052), and there was no significant difference when compared to ≥ 80-year-old patients ($P = 0.13$). The mortality rate within 90 days was 0.6% (25/4052), which was significantly lower than that of patients aged ≥ 80 years (data not shown).

Secondly, we hypothesized that, similar to age, reduced surgery would have a lower complication rate than standard surgery. Therefore, we compared Group A (80–84 years) and Group B (over 85 years) regarding the rate of complications of reduced surgery (pulmonary resection area and lymph node dissection area). However, no significant difference was observed between the two groups in terms of complications and length of hospital stay. In this study, the results of HOT introduction are included in the sum of complications. When HOT induction was omitted from the total number of complications, the complication rate in Group A was 39% (125/320), and the complication rate in Group B was 43% (32/74). Other studies have reported a complication rate of 27.8–40.8% for subjects aged over 80 years; therefore, our results are equivalent to those of previous studies [16–21] (Table 5). The operative mortality rate of 1.3% in this study was lower than those cited in recent studies with large sample sizes that described a 30-day mortality ranging from 1.4% to 7.8% [16–21]. Furthermore, the rate in the current study is also comparable to the mortality rate of lung cancer resection in the total population. In our hospital, the selection rate of limited resection was 27% (20/74) in patients over 85 years old. In addition, 58% (43/74) of the patients aged 85 years or older in our hospital had a lymph node dissection range of ND0-1. In previous studies, the selectivity of limited resection was 23.1–33.2%, and 48.0–65.4% of patients had a lymph node dissection range of ND0-1 [9, 16, 19, 22]. We believe that the indications for surgical procedures in the current study were similar to those in other papers.

Table 3 Univariate analysis of survival rate for clinical-stage I (a) Group A (*N* = 259) and (b) Group B (*N* = 63)

Variables	*n*	%	5-year survival rate (%)	*P* value
(a) Group A (*N* = 259)				
Age, median (range)	81 (80–84)			
Gender				
Male	157	61	51.4	< 0.05
Female	102	39	77.2	
Past medical history				
Yes	238	92	60.8	
No	21	8	77.9	0.68
Clinical T				
Clinical T1	183	71	65.3	
Clinical T2a	76	29	52.4	0.062
Operative				
Less than lobectomy	90	35	70.4	
Lobectomy or more	169	65	56.1	0.23
Nodal dissection				
ND0-1	153	59	64.1	
ND2	106	41	57.1	0.61
Postoperative complications				
Yes	108	42	43.2	
No	151	58	74.2	< 0.05
Pathology				
Adenocarcinoma	184	71	69.8	
Non-adenocarcinoma	75	29	40	< 0.05
Pathological stage				
p-stage I	203	78	69.1	
p-stage II or advanced	56	22	33.8	< 0.05
(b) Group B (*N* = 63)				
Age, median (range)	86 (85–91)			
Gender				
Male	32	51	48.4	
Female	31	49	72.2	< 0.05
Past medical history				
Yes	59	94	73	
No	4	6	100	0.31
Clinical T				
Clinical T1	39	62	73.9	
Clinical T2a	24	38	46.9	0.19
Operative				
Less than lobectomy	20	32	38.1	
Lobectomy or more	43	68	68.6	0.21
Nodal dissection				
ND0-1	46	73	69.1	
ND2	17	27	31.4	0.26
Postoperative complications				
Yes	31	49	52.8	
No	32	51	68	0.14
Pathology				
Adenocarcinoma	51	81	65	
Non-adenocarcinoma	12	19	32.6	0.16
Pathological stage				
p-stage I	55	87	69.7	
p-stage II or advanced	8	13	15	< 0.05

ND nodal dissection

Currently, studies on standard surgical procedures for lung cancer are ongoing in the JCOG0802/WJOG4607L and JCOG0804 trials [23], and the ongoing JCOG1413 study is on lymph node dissection. In the future, it will be necessary to increase the number of surgical cases in the elderly, as well as to conduct studies on the equivalence of age-related complications.

In recent years, there have been many cases where local treatment other than surgery has been selected for patients aged 80 years or older with clinical stage I, many of whom are high-risk for surgery. Stereotactic body radiotherapy (SBRT) has emerged as an alternative to surgical treatment for lung cancer in octogenarians with favorable outcomes. Indeed, Kreinbrink reported that local control was achieved in 100% and 92.3% of octogenarian lung cancer patients at 1 and 2 years after SBRT, respectively [24]. The European Society for Medical Oncology clinical guidelines still recommends SBRT as the first-line treatment in non-operable patients [25]. In the future, a randomized trial on the differences in selecting surgery or SBRT for lung cancer in elderly will be necessary.

