[Original]

Pre-operative Physical Performance Is Associated With Early Return to Work in Peri-operative Lung Cancer Patients

Hiroaki Teramatsu[1*], Hiroshi Yamato[2], Ying Jiang[2], Hiroaki Kako[1], Satoshi Kuhara[1], Ryosuke Ohya[1], Hideaki Itoh[3], Koji Kuroda[4], Yasuyuki Matsushima[3] and Satoru Saeki[3]

[1] *Department of Rehabilitation, University Hospital of Occupational and Environmental Health, Japan. 1-1, Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8556, Japan*
[2] *Department of Health Development, Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health, Japan. 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan*
[3] *Department of Rehabilitation Medicine, University of Occupational and Environmental Health, Japan. 1-1, Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan*
[4] *Second Department of Surgery, University of Occupational and Environmental Health, Japan. 1-1, Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan*

Abstract **:** Little is known about the factors related to return to work (RTW) in patients with peri-operative lung cancer (LC). This study aimed to investigate whether pre-operative physical performance is associated with early RTW in patients with peri-operative LC. A total of 59 patients who wished to resume work after lung resection surgery were included and were divided into three groups: early RTW (within 14 days after discharge), delayed RTW (within 15−90 days), and non-RTW (failure of RTW within 90 days). The early RTW group had significantly lower scores on the modified Medical Research Council dyspnea scale (mMRC) and significantly higher scores on the Euro Quality of Life 5-Dimension 3-Level (EQ-5D-3L) than the non-RTW group. Multivariate logistic regression analysis showed that EQ-5D-3L scores were significantly associated with early RTW, and mMRC scores and knee extensor strength tended to be associated with early RTW. Better pre-operative quality of life, mild dyspnea, and greater lower limb muscle strength tended to be associated with early RTW in patients with peri-operative LC.

Keywords **:** lung cancer, surgery, return to work, physical performance.

(Received May 2, 2022, accepted July 28, 2022)

Introduction

Cancer is one of the most prevalent diseases in the world, and the number of patients with cancer is expected to reach 21.6 million globally by 2030 [1]. The average life expectancy of cancer patients has increased in recent years due to early detection and improved treatment techniques, and the number of cancer survivors has also increased [2]. It is estimated that approximately only half of cancer survivors are employed, making employment support for cancer survivors an important issue [3]. Indeed, cancer patients face numerous challenges in their working environment, and they have a higher risk of losing their jobs than healthy individuals [4, 5].

Lung cancer (LC) is a highly prevalent disease not

*Corresponding Author: Hiroaki Teramatsu, Department of Rehabilitation, University Hospital of Occupational and Environmental Health, Japan. 1-1, Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan, Tel: +8193-603-1611, Fax: +8193-603-6691, E-mail: terateratera723@clnc.uoeh-u.ac.jp

only in Japan but also worldwide [6]. Surgical treatment is considered the standard therapy for patients with early-stage non–small cell LC [7]. The development of minimally invasive surgical techniques and peri-operative management has shortened hospital stays and improved prognosis in recent years [7]. A systematic review on return to work (RTW) among patients with LC reported that they are more likely to lose their jobs, take sick leave, change their job, or lose income than are other cancer patients [8]. Although there are several studies on the relationship between workers' occupation and LC incidence and prognosis [9], there are no reports, to our knowledge, on the status and factors related to RTW in patients with peri-operative LC. While several studies have shown that the physical performance of patients with peri-operative LC affects post-operative complications and prognosis [10], the relationship between physical performance and RTW in these patients remains unclear.

This study aimed to explore the status of RTW in patients with peri-operative employed LC and its associated factors. We also investigated whether pre-operative physical performance is associated with early RTW.

Methods

Study design and patients

This study included 83 employed patients (aged 20 years or older) who wished to resume work after discharge among the 325 patients admitted to our hospital for lung resection surgery between August 2018 and October 2019. We conducted a questionnaire survey 3 months after hospital discharge; 59 patients returned the questionnaire and were included in the analysis. The patients were divided into RTW and non-RTW groups. The RTW group was further dichotomized based on the average number of days from discharge to resumption of work, with the early RTW group defined as the mean number of days or less and the delayed RTW group defined as the mean number of days or more.

