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Risk factors for postoperative complications and long-term survival in lung cancer patients older than 80 years†

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Abstract

OBJECTIVES: The number of octogenarian lung cancer patients undergoing radical surgery has been increasing recently. However, knowledge regarding the risk factors for postoperative complications and reliable predictive factors for long-term survival is limited. This study aimed to investigate the risk factors of postoperative complications, and reliable prognostic factors, in lung cancer patients older than 80 years.

METHODS: Lung cancer patients aged 80 years or older who underwent radical surgery were retrospectively studied; a multi-institutional analysis was conducted from January 1998 to December 2015. Preoperative and postoperative clinical data, including age, gender, smoking history, body mass index, respiratory function, Charlson Comorbidity Index, Glasgow Prognostic Score, surgical procedure, cancer histology, clinical and pathological stage, surgical result and survival time, were collected.

RESULTS: A total of 337 patients, comprising 216 (64.1%) men and 121 (35.9%) women were enrolled. The median age was 82 (range 80–92) years. Of the 337 patients, 205 (60.8%) had preoperative comorbidities. Postoperative complications were observed in 119 (35.3%) patients; postoperative mortalities occurred in 6 (1.8%) patients. Univariate and multivariate analyses showed that male gender ($P = 0.01$) and operation time ($P = 0.047$) were associated with postoperative complications; in contrast, pathological Stage III ($P < 0.001$), male gender ($P = 0.01$), Charlson Comorbidity Index ≥ 2 ($P = 0.03$) and Glasgow Prognostic Score = 1/2 ($P = 0.04$) were independent prognostic factors for overall survival.

CONCLUSIONS: The risk factors for postoperative complications (male gender and operation time) and the predictive factors affecting long-term survival (male gender, Charlson Comorbidity Index, Glasgow Prognostic Score and P-stage) should be taken into account for the effective management of patients older than 80 years with lung cancer, undergoing surgery.

Keywords: Octogenarian • Multi-institutional analysis • Lung cancer surgery • Prognostic marker

INTRODUCTION

The number of elderly lung cancer patients, including octogenarians, has been increasing recently [1, 2]. According to the retrospective analyses for lung cancer surgery in octogenarians, the morbidity and the mortality rates were 8.4–48.0% and 1.1–8.8%, respectively; the 5-year overall survival rate was 27.0–57.5% [3–8]. Although these results are relatively acceptable, data regarding lung cancer are limited, and the surgical results and the risk evaluation in large elderly cohorts, particularly in octogenarians, were unclear. Apart from cancer staging, several useful prognostic scores that could predict long-term survival were reported. The Charlson Comorbidity Index (CCI) that was formulated in 1987 stipulates that 19 comorbidities have a significant effect on survival in breast cancer patients and has also been applied to primary lung cancer patients [9–11]. The more recent Glasgow Prognostic Score (GPS) that was first reported in 2001 stipulates that systemic inflammatory response predicted survival time of cancer patients, including lung cancer patients [12–14]. However, few studies for both CCI and GPS in an elderly cohort have been conducted. Therefore, this study

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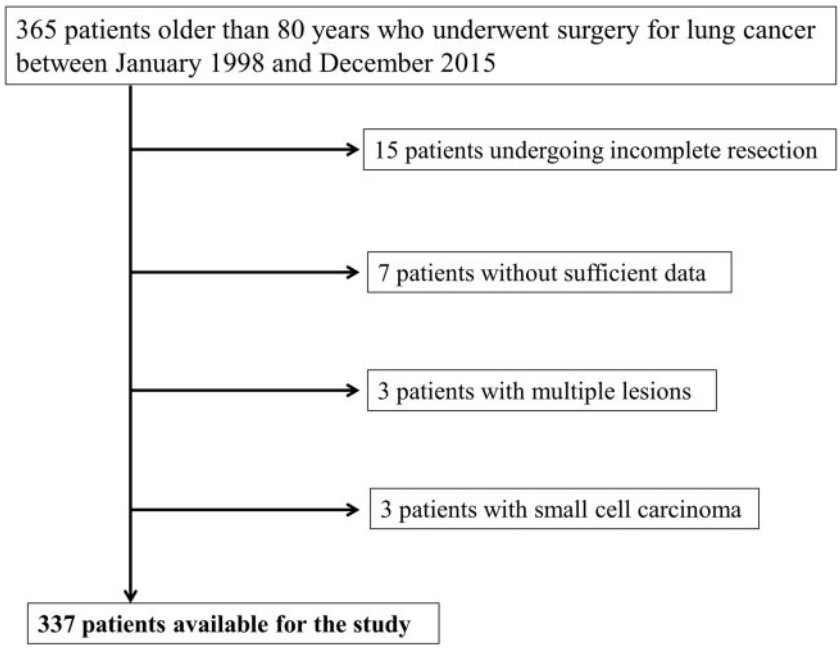

