The Perioperative Complications for Elderly Patients with Lung Cancer Associated with a Pulmonary Resection Under General Anesthesia

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Background: Surgery for elderly patients with lung cancer is relatively common due to the increasing elderly population. This study evaluated the perioperative complications associated with surgery in patients over 70 years of age with lung cancer.

Patients and Methods: A single-center retrospective evaluation was conducted of perioperative complications (1996–2006) in lung cancer surgical patients. We reviewed and analyzed the clinical records of 364 consecutive patients over 70 years of age and 392 control patients.

Results: The mean age of the elderly group was 75.5 years old and that of the control group was 59.4 years. A segmental or wedge resection was performed more frequently for the elderly group than in the control group, whereas pneumonectomies and lobectomies were performed more frequently in the control group. Preoperative comorbidities such as cardiac and thoracic diseases were more frequently recognized in the elderly group than in the control group. The quantity of propofol used as induction anesthesia in the elderly group was significantly smaller than that of the control group, furthermore, the operation time and operation room stay time of the elderly group were significantly shorter than that of the control group, however, extubation time was significantly prolonged. The ratio of thoracic complications in the elderly group was higher than that in the control group. The ratio of pulmonary leakage in the elderly group was higher than in the control group; however, there was no significant difference in length of stay in the hospital, the ratio of operative death and hospital death between the two groups.

Conclusions: Elderly patients more frequently have perioperative complications than younger patients; however, there was no statistical difference in mortality. A pulmonary resection for elderly patients may therefore be as feasible as in younger patients.

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As in many developed countries, lung cancer is now the first leading cause of cancer death in Japan. While the number of elderly patients with lung cancer has been increasing as life expectancy has increased, the surgical treatment of non-small cell lung cancer in the elderly patients remains challenging for the general thoracic surgeon. Surgical risk increases in elderly patients, especially in those over 65.[1] Aging results in physiological changes in the cardio-vascular and respiratory system and increases the frequency of other underlying diseases. Therefore, a surgical resection for elderly patients with lung cancer has a possibility of increasing the risk of life-threatening complications; however, in the setting of thoracic surgery in the elderly, recent reports in the literature have not clearly define the mortality risk, with such rates ranging from 2.8 to 3.7%.[2–4]

The present study, aimed at retrospectively analyzing the preoperative comorbidity and perioperative complications for surgery of elderly patients older than 70 years of age who underwent a pulmonary resection for lung cancer.

PATIENTS AND METHODS

Patients

There were 756 patients with lung cancer who were treated by a pulmonary resection from January 1996 to July 2006. Among the unselected and consecutive patients, 364 patients (48.1%) were older than 70 years of age (the elderly group) and 392 (51.9%) were less than 70 (the control group). Almost all the patients underwent an electrocardiogram and a respiratory function test and if necessary, an echocardiogram, a cardiac scintigram, and a pulmonary ventilation-blood flow scintigram. In our facility, the recommended lower limit value of postresection predicted forced expiratory volume in 1 second corrected for the area of body surface to allow a surgical resection is 600 ml/m^2. The preoperative data were collected from the medical records. Clinical staging was defined according to the 6th edition of the tumor, node, metastasis criteria of the International System for Staging

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Lung Cancer.[5] Histologic typing was carried out according to the World Health Organization histologic classifications.[6] The operative data reviewed from anesthesia charts included the age, sex, height, surgical methods, anesthetic methods, anesthetic drugs, operation time, length of stay in the operating room, extubation time, impossibility of extubation, and intraoperative complications. The length of stay in the operating room was defined as the period of time from when the patient was carried into the operating room to the time patient was carried out. Similarly, the extubation time was defined as the time from when the incision was closed to extubation. The body surface area (BSA) and body mass index (BMI) were calculated using the patients' height and weight (BSA = height $(cm)^{0.725} \times$ weight $(kg)^{0.425} \times 0.007184$, BM I= weight (kg)/height $(m)^2$) at the time of surgery. The Alveolar-arterial Oxygen Difference (AaDO2) was defined as follows: $AaDO2 = PAO_2 - PaO_2$. Postoperative information, including postoperative complications and mortality, were analyzed using medical records. Operative death was defined as death within 30 days after the operation, and Hospital death was defined as death related to operation in hospital after 31st postoperative day without leaving hospital.