This study was approved by the ethics committee of the University of Occupational and Environmental Health (No. H30-157). The patients were informed via verbal and written communication outlining the objectives of the study, the requirements for withdrawal, and the freedom to decline participation without any disadvantage. Voluntary consent was obtained from each patient.

Data collection

We collected the following data from electronic medical records: basic characteristics, physical measurements, cancer histology, cancer stage, respiratory function, surgical procedures, and post-operative course. We used questionnaires to survey the patients' work and living environments before admission and their RTW status 3 months after discharge. The Work Ability Index (WAI) was used to assess the ability to adapt to work [11].

Assessment of physical performance

Assessment of physical performance included the modified Medical Research Council dyspnea scale (mMRC), the Eastern Cooperative Oncology Group Performance Status (ECOG-PS), upper arm circumference, calf circumference, knee extensor strength (KES), grip strength, Short Physical Performance Battery (SPPB), 10-meter walk time, 6-minute walk test, and the Euro Quality of Life (QOL) 5 dimension 3-level (EQ-5D-3L). The mMRC was used to assess dyspnea [12], and ECOG-PS was used as a measure of general health status and limitations of activities of daily living (ADL) [13]. Upper arm and calf circumferences were used as anthropometric measurements. KES and grip strength were used to assess muscle strength [14], and SPPB was used as a simple physical performance battery [15]. The 10-meter walk time and 6-minute walk test were used as gait assessments [16]. EQ-5D-3L was used to assess health-related QOL [17]. Details of the physical performance assessment are described in previous reports [12−17].

Department of Occupational Medicine

The University Hospital of Occupational and Environmental Health, Japan, established Japan's first Department of Occupational Medicine in 2018, specializing in health promotion and employment support. The Department of Occupational Medicine arranges and proposes solutions to employment issues from the standpoint of a medical institution in cooperation

with the attending physician's department and issues a written opinion from the attending physician to the employer when necessary [18].

Statistical analysis

The Kaplan–Meier survival curve was used to calculate the cumulative RTW rates in the patients. The chi-square test was used for categorical variables and the Kruskal–Wallis test was used for continuous variables to assess the differences between the three groups. Bonferroni's multiple comparison method was used for items with significant differences among the three groups. Logistic regression analysis was used to investigate whether the physical performance was associated with early RTW. A univariate analysis was conducted first, followed by a multivariate analysis adjusted for age and sex. A logistic regression analysis, excluding patients who received adjuvant therapy, was also performed as a subgroup analysis. All statistical analyses were performed using SPSS Statistics, version 25 (IBM Corp., Armonk, NY). Statistical significance was set at $P<0.05$.

Results

The average RTW period for the RTW group was 14.6 days. We divided the patients into three groups: the early RTW group, who resumed work within 14 days of discharge (31 patients), the delayed RTW group, who resumed work between 15 and 90 days after discharge (13 patients), and the non-RTW group, who failed to resume work within 90 days (15 patients) (Figure 1). The cumulative RTW rates of all the patients are shown in Figure 2. The cumulative