Figure 1: Flow chart of the number of patients eligible for this study.

aimed to analyse the surgical results and elucidate the risk factors for postoperative complication and the long-term predictive values for lung cancer patients in octogenarians undergoing radical surgery in Japanese multi-institutional cohorts.

MATERIALS AND METHODS

This study included lung cancer patients aged 80 years or older who underwent surgery at any of the 7 institutions from January 1998 through December 2015. Clinical characteristics, including age, gender, preoperative comorbidity, preoperative blood test results [C-reactive protein (CRP) and albumin levels], respiratory function, tumour histology, clinical and pathological stage (C-stage and P-stage), operative procedure, operative time, postoperative complication, survival time and cause of death, were retrospectively collected from the databases of each institute. The preoperative examination for cancer staging included computed tomography of the chest and upper abdomen, computed tomography or magnetic resonance imaging of the brain and bone scintigraphy or ^{18}F-fluorodeoxyglucose–positron emission tomography. Although endobronchial ultrasonography was performed in selected cases, mediastinoscopy was not performed in 7 institutes. The tumour stage was determined according to the seventh edition of the tumour, node and metastasis (TNM) staging system of the International Union for Cancer Control; the histological tumour type was determined according to the third edition of the World Health Organization (WHO) classification [15, 16]. Operative indication was determined based on the following factors decided on by the surgeons of each institute: performance status, 0–1; postoperative predicted forced expiratory volume in 1 s, ≥800 ml [17]; clinical Stage, I–IIIA expected to be completely resectable; and mental status, not senile. Limited lung resection, defined as partial resection in this study, was selected if the patient had lower pulmonary function or multicomorbidities. Video-assisted thoracic surgery was treatment option, but if a patient was contraindicated for video-assisted thoracic surgery, open thoracotomy was used. Contraindications for video-assisted thoracic surgery included pulmonary artery or bronchial plasty, chest wall resection or the presence of giant tumour. The CCI was scored according to 19 preoperative comorbidities; this method was consistent with that of Charlson *et al.* [9]. The GPS was defined as follows: score 0, albumin level ≥3.5 g/dl and CRP level <0.5 mg/dl; score 1, albumin level <3.5 g/dl or CRP level ≥0.5 mg/dl and score 2, albumin level <3.5 g/dl and CRP ≥0.5 mg/dl. This was similar to that of by McMillan *et al.* [12]. The National Clinical Database (NCD) in Japan defined postoperative pulmonary complication as follows: pulmonary fistula is prolonged air leakage over 7 postoperative days or the need for reoperation or pleurodesis. Postoperative pneumonia is the new infiltration on chest roentgenogram (X-P) or computed tomography, which needed antibiotics therapy. Respiratory failure was defined as management with a ventilator over 2 postoperative days or the need for reintubation or tracheotomy. The overall survival time was calculated from the date of surgery to the time of death or the last follow-up. The Research Review Board at The University of Tokyo Graduate School of Medicine (approval number 11146) and the respective ethics committees of the other 6 institutions approved this study. Statistical analysis was performed using JMP 12.0 pro (SAS institute Inc., Cary, NC, USA). The unpaired *t*-test was used for continuous variables. The Spearman's correlation analysis was used to assess the covariant of 2 variables. The risk factors for postoperative complications were assessed using univariate and multivariate logistic regression analyses. P-stage was analysed as a categorical variable. Survival curves were calculated via the Kaplan–Meier method; differences in survival were assessed using the log-rank test. Univariate and multivariate analyses for long-term survival were calculated via the Cox proportional hazard model. A *P*-value <0.05 was considered statistically significant.