Operation and Anesthesia Methods

The surgical procedures and anesthesia methods for each group are shown in Table 1. An anatomic resection was followed by a complete systemic mediastinal lymph nodes dissection while segmental and wedge resections were followed by mediastinal lymph nodes sampling. All operations were performed under general anesthesia and/or epidural analgesia. Propofol was mainly used in anesthesia induction and its concentration was controlled using a target controlled infusion system (Diprifusor). In this system, the concentration of propofol was determined by the patient's age and weight.[7] The preservation of anesthesia for almost all patients was performed with sevoflurane, together with nitrous oxide gas if necessary. No epidural analgesia was used in from 2.3 to 4.4% of the patients in the two groups because of their use of anticoagulating agents such as antiplatelet or antithrombotic agents, or because of difficulty in inserting epidural

TABLE 1. Patients Characteristics

	Elderly Group (%)	Control Group (%)	p[a]
No. of patients	364	392	
Female (%)	131 (36.0)	120 (30.6)	NS
Mean age (range)	75.5 (70–90)	59.4 (20–69)	
Smoking history			0.0336
Former or current smoker	143 (39.3)	176 (44.9)	
Nonsmoker	72 (19.8)	51 (13.0)	
Unknown	149 (40.9)	165 (42.1)	
BSA[b] ($m^2 \pm$ SD[c])	1.54 ± 0.16	1.62 ± 0.17	<0.0001
BMI[d] ($kg/m^2 \pm$ SD[c])	22.4 ± 3.5	22.7 ± 3.2	NS
Clinical stage			NS
IA/IB	138 (37.9)/108 (29.7)	168 (42.9)/85 (21.7)	
IIA/IIB	7 (1.9)/28 (7.7)	9 (2.3)/19 (4.8)	
IIIA/IIIB	30 (8.2)/25 (6.9)	43 (11.0)/39 (9.9)	
IV/Unknown	21 (5.8)/7 (1.9)	20 (5.1)/9 (2.3)	
Histology[e]			NS
AD	202 (55.5)	250 (63.8)	0.0203
SQ	113 (31.0)	89 (22.7)	0.0096
LC	6 (1.6)	6 (1.5)	NS
AD-SQ	12 (3.3)	9 (2.3)	NS
SCLC	13 (3.6)	12 (3.1)	NS
Others	18 (4.9)	26 (6.6)	
Operation[f]			<0.0001
EPP/Pneumo	2 (0.5)/5 (1.4)	3 (0.8)/17 (4.3)	NS/0.0154
Lobe/Bil	236 (64.8)/16 (4.4)	296 (75.5)/13 (3.3)	0.0013/NS
Seg/Wedge	33 (9.1)/62 (17.0)	12 (3.1)/36 (9.2)	0.0005/0.0013
Exploration/other	5 (1.4)/5 (1.4)	7 (1.8)/8 (2.0)	NS/NS
Anesthesia methods			NS
Epidural + general anesthesia	348 (95.6)	383 (97.7)	
General anesthesia	16 (4.4)	9 (2.3)	

[a] NS, not significance.
[b] BSA, body surface area.
[c] SD, standard deviation.
[d] BMI, body mass index.
[e] AD, adenocarcinoma; SQ, squamous cell carcinoma; LC, large cell carcinoma; AD-SQ, adenosquamous cell carcinoma; SCLC, small cell lung cancer.
[f] EPP, extrapleural pneumonectomy; Pneumo, pneumonectomy; Lobe, lobectomy; Bil, bilobectomy; Seg, segmental resection; Wedge, Wedge resection.

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tubing and minor invasive operations by video-assisted thoracic surgery such as a wedge resection.

Statistical Analysis

Continuous variables are presented as the mean ± SD. The statistical analysis was performed using independent Student's *t*-tests for continuous variables. A χ^2 analysis was used for categorical variables. A Kruskal-Wallis test was performed to compare the medians across groups. In all statistical analyses, a p value of less than 0.05 was considered to be significant.