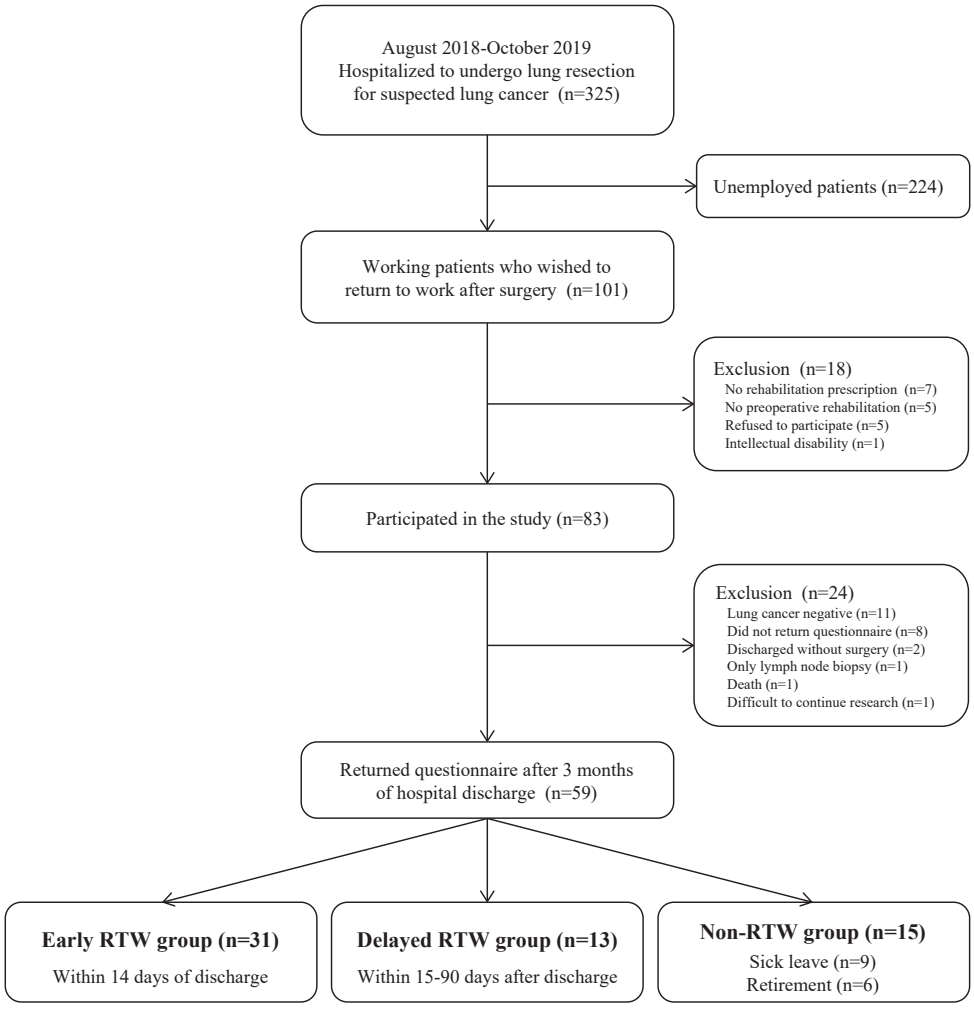

Figure 1. Study flow diagram. RTW: return to work.

RTW rates within 14 and 90 days were 52.5% (31/59) and 74.6% (44/59), respectively. There were changes in work content (e.g., reduction in workload) after recommencing work for two patients in the early RTW group and four patients in the delayed RTW group. Nevertheless, all patients in the RTW group resumed a full-time status on the first day back at work.

The clinical characteristics of patients are presented in Table 1 and Table 2. There were no significant differences in age or sex, but all the patients except one in the non-RTW group were over 60 years old, and the proportion of female in the non-RTW group was 53%,

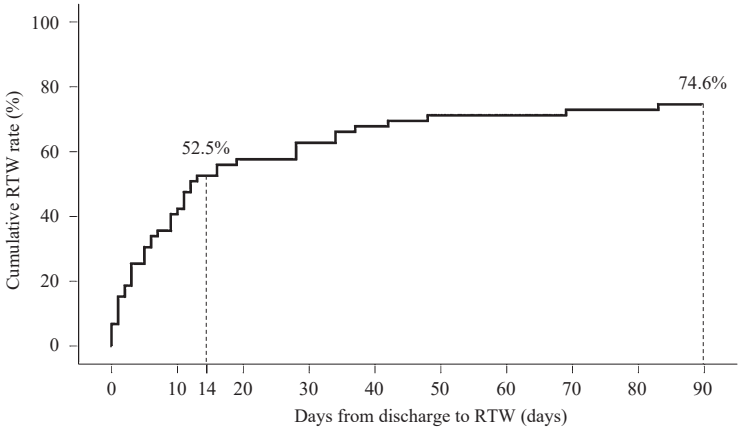

Figure 2. Cumulative RTW rate from the initial day of discharge. RTW: return to work.