RESULTS

A total of 365 patients aged 80 years or older who underwent surgery for lung cancer were initially enrolled, but 28 were excluded due to incomplete resection [15], insufficient data [7],

Table 1: Clinical characteristics of the 337 octogenarian lung cancer patients who underwent radical surgery

Clinical characteristics	
Male/female	216/121
Age (years)	80–92 (median 82)
Body mass index	15.1–31.8 (mean 22.5)
Brinkman index 0/<200/<600/≥600/unknown	120/12/41/158/6
%VC (%)	50.5–162.6 (mean 99.7)
FEV_1/FVC (%)	31.0–98.7 (mean 69.0)
Preoperative comorbidity (yes), *n* (%)	207 (61.4)
Clinical tumour size (cm)	0.8–9.4 (mean 2.9)
Clinical lymph node stage (N0/N1/N2)	299/24/14
Clinical stage (IA/IB/IIA/IIB/IIIA)	191/86/31/14/15
Procedure, *n* (%)	
Partial resection	66 (19.6)
Segmentectomy	28 (8.3)
Lobectomy	237 (70.3)
Bilobectomy	5 (1.5)
Pneumonectomy	1 (0.3)
Surgical approach, *n* (%)	
Thoracotomy	78 (23.1)
Hybrid VATS	97 (28.8)
VATS	146 (43.3)
Conversion to thoracotomy	16 (4.7)
Era change for surgical procedure of VATS, *n* (%)	
1998–2005	19/46 (41.3)
2006–2015	224/291 (77.0)
Lymph node dissection, *n* (%)	
ND0	82 (24.3)
ND1	105 (31.2)
ND2	145 (43.0)
Unknown, others, *n* (%)	5 (1.5)
Operation time (min)	37–604 (mean 211.8)
Bleeding (ml)	0–4338 (mean 218.7)
Pathological tumour size (cm)	0.6–11.0 (mean 3.1)
Pathological lymph node stage (N0/N1/N2/Nx)	216/28/27/66
Pathological stage (IA/IB/IIA/IIB/IIIA)	191/86/31/14/38
Histology (Ad/Sq/others)	217/90/30
Drainage time (days)	1–26 (median 4)
Postoperative stay (days)	3–391 (median 11)
Postoperative adjuvant therapy for pathological stage IIIA (none/chemotherapy/radiotherapy/chemoradiotherapy)	30/5/2/1
Observation time (months)	0.1–152.8 (median 29.9)

Ad: adenocarcinoma; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; VATS: video-assisted thoracoscopic surgery; ND: lymph node dissection; ND0: without any lymph node dissection; ND1: hilar lymph node dissection; ND2: hilar and mediastinal lymph node dissection; Sq: squamous cell carcinoma; VC: vital capacity.

Table 2: Prevalence of comorbidity scored via the CCI and the GPS

Score	Comorbidity	*n* (%)	Total score of CCI	*n* (%)
1	Coronary artery disease	44 (13.1)	0	132 (39.2)
1	Congested heart failure	3 (0.9)	1	68 (20.2)
1	Peripheral vascular disease	8 (2.4)	2	87 (25.8)
1	Cerebrovascular disease	24 (7.1)	3	40 (11.9)
1	Dementia	3 (0.9)	4	6 (1.8)
1	Chronic pulmonary disease	24 (7.1)	5	2 (0.6)
1	Connective tissue disease	15 (4.5)	6	1 (0.3)
1	Peptic ulcer disease	33 (9.8)	7	0 (0)
1	Mild liver disease	0 (0)	8	1 (0.3)
1	Diabetes	45 (13.4)	Total	337 (100)
2	Hemiplegia	2 (0.6)		
2	Moderate-to-severe renal disease	1 (0.3)		
2	Diabetes with organ damage	5 (1.5)		
2	Any prior tumour (within 5 years)	86 (25.5)		
2	Leukaemia	0 (0)		
2	Lymphoma	1 (0.3)		
3	Moderate-to-severe liver disease	0 (0)		
6	Metastatic solid tumour	2 (0.6)		
6	AIDS	0 (0)		
Score	Preoperative state	*n* (%)	Total score of GPS	*n* (%)
0	Albumin ≥3.5 g/dl and CRP <0.5 mg/dl	240 (71.2)	0	240 (71.2)
1	Albumin <3.5 g/dl and CRP <0.5 mg/dl	11 (3.3)	1	
1	Albumin ≥3.5 g/dl and CRP ≥0.5 mg/dl	49 (14.5)	1	60 (17.8)
2	Albumin <3.5 g/dl and CRP ≥0.5 mg/dl	20 (5.9)	2	20 (5.9)
	Unknown	17 (5.0)	Unknown	17 (5.0)
			Total	337 (100)