RESULTS

The details of the patients' preoperative characteristics are shown in Table 1. There were 233 males (64.0%) and 131 females (36.0%) in the elderly group and 272 males (69.4%) and 120 females (30.6%) in the control group. The mean age was 75.5 years (range, 70–90 years) in the elderly and was 59.4 years (range, 20–69 years) in the control group. In this study, we could review about 60% of all patients with or without smoking, and elderly patients tended to smoke less than the control patients based on their smoking history. The mean BSA and BMI of the elderly and control groups were: BSA; 1.54 and 1.62, respectively ($p < 0.0001$), BMI; 22.4 and 22.7, respectively (not significant). The elderly and control groups did not significantly differ when the stage grouping was considered. In this study, the histologic type of squamous cell carcinoma (SQ) was more frequently observed in the elderly group, whereas adenocarcinoma (AD) in the control group. A pneumonectomy or lobectomy was performed much more frequently in the control in comparison to segmental and wedge resections in the elderly. There was no significant difference in the anesthesia methods between the two groups.

Preoperative comorbidities are shown in Table 2. The elderly group had more cardiac and thoracic comorbidities than the control group. The major cardiac diseases in the elderly were hypertension, ischemic heart disease, cerebrovascular disease, arteriosclerosis obliterans, and abdominal aortic aneurysm and major thoracic diseases was emphysema.

Intraoperative observations and complications are shown in Table 3. The required amount of propofol was significantly decreased in the elderly group while that of sevoflurane showed no such statistical decrease. The ratio of propofol/BMI and propofol/BSA also showed a significant difference among the two groups, while the ratio of sevoflurane/BMI and sevoflurane/BSA showed no statistical difference between the two groups. Both the operation time and the length of stay in the operating room were significantly shorter in the elderly than in the controls, and the difference in the operation time duration is due to the fact that elderly patients underwent more limited resections in comparison to the other group. However, the extubation time was significantly increased in the elderly group. In the present study, 18 elderly patients and 14 control patients were impossible to extubate and were cared for in an intensive care unit with tracheal intubation. They were no significant differences in the ratio of patients for who it was impossible to extubate in the two groups. Furthermore, there was no significant difference in the total intraoperative cardiac complications; however, there was a higher frequency of hypertension in the elderly than in the control. Thoracic complications, especially, hypoxia, an increased AaDO2 level and atelectasis, all significantly increased in the elderly group.

TABLE 2. Preoperative Comorbidities

	Elderly Group (%)	Control Group (%)	p^a
Cardiac disease[b]	170 cases (46.7)	90 cases (23.0)	<0.0001
Hypertension	122 (33.5)	69 (17.6)	<0.0001
IHD	44 (12.1)	18 (4.6)	0.0002
CVD	34 (9.3)	20 (5.1)	0.0238
ASO	13 (3.6)	4 (1.0)	0.0181
AAA	10 (2.7)	0 (0)	0.0010
Thoracic disease[c]	94 cases (25.8)	68 cases (17.3)	0.0045
Emphysema	48 (13.2)	24 (6.1)	0.0009
Old TB	25 (6.9)	20 (5.1)	NS
Fibrosis/IP	16 (4.4)	8 (2.0)	NS
Asthma	12 (3.3)	10 (2.6)	NS
Bronchiectasis	4 (1.1)	1 (0.3)	NS
Others[d]	86 cases (23.6)	71 cases (18.1)	NS
DM	49 (13.5)	41 (10.5)	NS
Liver disorder	15 (4.1)	15 (3.8)	NS
Renal disorder	13 (3.6)	11 (2.8)	NS
Rheumatic disease	7 (1.9)	6 (1.5)	NS

[a] NS, not significance.
[b] IHD, ischemic heart disease; ASO, arterio sclerosis obliterance; AAA, abdominal aortic aneurysm; CVD, cerebrovascular disease.
[c] IP, interstitial pneumonia; TB, tuberculosis.
[d] DM, diabetes mellitus.

Postoperative complications and mortality due to the operation are shown in Table 4. Postoperative cardiac complications between the two groups showed no statistical difference. The total postoperative thoracic complications showed statistical differences, specifically, the ratio of pulmonary leakage was significantly prolonged in the elderly group ($p = 0.0070$) and this complication statistically influenced the total thoracic complications ($p = 0.0375$). In this series, the length of hospital stay, operative death and hospital death showed no statistical difference between the two groups.