Table 1. Clinical characteristics of the patients

	Early RTW (n=31) n (%); mean±SD	Delayed RTW (n=13) n (%); mean±SD	Non-RTW (n=15) n (%); mean±SD		*P*-value
Age	63.1 ± 10.7	58.8 ± 12.4	66.8 ± 6.5		0.16
Range (youngest - oldest)	28 – 86	36 – 73	50 – 79		
Sex (male : female)	22 : 9	8 : 5	7 : 8		0.29
Charlson Comorbidity Index					0.06
0 (low risk)	15 (48)	5 (38)	4 (27)		
1−2 (moderate risk)	12 (39)	6 (46)	4 (27)		
3−4 (high risk)	3 (10)	2 (15)	4 (27)		
≥5 (very high risk)	1 (3)	0	3 (20)		
Surgical approach				c	0.01*
VATS	20 (65)	12 (92)	7 (47)		
RATS	8 (26)	1 (8)	2 (13)		
Thoracotomy	3 (10)	0	6 (40)		
Hospital stay (days)	11 ± 5	11 ± 7	14 ± 7		0.13
Adjuvant therapy	1 (3)	1 (8)	4 (27)		0.45
Type of occupation					0.27
Clerical and research	13 (42)	3 (23)	3 (20)		
Sales, technical, and engineering	16 (52)	9 (69)	12 (80)		
Others	2 (6)	1 (8)	0		

Duties					0.59
Manager	10 (32)	1 (8)	2 (13)		
Supervisor	3 (10)	3 (23)	3 (20)		
General	6 (19)	3 (23)	3 (20)		
Others	12 (39)	6 (46)	7 (47)		
Employment status					<0.05*
Regular	12 (39)	4 (31)	4 (27)		
Re-employment	6 (19)	2 (15)	2 (13)		
Part-time	1 (3)	5 (38)	4 (27)		
Self-employed	4 (13)	1 (8)	4 (27)		
Others	8 (26)	1 (8)	1 (7)		
Business trip (yes)	12 (39)	1 (8)	1 (7)		0.03*
Occupational physician					0.95
Full-time doctor	2 (6)	1 (8)	1 (7)		
Part-time doctor	10 (32)	4 (31)	3 (20)		
None	19 (61)	8 (62)	11 (73)		
WAI dimensions					
6. Own prognosis of work ability after 2 years †	5.0 ± 2.1	6.5 ± 1.2	3.5 ± 1.7	c	<0.01**
Family or partner (yes)	30 (97)	9 (69)	15 (100)	a, c	<0.01**
Intervention from the Department of Occupational Medicine	0	2 (15)	1 (7)		0.06
Physical performance					
mMRC dyspnea scale §				b, c	0.01*
0 (normal)	26 (84)	11 (85)	7 (47)		
1	5 (16)	2 (15)	7 (47)		
>2	0	0	1 (7)		
ECOG-PS §					0.35
0 (normal)	29 (94)	12 (92)	12 (80)		
1	2 (6)	1 (8)	3 (20)		
Upper arm circumference † (cm)	26.2 ± 2.7	27.6 ± 4.0	24.4 ± 2.8		0.08
Calf circumference † (cm)	34.8 ± 3.3	37.0 ± 5.3	33.0 ± 2.6		0.05
Knee extensor strength † (%)	58 ± 11	50 ± 8	52 ± 16		0.07
Grip strength † (kg)	34.1 ± 10.0	32.7 ± 13.2	27.2 ± 6.4		0.05
Short Physical Performance Battery † (points)	12.0 ± 0.2	11.7 ± 1.1	11.9 ± 0.3		0.77
10-meter walk time § (seconds)	6.1 ± 1.1	6.0 ± 1.3	6.4 ± 1.0		0.72
6-minute walk distance † (m)	537 ± 67	522 ± 95	493 ± 139		0.66
EQ-5D-3L †	0.98 ± 0.07	0.93 ± 0.12	0.88 ± 0.17	b	0.03*