AIDS: acquired immune deficiency syndrome; CCI: Charlson Comorbidity Index; CRP: C-reactive protein; GPS: Glasgow Prognostic Score.

multiple lesions [3] and diagnosis of small-cell carcinoma [3]. Finally, 337 patients were included for analysis (Fig. 1). The clinical characteristics of these patients are presented in Table 1. Preoperative comorbidity was noted in 205 (60.8%) patients; 237 (70.3%) patients underwent radical lobectomy, and mediastinal lymph node dissection was performed in 145 (43.0%) patients. The prevalence of the comorbidity in accordance with the CCI score and the GPS is described in Table 2. The most common comorbidity was malignant disease within 5 years (86 cases, 25.5%). A total of 119 (35.3%) patients developed postoperative complications, whereas 6 (1.8%) patients died due to surgery-related causes (Table 3). Thirty-day mortality was observed in 4 patients, whereas 90-day mortality was observed in only 1 patient. According to the univariate and multivariate logistic regression analyses, male gender (odds ratio 2.18, $P = 0.01$) and operation time (odds ratio 5.89, $P = 0.047$) were independent significant risk factors for postoperative complications (Table 4). The results of Cox proportional hazards model of the univariate and multivariate analyses for long-term survival are presented in Table 5. P-stage [P-stage III: hazard ratio (HR) 4.07, $P < 0.001$), male gender (HR 2.09, $P = 0.01$), CCI ≥2 (HR 2.25, $P = 0.03$) and GPS = 1/2 (HR 2.12, $P = 0.04$) were significant risk factors for poor overall survival. The 5-year overall and recurrence-free survival rates of all 337 patients were 66.1% [95% confidence interval (CI) 59.5–72.1%] and 60.3% (95% CI 53.8–66.4%), respectively. The Kaplan–Meier curves stratified based on gender, CCI, GPS and P-stage are shown in Fig. 2A–D, respectively. The 5-year overall survival rates were 57.7% (95% CI

Table 3: Prevalence of postoperative complications, surgery-related deaths and long-term outcome

	n (%)
Postoperative complications	
Pulmonary fistula	41 (12.1)
Postoperative pneumonia	35 (10.3)
Arrhythmia	21 (6.2)
Delirium	11 (3.2)
Chylothorax	10 (2.9)
Respiratory failure	9 (2.7)
Empyema	8 (2.3)
Atelectasis	7 (2.1)
Brain infarction/bleeding	5 (1.5)
Postoperative reoperation	5 (1.5)
Postoperative bleeding	4 (1.2)
Heart failure	4 (1.2)
Renal failure	3 (0.9)
Exacerbation of interstitial pneumonia	3 (0.9)
Recurrent nerve palsy	2 (0.6)
Wound abscess	2 (0.6)
Liver failure	1 (0.3)
Total	119 (35.3)
Causes of surgery-related deaths	
Exacerbation of interstitial pneumonia	3 (0.9)
Postoperative pneumonia	2 (0.6)
Asthma	1 (0.3)
Total	6 (1.8)
Long-term outcome	
Alive without cancer	174 (51.6)
Alive with cancer	40 (11.9)
Died of cancer	52 (15.4)
Died of non-cancer-related death	44 (13.1)
Died of surgery-related death	6 (1.8)
Unknown	21 (6.2)
Total	337 (100)