DISCUSSION

The definition of an older or elderly person was proposed by the World Health Organization.[8] According this definition, most developed world countries have accepted the chronological age of 65 years as a definition of an elderly person. However, a survey of the Organization of the Japanese Ministry of Health, Labor and Welfare showed most Japanese persons felt that elderly age was defined as more than 70 years.[9] In this present study, an elderly age was defined as 70 years and the correlation between surgical complications and age were analyzed.

In recent years, the number of patients with AD, especially nonsmokers or females, increased and those with SQ

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TABLE 3. Intraoperative Stats and Complications

	Elderly Group (%)	Control Group (%)	p^a
Anesthetic[b]			
Propofol (mg ± SD)	375.8 ± 299.2	493.3 ± 399.5	<0.0001
Revised propo value (BMI)	16.7 ± 12.7	21.7 ± 17.0	<0.0001
Revised propo value (BSA)	241.9 ± 186.0	301.7 ± 234.3	0.0001
Sevoflurane (ml ± SD)	82.2 ± 46.0	86.5 ± 45.1	NS
Revised sevo value (BMI)	3.7 ± 2.2	3.9 ± 2.1	NS
Revised sevo value (BSA)	53.6 ± 29.7	53.3 ± 27.5	NS
Operation time (min ± SD)	203.8 ± 83.9	224.3 ± 87.2	0.0011
OR[c] stay time (min ± SD)	309.8 ± 87.3	323.6 ± 94.4	0.0377
Difficult thoracheal intubation	10 (2.7)	5 (1.3)	NS
Extubation time (min ± SD)	28.2 ± 19.0 (n = 346)	23.6 ± 12.9 (n = 378)	0.0001
Impossibility of extubation	18 (4.9)	14 (3.6)	NS
Cardiac disease	254 cases (69.8)	261 cases (66.6)	NS
Hypotension	186 (51.1)	217 (55.4)	NS
Hypertension	58 (15.9)	31 (7.9)	0.0006
Arrythmia	62 (17.0)	76 (19.4)	NS
Thoracic disease	64 cases (17.6)	46 cases (11.7)	0.0227
Hypoxia	19 (5.2)	9 (2.3)	0.0334
Hypercapnia	14 (3.8)	16 (4.1)	NS
AaDO2[d] ↑	30 (8.2)	16 (4.1)	0.0168
Atelectasis	9 (2.5)	2 (0.5)	0.0244

[a] NS, not significance.
[b] SD, standard deviation; BMI, body mass index; BSA, body surface area.
[c] OR, operation room.
[d] AaDO2, Alveolar-arterial oxygen gradient.

TABLE 4. Postoperative Complications and Mortality

	Elderly group (%)	Control group (%)	P^a
Cardiac disease	16 cases (4.4)	17 cases (4.3)	NS
Heart failure	1 (0.3)	5 (1.3)	NS
Arrythmia	13 (3.6)	14 (3.6)	NS
Cerebral infarction	3 (0.8)	1 (0.3)	NS
Thoracic disease	87 cases (23.9)	69 cases (17.6)	0.0325
Respiratory failure	5 (1.4)	11 (2.8)	NS
Pneumonia	10 (2.7)	11 (2.8)	NS
Pulmonary leakage	51 (14.0)	31 (7.9)	0.0070
Bronchial leakage	7 (1.9)	11 (2.8)	NS
Chyle leakage	8 (2.2)	4 (1.0)	NS
Empyema	4 (1.1)	9 (2.3)	NS
Atelectasis	4 (1.1)	4 (1.0)	NS
Pulmonary embolization	1 (0.3)	0 (0)	NS
Others	12 cases (3.3)	20 cases (5.1)	NS
Liver disorder	2 (0.5)	4 (1.0)	NS
Renal disorder	1 (0.3)	4 (1.0)	NS
Infection	1 (0.3)	1 (0.3)	NS
Bleed	2 (0.5)	6 (1.5)	NS
Length of stay[b] (day)	18.1	20.4	NS
Operative death	6 cases (1.6)	5 cases (1.3)	NS
Hospital death	7 cases (1.9)	3 cases (0.8)	NS

[a] NS, not significance.
[b] Except for patients with operative death.