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as numbers (%). RTW: return to work, VATS: video-assisted thoracic surgery, RATS: robot-assisted thoracic surgery, WAI: work ability index, mMRC: modified Medical Research Council, ECOG-PS: Eastern Cooperative Oncology Group performance status, EQ-5D-3L: Euro Quality of Life 5 dimension 3-level, SD: standard deviation. * $P<0.05$, ** $P<0.01$. †: High value is a good indicator, §: Low value is a good indicator. a: Significant difference between early RTW group and delayed RTW group. b: Significant difference between early RTW group and non-RTW group. c: Significant difference between delayed RTW group and non-RTW group.

Table 2. Clinical characteristics of the patients

	Early RTW (n=31) n (%); mean ± SD	Delayed RTW (n=13) n (%); mean ± SD	Non-RTW (n=15) n (%); mean ± SD	*P*-value
Preoperative pulmonary function test				0.86
%FVC (%)	101 ± 14	100 ± 11	107 ± 24	
%FEV_1 (%)	86 ± 17	87 ± 17	87 ± 29	
%DL_{CO} (%)	92 ± 24	96 ± 30	90 ± 25	
Histological type (with overlap)				0.76
Adenocarcinoma	27 (87)	12 (92)	12 (80)	
Squamous cell carcinoma	2 (6)	1 (8)	3 (20)	
Others	2 (6)	0	0	
Pathological stage				0.65
0	3 (10)	1 (8)	0	
1	23 (74)	10 (77)	9 (60)	
2	1 (3)	1 (8)	2 (13)	
3	3 (10)	1 (8)	2 (13)	
Unknown	1 (3)	0	2 (13)	
Work style				0.99
Full-time work	18 (58)	6 (46)	8 (53)	
Shift work	3 (10)	1 (8)	1 (7)	
Discretionary work	5 (16)	2 (15)	2 (13)	
Part-time work	5 (16)	4 (31)	4 (27)	
Company size				0.53
1−49	22 (71)	8 (62)	12 (80)	
50−299	5 (16)	4 (31)	2 (13)	
300−999	1 (3)	0	1 (7)	
>1000	3 (10)	1 (8)	0	
WAI dimensions				
1. Subjective estimation of present work ability compared with lifetime best †	7.3 ± 2.0	7.5 ± 2.1	8.2 ± 1.8	0.33
2. Subjective work ability in relation to both the physical and the mental demands of work †	7.6 ± 1.8	8.5 ± 1.5	8.0 ± 1.9	0.27
3. Number of diagnosed diseases †	4.0 ± 1.7	4.3 ± 1.7	4.1 ± 1.4	0.82
4. Subjective estimation of work impairment due to diseases †	5.5 ± 1.2	5.5 ± 0.7	5.0 ± 1.4	0.29
5. Sickness absenteeism during the past year †	4.0 ± 1.1	3.8 ± 1.2	3.5 ± 1.5	0.63
7. Enjoying daily tasks; active and alert; full hope for the future †	2.9 ± 1.0	2.7 ± 1.1	2.8 ± 1.1	0.82
WAI summary score †	36.2 ± 6.4	35.9 ± 12.3	32.2 ± 10.7	0.32

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as numbers (%). RTW: return to work, WAI: work ability index, SD: standard deviation, FVC: forced vital capacity, FEV_1: forced expiratory volume in the first second, DL_{CO}: diffusing capacity for carbon monoxide. * $P<0.05$, ** $P<0.01$. †: High value is a good indicator, §: Low value is a good indicator.