50.4–66.7%) and 79.0% (68.2–86.9%) for the male and female patients, 74.0% (95% CI 66.3–80.6%) and 52.3% (95% CI 40.7–63.7%) for the patients with CCI = 0 or 1 and CCI ≥2 and 70.6% (95% CI 62.9–77.3%) and 48.5% (95% CI 33.6–63.7%) for the patients with GPS = 0 and GPS 1/2, respectively ($P < 0.001$). The 5-year overall survival rates in P-Stage I, II and III were 72.8% (95% CI 65.2–79.3%), 54.3% (95% CI 39.3–68.6%) and 41.9% (95% CI 23.7–62.5%), respectively (P-Stage I vs II: $P = 0.002$ and P-stage II/III: $P = 0.55$). The 5-year recurrence-free survival rates were 62.1% (95% CI 54.3–69.4%) and 60.0% (95% CI 44.6–66.8%) for the patients with CCI = 0 or 1 and CCI ≥2 ($P = 0.92$) and 63.1% (95% CI 55.6–70.0%) and 48.5% (95% CI 33.3–64.0%) for the patients with GPS = 0 and GPS 1/2 ($P = 0.03$) (Supplementary Material, Figs S1A and B). The 5-year disease-specific survival rates were 85.3% (95% CI 78.2–90.3%) and 70.4% (95% CI 57.5–80.7%) for the patients with CCI = 0 or 1 and CCI ≥2 ($P = 0.01$) and 81.7% (95% CI 76.1–88.2%) and 70.7% (95% CI 54.4–83.0%) for the patients with GPS = 0 and GPS 1/2 ($P = 0.06$) (Supplementary Material, Figs S1C and D). The Spearman's correlation analysis revealed that CCI was not significantly correlated with the GPS ($P = 0.16$) and that the GPS and P-stage and CCI and P-stage had no correlations either ($P = 0.80$ and $P = 0.82$, respectively; Supplementary Material, Fig. S2). The combined analysis of the GPS and the CCI revealed that the 5-year overall survival rates were 77.8% (95% CI 68.7%–84.8%) in patients with CCI = 0 or 1 and GPS = 0, 57.1% (95% CI 45.8%–67.7%) in patients with either CCI ≥2 or GPS = 1/2 and 36.6% (95% CI 16.7–62.4%) in patients with a CCI ≥2 and GPS = 1/2 ($P < 0.001$; Fig. 3).

DISCUSSION

Recently, the number of elderly lung cancer patients undergoing radical surgery has been increasing, particularly in Japan. In this study, data from a large number of lung cancer patients with Stage I–IIIA disease aged 80 years or older who had undergone surgery were collected, and the analysis results were acceptable and relatively superior to prior studies [3–8]. The most common complications after lung surgery in elderly patients are arrhythmia, postoperative pneumonia and prolonged air leak; these results were the same in this study [4–8]. Preoperative coronary artery disease, chronic obstructive pulmonary disease and CCI are significant risk factors for postoperative complications after lung cancer surgery [18–21]. In contrast, another Japanese cohort study demonstrated that the development of complications in 57 consecutive lung cancer patients was not associated with a CCI score of over 2 [22]. This study revealed that male gender and operation time were the significant risk factors for postoperative complications. The difference between the results from prior studies and that of this study might be due to patient selection bias and the surgeon's choice of procedure. First, in our study, almost 40% of the patients had no preoperative comorbidity. Second, limited lung resection (partial resection) was performed in 48 of 287 (16.7%) patients with CCI = 0, 1 or 2; limited lung resection was performed in 18 of 50 (36.0%) patients who had a CCI ≥3 ($P = 0.001$). These results demonstrated that the surgeons preferred minimal resection for patients with multiple comorbidities to reduce the postoperative complications. Operation time, which has a large influence on the extent of lung resection, was found to have a significant effect on postoperative morbidity in our cohort.

Any surgical procedure, e.g. lymph node dissection, is critical for elderly patients. In our study, mediastinal lymph node dissection did not have any impact on postoperative complication and long-term survival. In a previous study, lymph node dissection was highly frequent in elderly patients over 70 years old because of a higher incidence of advanced lymph node metastases in elderly than in young patients [23]. In contrast, pulmonary resection without complete mediastinal lymph node dissection should be considered in octogenarians, because it had a minimal effect on long-term survival and had a low risk of worsening performance status at discharge [24]. It is assumed that more cardiopulmonary comorbidities, frailty and longer operation time had an influence on the postoperative complications and performance status. Therefore, the indication for lymph node dissection must be considered carefully based on comorbidities, gender and several prognostic markers, including the CCI and the GPS.

As for other important alternative treatments, stereotactic body radiotherapy has been indicated, especially for multiple comorbid elderly lung cancer patients. Although the number was limited, equivalent results in regards short- and long-term survival following stereotactic body radiotherapy, in comparison with surgery, have also been reported recently [25]. Analyses on stereotactic body radiotherapy with a greater number of patients might provide more precise information on morbidity and mortality, and long-term survival in the near future.