Multivariate analysis identified advanced pathological stage and sex (male) as significant factors that influenced long-term survival in clinical stage I patients. We narrowed down cases to clinical stage I for two reasons. The first reason is that in clinical stage I, surgery can be expected to cure the disease. However, in clinical stage II and III cases, recurrence is likely to occur, and whether or not subsequent treatment is possible depends more on the person's basic physical strength than on surgery. Another reason is that clinical stage I cases account for most of the Group A (81%) and Group B (85%) cases; in our study, postoperative complications were a prognostic predictor in Group A, but not in Group B. There were 12 cases (38%) of men and 20 cases (72%) of women, with postoperative complications (Table 3), and there were no postoperative complications in 20 (65%) men and 11 (35%) women. There were 80 cases (53%) of men and 71 cases (47%) of women, with postoperative complications (Table 3). There were no postoperative complications in 77 (71%) men and 31 (29%) women. In other words,

Table 4 Multivariate analysis of survival rate for clinical-stage I (a) Group A ($N=259$) and (b) Group B ($N=63$)

Variable	Reference	OR	95% CI	*P* value
(a) Group A ($N=259$)				
Sex (male)	Female	2.264	1.215–4.217	0.01
Postoperative complications (Yes)	No	2.061	1.228–3.461	0.006
Pathology (adenocarcinoma)	Non-adenocarcinoma	0.762	0.442–1.312	0.33
Pathological stage (p-stage II or advanced)	p-stage I	2.408	1.430–1.312	0.001
(b) Group B ($N=63$)				
Sex (male)	Female	12.08	2.821–51.692	0.001
Pathological stage (p-stage II or advanced)	p-stage I	15.88	4.123–61.16	0.0001

OR odds ratio, *CI* confidence interval

in Group B, the proportion of women with postoperative complications was higher than in the other groups, so it is possible that there was no significant difference in Table 3. Other papers have reported that advanced pathological stage, comorbidity, sex (male), coronary artery disease, and interstitial pneumonia are prognostic factors [16–19]. There are several possible reasons for these differences. First, this study was limited to preoperative stage I patients. Secondly, as expected from the country with the world's highest life expectancy (81.0 years for men and 87.1 years for women) [1], Japanese octogenarians may have better physiological and medical conditions than the elderly in other countries. Therefore, surgeons should especially consider females when selecting elderly patients most likely to achieve long-term benefit from pulmonary resection.

This study has limitations including selection bias and the lack of a comparative analysis between octogenarians and younger groups, which may have been partially mitigated by propensity matching. Furthermore, the two groups are similar, but not completely the same, and the numbers suggest bias in the patient selection (particularly in Group B). The main focus of this study was whether we could offer worthy outcomes for surgery in patients aged ≥ 85 years, compared to those aged 80–84 years. However, it is different to come to any definite conclusions given the inherent biases of the study. Indeed, we do not know how many elderly patients will visit the hospital and eventually decline surgery. Moreover, the number of patients was small because the data were collected from a single institution. Third, the study design was retrospective. Therefore, we believe that a large-scale prospective observational study is necessary in the future in order to fully address these issues.

Conclusion

In conclusion, the 2-year survival rate of elderly patients aged over 85 years was 79.0%, the 3-year survival rate was 74.7%, and the 5-year survival rate was 53.6%. In those aged over 85 years, female, and early stage (pathological stage I) were independent prognostic factors in clinical stage I non-small cell lung cancer. In a limited number of cases that were able to undergo surgery, surgical resection was safely performed for patients aged over 85 years with equivalent survival to those aged 80–84 years.

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Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest.

References

1. National Institute of Aging: Global aging. https://www.nia.nih.gov/sites/default/files/2017-06/global_health_aging.pdf. Accessed 2 Aug 2019.
2. Evans JR, Fletcher AE, Wormald RP, Ng ES, Stirling S, Smeeth L, et al. Prevalence of visual impairment in people aged 75 years and older in Britain results from the MRC trial of assessment and management of older people in the community. Br J Ophthalmol. 2002;86:795–800. https://doi.org/10.1136/bjo.86.7.795.
3. Desai M, Pratt LA, Lentzner H, Robinson KN. Trend in vision and hearing among older Americans. Aging trends. Hyattsville. MD: National Center for Health Statistics; 2001.
4. Butler AA, Menant JC, Tiedemann AC, Lord SR. Age and gender differences in seven tests of functional mobility. J Neuroeng Rehabil. 2009;6:31. https://doi.org/10.1186/1743-0003-6-31.
5. He W, Larsen LJ. U.S. Census Bureau, American Community Survey reports, ACS-29, Older Americans with a disability: 2008–2012. Washington, DC: U.S. Government Printing Office; 2014.
6. Dodds RM, Granic A, Davies K, Kirkwood TB, Jagger C, Sayer AA. Prevalence and incidence of sarcopenia in the very old: findings from the Newcastle 85 + study. J Cachexia Sarcopenia Muscle. 2017;8:229–37. https://doi.org/10.1002/jcsm.12157.
7. Goya T, Asamura H, Yoshimura H, et al. Prognosis of 6644 resected non-small cell lung cancer in Japan: a Japanese lung cancer registry study. Lung Cancer. 2005;50:227–34.
8. Zhang Z, Mostofian F, Ivanovic J, et al. All grades of severity of postoperative adverse events are associated with prolonged length