which was higher than that in the other two groups. In terms of the Charlson Comorbidity Index (CCI), which indicates the degree of comorbidity and the risk of post-operative complications, the proportion of patients at higher risk was greater in the non-RTW group than in the other two groups (CCI≥3: early RTW group, 13% vs. delayed RTW group, 15% vs. non-RTW group, 47%). More than half of the patients in all three groups underwent minimally invasive surgery, such as video-assisted or robot-assisted thoracic surgery. No patients in the delayed RTW group underwent thoracotomy. The proportion of patients in the non-RTW group who underwent thoracotomy was higher than that in the other two groups (10% vs. 0% vs. 40%). There was a significant difference ($P=0.01$) in the distribution of surgical approach among the three groups, and the proportion of patients who received adjuvant therapy was higher in the non-RTW group than in the other two groups (3% vs. 8% vs. 27%).

The early RTW group had a higher proportion of clerical and research workers (42% vs. 23% vs. 20%), managers (32% vs. 8% vs. 13%), and regular employees (39% vs. 31% vs. 27%). The delayed RTW and non-RTW groups had a higher proportion of part-time workers (3% vs. 38% vs. 27%), and the non-RTW group had a higher proportion of self-employed workers (13% vs. 8% vs. 27%). There was a significant difference ($P<0.05$) in the distribution of employment status among the three groups. Patients in the early RTW group had a higher number of business trips than those in the other two groups (39% vs. 8% vs. 7%, $P=0.03$). In all three groups, more than half of the patients did not have an occupational physician at their workplace (61% vs. 62% vs. 73%). The WAI "own prognosis of work ability after 2 years" was lower in the early RTW group than in the delayed RTW group, and higher than in the non-RTW group (5.0 ± 2.1 vs. 6.5 ± 1.2 vs. 3.5 ± 1.7, $P<0.01$). The proportion of patients living with a family member or partner was significantly lower in the delayed RTW group than in the other two groups (97% vs. 69% vs. 100%, $P<0.01$). The number of patients who received interventions from the Department of Occupational Medicine was only 2 in the delayed RTW group, 1 in the non-RTW group, and 0 in the early RTW group.

In terms of pre-operative physical performance, the early RTW group had lower mMRC scale scores (0 [0−0] vs. 1 [0−1] vs. 1 [0−1], $P=0.01$), higher KES (58 ± 11% vs. 50 ± 8% vs. 52 ± 16%), higher grip strength (34.1 ± 10.0 kg vs. 32.7 ± 13.2 kg vs. 27.2 ± 6.4 kg), and higher EQ-5D-3L scores (0.98 ± 0.07 vs. 0.93 ± 0.12 vs. 0.88 ± 0.17, $P=0.03$) than the other two groups. The delayed RTW group had larger upper arm (26.2 ± 2.7 vs. 27.6 ± 4.0 vs. 24.4 ± 2.8) and calf circumferences (34.8 ± 3.3 vs. 37.0 ± 5.3 vs. 33.0 ± 2.6) than the other two groups.

The results of the logistic regression analysis are presented in Table 3. Multivariate analysis adjusted for age and sex showed that the EQ-5D-3L scores (odds ratio [OR]=1.01, 95% confidence interval [CI]=1.00−1.01, $P=0.03$) were significantly associated with early RTW; mMRC scores (OR=0.35, 95% CI=0.10−1.20, $P=0.09$) and KES (OR=1.05, 95% CI=1.00−1.11, $P=0.07$) tended to be associated with early RTW. The subgroup analysis of 53 patients, excluding 6 patients in adjunctive therapy, showed that the EQ-5D-3L scores (OR=1.01, 95% CI=1.00−1.01, $P=0.03$) and KES (OR=1.06, 95% CI=1.00−1.12, $P<0.05$) were significantly associated with early RTW (Table 4).