In terms of the prognostic markers other than CCI and GPS, long-term survival was affected by male gender, extent of lung resection, dyspnoea and P-stage in 294 octogenarian lung cancer

Table 4: Univariate and multivariate logistic regression analyses of variables associated with postoperative minor and major complications

Variables	Complicated group (119 cases)	Non-complicated group (218 cases)	Univariate analysis		Multivariate analysis	
			Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Age (years)	80–92 (mean 82.5)	80–91 (mean 82.2)	1.06 (0.96–1.17)	0.28		
Gender (male/female)	92/27	124/94	2.58 (1.57–4.34)	<0.001	2.06 (1.13–3.84)	0.02*
BI (≥600/<600)	68/49	90/124	1.91 (1.21–3.03)	0.005	1.27 (0.70–2.29)	0.42
Body mass index	17.1–30.1 (mean 22.5)	15.1–31.8 (mean 22.5)	1.00 (0.93–1.07)	0.92		
%VC	50.5–144.4 (mean 96.6)	57.0–162.6 (mean 101.4)	0.98 (0.97–0.997)	0.02	0.99 (0.97–1.00)	0.15
FEV_1/FVC	38.0–97.7 (mean 69.6)	31–98.7 (mean 68.6)	1.00 (0.99–1.03)	0.50		
Coronary artery disease (yes/no)	12/107	33/185	0.63 (0.30–1.24)	0.18		
Diabetes mellitus (yes/no)	17/102	28/190	1.13 (0.58–2.15)	0.71		
Comorbidity (yes/no)	81/38	124/94	1.62 (1.02–2.60)	0.04	1.21 (0.72–2.04)	0.48
GPS (1 or 2/0)	29/83	51/156	1.08 (0.63–1.81)	0.78		
CCI (≥2/0 or 1)	68/51	86/132	1.15 (0.73–1.81)	0.54		
Procedure (radical/limited)	113/16	168/50	1.92 (1.06–3.63)	0.03	1.46 (0.70–3.11)	0.31
Surgical approach (VATS/thoracotomy)	85/34	158/60	1.05 (0.63–1.72)	0.84		
LN dissection (ND2/ND0 or ND1)	54/63	91/124	1.16 (0.74–1.84)	0.50		
Operative time (min)	52–551 (mean 232.5)	37–604 (mean 200.0)	9.53 (2.28–42.42)	0.002	5.89 (1.04-35.94)	0.047*
Haemorrhage (mL)	0–4030 (mean 278.8)	0–4338 (mean 183.9)	1.00 (0.99–1.00)	0.07		
Pathology (non-Ad/Ad)	49/70	66/152	1.61 (1.01–2.57)	0.04	1.16 (0.67–1.99)	0.60
P-stage (I/II/III)	74/31/14	165/29/24	P-Stage I 1			
			P-Stage II 2.38 (1.34–4.26)	0.003		
			P-Stage III 1.30 (0.62–2.63)	0.47		

Ad: Adenocarcinoma; BI: Brinkman index; CCI: Charlson Comorbidity Index; CI: confidence interval; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; GPS: Glasgow Prognostic Score; limited: limited lung resection; LN: lymph node; ND: lymph node dissection; ND0: without any lymph node dissection; ND1: hilar lymph node dissection; ND2: hilar and mediastinal lymph node dissection; P-stage: pathological stage; radical: radical lung resection; VATS: video-assisted thoracoscopic surgery; VC: vital capacity.

Table 5: Univariate and multivariate analyses with Cox proportional hazards model for overall survival in 337 lung cancer octogenarians who underwent surgery

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Age (years)	1.00 (0.91–1.10)	0.95		
Gender (male/female)	2.40 (1.52–3.94)	<0.001	2.22 (1.21–4.21)	0.01*
BI (≥600/<600)	2.12 (1.41–3.22)	<0.001	1.51 (0.87–2.66)	0.14
Body mass index	0.96 (0.90–1.03)	0.25		
%VC	0.99 (0.97–0.99)	0.01	0.99 (0.98–1.01)	0.38
FEV_1/FVC	1.00 (0.98–1.01)	0.72		
GPS (1 or 2/0)	2.16 (1.38–3.33)	0.001	1.82 (1.04–3.11)	0.04*
CCI (≥2/0 or 1)	1.88 (1.09–3.30)	0.02	1.70 (1.09–2.68)	0.02*
Procedure (limited/radical)	1.16 (0.70–1.84)	0.55		
LN dissection (ND2/ND0 or ND1)	0.78 (0.52–1.16)	0.23		
Surgical approach (VATS/thoracotomy)	0.66 (0.45–0.99)	0.046	0.84 (0.53–1.37)	0.48
Postoperative complication (yes/no)	1.19 (0.79–1.78)	0.40		
Pathology (non-Ad/Ad)	1.62 (1.08–2.41)	0.02	0.76(0.44–1.30)	0.32
P-stage (I, II, III)	P-Stage I 1		1	
	P-Stage II 2.11 (1.29–3.37)	0.004	1.59 (0.88–2.75)	0.12
	P-Stage III 2.49 (1.44–4.11)	0.002	4.06 (2.12–7.42)	<0.001*