decreased in Japan.[9] In the current data, 452 of 756 patients (59.8%) had AD and 202 of 756 patients (26.7%) had SQ. These data can be attributed to the fact that the rate of smoking has decreased, whereas, the rate of women smokers has increased in Japan.[9] With regard to the surgical methods, these data was almost as same as a previously report of a multicenter survey for octogenarians[10] and the current study showed that more than 65% of the elderly patients underwent a lobectomy and/or a pneumonectomy with less frequent fatal complications. In addition, there were no statistical differences in the anesthesia methods between the two groups. Lung cancer surgery, including a lobectomy and systematic lymph node dissection, was feasible for elderly patients if the thoracic and cardiovascular functions were tolerable for surgery. The preoperative comorbidities are shown in Table 2. Clearly, cardiac and thoracic comorbidities were more frequent in the elderly group than in the control group. Hypertension, ischemic heart disease, abdominal aortic aneurism, and emphysema were found more frequently in the elderly than in the controls. It is important to prevent perioperative complications and control preoperative comorbidity in elderly patients before surgery.

The surgical outcomes are shown in Table 3. The induction of anesthesia was performed with propofol followed by sevoflurane. The quantity of propofol in control was significantly greater than in the elderly, whereas that of sevoflurane showed no difference between the two groups. The quantity of these anesthesia drugs was adjusted by the BMI and BSA to clarify the differences between the two

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groups. The quantity of propofol and its revised value in the controls were statistically greater than in the elderly. Furthermore, there was a similar tendency with sevoflurane. However, the extubation time was obviously longer in the elderly than in the control group. Elderly patients are normally able to undergo anesthesia with a smaller dose of anesthetics. This might suggest that the quantity of anesthetics for the elderly was unexpectedly excessive and the anesthesia for elderly might require a smaller dose if their general conditions are tolerable for surgery and general anesthesia. Thoracic complications occurred more frequently in the elderly than in the controls, especially, hypoxia, increasing AaDO2 and atelectasis. This was probably because elderly patients had poorer pulmonary functions than the controls and, in particular, there was a comparatively higher incidence of atelectasis due to hypersecresion, such as emphysema, old-tuberculosis and the results of long years of smoking. In this investigation, we confirmed that about 40% of the elderly patients had a smoking history, and these elderly patients with a history of smoking statistically had much more postoperative complications, especially thoracic complications, than those with no history of smoking (data not shown). Furthermore, the poor pulmonary function observed in the elderly may explain the increased incidence of postoperative thoracic complications such as pulmonary leakage due to emphysema, as shown in Table 4. Regarding the forced expiratory volume in 1 second/BSA value after a pulmonary resection, we considered a setting higher than 600 ml/m^2 to be necessary in elderly patients. However, there was no difference of intra and postoperative complications between the two groups in spite of the greater frequency of preoperative cardiac comorbidities in the elderly than in the controls. The use of thoracic epidural anesthesia for coronary artery bypass grafting and ischemic heart disease has focused predominantly on its advantageous effects on coronary blood flow and hemodynamic stability.[11,12] Therefore, proper anesthesia may have steadied the cardiac function and decreased both the number of intra- and postoperative complications.

In the present investigation, there were six operative deaths among the elderly and five among the control patients. The reasons for operative death were as follows: for the elderly; three respiratory failures due to a bronchial fistula, one cerebral infarction, one pulmonary embolization and one hemoptysis due to a pulmonary-bronchial fistula, for the controls; three respiratory failures due to acute interstitial pneumonia, one intraoperative circulation failure and one esophageal fistula. Thoracic complications introduced the possibility of fatal complications for not only the elderly but also the control group and these should therefore be prevented. However, there were no statistical differences in the incidence of operative death, hospital death, and length of stay in hospital between the elderly and control patients. With regard to the operation, 7 elderly patients (1.9%) had undergone a pneumonectomy including an extrapleural pneumonectomy, however, these patients had no serious perioperative complications and all were discharged from the hospital without any trouble.

In conclusion, though there may be a possibility of bias regarding our data due to the fact that it was only a single-center retrospective study, pulmonary resections may be as feasible in elderly patients as in younger patients if the elderly patients are carefully selected and perioperative complications can also be sufficiently prevented.

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