Discussion

This is the first study to investigate whether pre-operative physical performance is associated with early RTW in patients with peri-operative LC. With the latest minimally invasive surgery and peri-operative management techniques, more than half of the patients were able to resume work within 14 days. In addition, better pre-operative QOL, mild dyspnea, and stronger lower limb muscles tended to be associated with early RTW.

RTW rate and its characteristics

The RTW rate within 14 days after discharge for patients with peri-operative LC was 52.5%, and the RTW rate within 90 days was 74.6%. A previous study conducted in 2016 among patients with LC in Japan reported that the RTW rate was 75%, and the median time from sick leave to RTW was 96.5 days [19]. Although this report included cases of advanced LC that were not indicated for surgery, the results cannot be simply compared with our study, which included pa-

Table 3. Odds ratios of physical performance related to early RTW determined via logistic regression analysis

	Univariate model				Multivariate model			
	OR	95% CI		*P*-value	OR	95% CI		*P*-value
		Lower	Upper			Lower	Upper	
Modified MRC dyspnea scale§	0.36	0.11	1.14	0.08	0.35	0.10	1.20	0.09
ECOG-PS§	0.41	0.07	2.46	0.33	0.39	0.06	2.56	0.33
Upper arm circumference†	1.04	0.88	1.23	0.65	1.01	0.84	1.21	0.95
Calf circumference†	1.10	0.88	1.15	0.98	0.97	0.82	1.14	0.69
Knee extensor strength†	1.05	1.00	1.10	0.04*	1.05	1.00	1.11	0.07
Grip strength†	1.04	0.99	1.10	0.11	1.04	0.96	1.13	0.38
Short Physical Performance Battery†	2.02	0.39	10.44	0.40	1.79	0.33	9.67	0.50
10-meter walk time §	0.99	0.58	1.47	0.73	0.96	0.57	1.63	0.88
6-minute walk distance†	1.00	1.00	1.01	0.23	1.00	1.00	1.01	0.20
EQ-5D-3L†	1.01	1.00	1.01	0.02*	1.01	1.00	1.01	0.03*

Age and sex were included in the multivariate logistic regression model. OR: odds ratio, CI: confidence interval, MRC: Medical Research Council, ECOG-PS: Eastern Cooperative Oncology Group performance status, EQ-5D-3L: Euro Quality of Life 5 dimension 3-level. * $P<0.05$. †: High value is a good indicator, §: Low value is a good indicator.

Table 4. Odds ratios of physical performance related to early RTW determined via logistic regression analysis (Excluding patients who received adjuvant therapy)

	Univariate model				Multivariate model			
	OR	95% CI		*P*-value	OR	95% CI		*P*-value
		Lower	Upper			Lower	Upper	
Modified MRC dyspnea scale§	0.45	0.15	1.41	0.17	0.41	0.12	1.38	0.15
ECOG-PS§	0.48	0.07	3.12	0.44	0.43	0.06	3.14	0.41
Upper arm circumference†	1.01	0.85	1.20	0.89	1.00	0.83	1.20	0.99
Calf circumference†	0.96	0.83	1.11	0.59	0.94	0.79	1.12	0.48
Knee extensor strength†	1.05	1.00	1.11	<0.05*	1.06	1.00	1.12	<0.05*
Grip strength†	1.03	0.98	1.09	0.28	1.04	0.96	1.14	0.32
Short Physical Performance Battery†	1.32	0.08	22.26	0.85	1.28	0.07	23.01	0.87
10-meter walk time §	0.97	0.60	1.59	0.91	0.96	0.55	1.66	0.88
6-minute walk distance†	1.00	1.00	1.01	0.31	1.00	1.00	1.01	0.24
EQ-5D-3L†	1.01	1.00	1.01	0.03*	1.01	1.00	1.01	0.03*

Age and sex were included in the multivariate logistic regression model. OR: odds ratio, CI: confidence interval, MRC: Medical Research Council, ECOG-PS: Eastern Cooperative Oncology Group performance status, EQ-5D-3L: Euro Quality of Life 5 dimension 3-level. * $P<0.05$. †: High value is a good indicator, §: Low value is a good indicator.

tients with operable early-stage LC. Our results showed that, thanks to the latest minimally invasive surgery and peri-operative management techniques, more than half of the patients succeeded in early RTW, whereas approximately 25% were unable to resume work within 90 days.