Ad: adenocarcinoma; BI: Brinkman index; CCI: Charlson Comorbidity Index; CI: confidence interval; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; GPS: Glasgow Prognostic Score; HR: hazard ratio; limited: limited lung resection; ND: lymph node dissection; ND0: without any lymph node dissection; ND1: hilar lymph node dissection; ND2: hilar and mediastinal lymph node dissection; P-stage: pathological stage; radical: radical lung resection; VATS: video-assisted thoracoscopic surgery; VC: vital capacity.

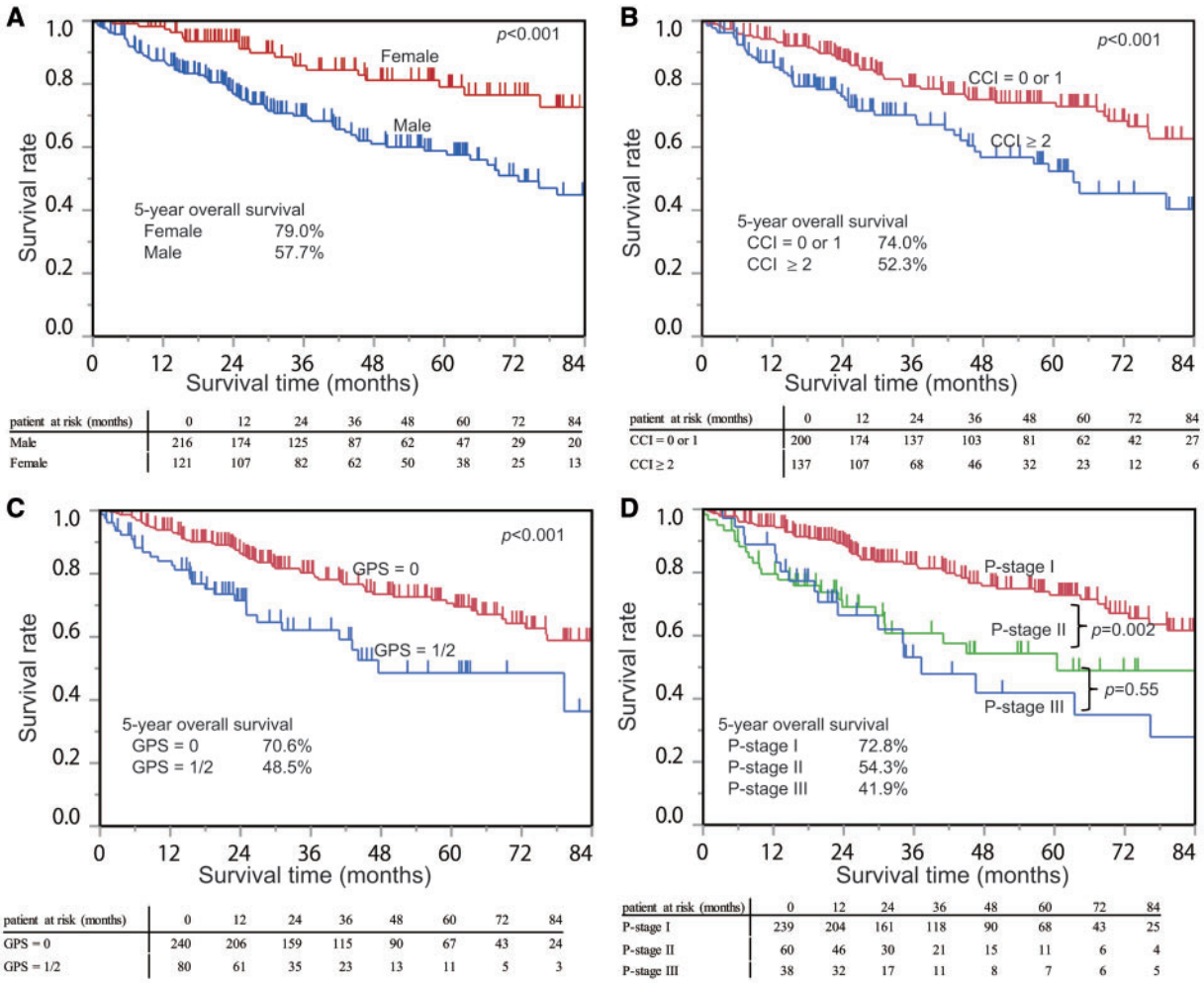

Figure 2: Comparisons of overall survival curves between (**A**) male and female, (**B**) CCI = 0 or 1 and CCI ≥2, (**C**) GPS = 0 and 1/2 and (**D**) P-stage I, II and III patients. CCI: Charlson Comorbidity Index; GPS: Glasgow Prognostic Score; P-stage; pathological stage.

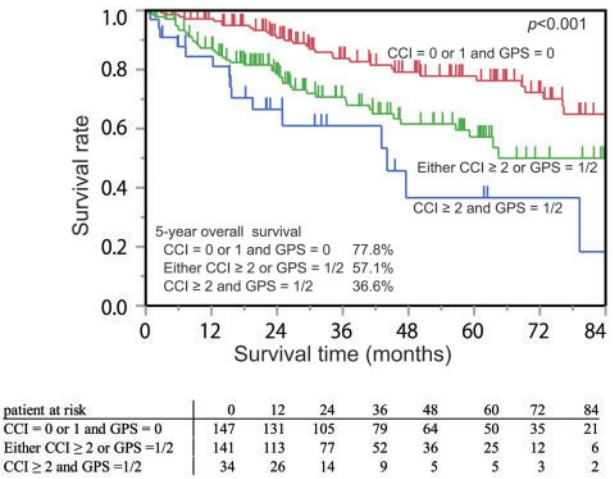

Figure 3: Comparison of overall survival curves between patients with a CCI = 0 or 1 and GPS = 0, either CCI ≥2 or GPS = 1/2 and CCI ≥2 and GPS = 1/2. CCI: Charlson Comorbidity Index; GPS: Glasgow Prognostic Score.

patients who underwent surgeries [3]. In this study, we initially showed that both the CCI and the GPS can be used to predict overall survival as well as P-stage and male gender. According to the results of recurrence-free and disease-specific survival times for CCI and GPS (Supplementary Material, Fig. S1) in our study, both the CCI and the GPS had some correlation with cancer-related deaths. There could be a possibility that the results are obscured due to some irregular non-cancer-related death. A previous study of a limited number of octogenarian lung cancer patients showed that CCI predicted overall survival in patients with non-small-cell lung cancer [26]. The CCI thus proved to be a reliable predictive marker.