of stay after lung cancer resection. J Thorac Cardiovasc Surg. 2018;15:798–807.
9. Saji H, Ueno T, Nakamura H, et al. A proposal for a comprehensive risk scoring system for predicting postoperative complications in octogenarian patients with medically operable lung cancer: JACS1303. Eur J Cardiothorac Surg. 2018;53:835–41.
10. Rueth NM, Parson HM, Habermann EB, et al. The long-term impact of surgical complications after resection of stage I non-small cell lung cancer: a population-based survival analysis. Ann Surg. 2011;254:368–74.
11. Farjah F, Backhus L, Cheng A, et al. Failure to rescue and pulmonary resection for lung cancer. J Thorac Cardiovasc Surg. 2015;149:1365–71.
12. Bernard A, Rivera CM, Pages PB, et al. Risk model of in-hospital mortality after pulmonary resection for cancer: a national database of the French Society of Thoracic and Cardiovascular Surgery (Epithor). J Thorac Cardiovasc Surg. 2011;141:449–58.
13. Raghu G, Collard HR, Egan JJ, Martinez FJ, Bejr J, Brown KK, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. Am J Respir Crit Care Med. 2011;183:788–824.
14. Sobin LH, Gospodarowicz MK, Wittekind C. Lung and pleural tumors: UICC International Union against cancer TNM classification of malignant tumours. 7th ed. Oxford: Wiley-Blackwell; 2009. p. 138–146.
15. Travis WD, Brambilla E, Muller-Hermelink HK, Harris CC. Pathology and genetic of tumours of the lung, pleura, thymus and heart: World Health Organization classification of tumours. Lyon: IARC Press; 2004. p. 9–124.
16. Okami J, Higashiyama M, Asamura H, Goya T, Koshiishi Y, Sohara Y, et al. Pulmonary resection in patients aged 80 years or over with clinical stage I non-small cell lung cancer: prognostic factors for overall survival and risk factors for postoperative complications. J Thorac Oncol. 2009;4(10):1247–53.
17. Miura N, Kohno M, Ito K, Senba M, Kajiwara K, Hamaguchi N, et al. Lung cancer surgery in patients aged 80 years or older: an analysis of risk factors, morbidity, and mortality. Gen Thorac Cardiovasc Surg. 2015;63(7):401–5.
18. Schulkes KJG, Pouw CAM, Driessen EJM, van Elden LJR, van den Bos F, Janssen-Heijnen MLG, et al. Lung cancer in the oldest old: a nation-wide study in the Netherlands. Lung. 2017;195(5):627–34.
19. Hino H, Karasaki T, Yoshida Y, Fukami T, Sano A, Tanaka M, et al. Competing risk analysis in lung cancer patients over 80 years old undergoing surgery. World J Surg. 2019;43(7):1857–66.
20. Pagès PB, Mariet AS, Pforr A, Cottenet J, Madelaine L, Abou-Hanna H, et al. Does age over 80 years have to be a contraindication for lung cancer surgery—a nationwide database study. J Thorac Dis. 2018;10(8):4764–73.
21. Detillon DD, Veen EJ. Postoperative outcome after pulmonary surgery for non-small cell lung cancer in elderly patients. Ann Thorac Surg. 2018;105(1):287–93.
22. Shinohara S, Kobayashi K, Kasahara C, Onitsuka T, Matsuo M, Nakagawa M, et al. Long-term impact of complications after lung resections in non-small cell lung cancer. J Thorac Dis. 2019;11(5):2024–33.
23. Suzuki K, Saji H, Aokage K, Watanabe S, Okada M, Mizusawa J, et al. Comparison of pulmonary segmentectomy and lobectomy: safety results of a randomized trial. J Thorac Cardiovasc Surg. 2019;158(3):895–907.
24. Kreinbrink P, Blumenfeld P, Tolekidis G, et al. Lung stereotactic body radiation therapy (SBRT) for early-stage non-small cell lung cancer in the very elderly (≥ 80 years old): extremely safe and effective. J Geriatr Oncol. 2017;8(5):351–5.
25. Vansteenkiste J, De Ruysscher D, Eberhardt WE, et al. Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up. Ann Oncol. 2013;24(Suppl 6):ci89–98.