The GPS was also useful in predicting the survival of various cancer patients from previous analysis [12]. The modified GPS correlated with the Edmonton Frailty Scale and clinical cancer staging in 52 solid tumour patients aged 65 years or older at diagnosis [27]. The GPS and P-stage were significant prognostic factors in 98 patients aged 80 years and older who have clinical Stage I lung cancer [28]. Hence, the CCI and the GPS should be determined when considering the operative indication and the type of procedure for elderly lung cancer patients.

Limitations

This study has several limitations, including selection bias, because of its retrospective and multi-institutional design, and because no comparative analysis was performed between patients older than 80 years and those younger than 80 years. In

particular, almost 40% of patients had no comorbidities, because Japanese people generally live longer than those in other countries do; the average lifespan is 79 years for men and 86 years for women. Patients in their 80s with good performance status are also increasing in this country. According to the annual report in Japan, the proportion of lung cancer surgery in patients over the age of 80 years increased from 8.7%, in 2007, to 12.1%, in 2014 [2]. This could be suggestive of a patient selection bias. However, data were collected from a large number of Stage I–IIIA lung cancer patients aged 80 years or older who underwent surgery, and both the short- and long-term results were analysed.

CONCLUSIONS

We concluded that the risk factors for postoperative morbidity were male gender and operation time and that the predictive factors for long-term survival were male gender, CCI, GPS and P-stage in this single-arm retrospective analysis, which we should keep in mind for lung cancer surgery in the elderly. In addition, the Japanese Association for Chest Surgery is currently conducting an ongoing prospective multi-institutional study, comparing patients older than 80 years with lung cancer with those younger than 80 years. We expect the results of this study to support the findings of our research.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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Conflict of interest: none declared.

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