The early RTW group had a higher proportion of patients who had a family or partner compared with those in the delayed RTW group. The WAI "own prognosis of work ability after 2 years" was worse in the early RTW group than in the delayed RTW group. This may have been due to pre-operative anxiety regarding their ability to adapt to work after RTW, the financial burden of medical expenses and decreased income, as well as the pressure to continue working to support their families [20, 21]. Patients who required

early RTW, due to these abovementioned reasons, may have resumed work without adequate home care after discharge and thus continued to be affected by the physical burden of surgery. It is important to identify patients who need early RTW by assessing their ability to adapt to work before surgery and considering the implementation of rehabilitative interventions. The Department of Occupational Medicine can play a major role in supporting a smooth early RTW.

Patients in the early RTW group had a higher percentage of business trips than those in the other two groups, and the distribution of difference was also significant (39% vs. 8% vs. 7%, P=0.03); however, the reason for this phenomenon is unknown. Patients in the early RTW group belonged to larger workplaces than those in the other two groups and had a higher percentage of clerical, research, and managerial positions. We speculate, therefore, that the early RTW group had stronger pressure to return than the other two groups did.

The delayed RTW group had a larger limb circumference but a lower KES. Logistic regression analysis showed that the KES tended to be associated with early RTW, suggesting that the low KES in the delayed RTW group was an obstacle to early RTW. Pre-operative rehabilitation focusing on strengthening the muscles of the lower limbs may contribute to a smooth RTW.

The majority of patients in the non-RTW group were over 60 years old, with a higher proportion of women and non-desk workers. In a systematic review of the RTW status in cancer survivors in Europe, "age 50 years or older," "female," and "physically demanding occupation" were cited as obstacles to RTW [5]. These characteristics were similar to those of the non-RTW group in our study. Patients in the non-RTW group had more comorbidities, invasive surgeries, and adjuvant therapies, as well as lower physical performance. These results suggest that the patients who wished to resume work (but were unable to do so) had characteristics that made RTW difficult, and their poor general condition before surgery may have acted as an additional obstacle. Successful RTW in such patients may require early intervention by the Department of Occupational Medicine, in addition to aggressive rehabilitation before surgery.

Physical performance related to early RTW

Multivariate analysis showed that high EQ-5D-3L was a predictor of early RTW within 14 days. Similar results were obtained in a subgroup analysis that excluded patients who received adjuvant therapy. The EQ-5D-3L is a self-administered questionnaire for the quantitative assessment of comprehensive health-related QOL and is widely used in clinical practice [17]. Our results suggest that the EQ-5D-3L can be used pre-operatively to predict patients who will have difficulty with RTW soon after surgery. The EQ-5D-5L, a more accurate five-level scale, was recently developed and has been reported to be a good indicator of the risk of post-operative complications in LC patients [22]. Future studies of RTW using EQ-5D-5L in patients with peri-operative LC are needed.

Low mMRC and high KES scores also tended to be favorable for early RTW. The mMRC can be used to easily and rapidly evaluate dyspnea and movement disorders. It has also been reported to be a prognostic indicator for elderly patients, as well as patients with the chronic obstructive pulmonary disease [23, 24]. KES is widely used in the field of rehabilitation as an indicator of the acquisition of ADL. KES has also been reported to be related to prognosis in cancer patients; it is used not only as an ADL index but also as a prognostic index [25]. The results of this study indicate that mMRC and KES may be used as predictors of early RTW and clinical outcomes. However, the significant associations of mMRC and KES with early RTW attenuated this trend after adjustment for age and sex, suggesting that these indices may not be independent factors of early RTW, and that other factors may be involved. Several factors other than age and sex have been reported to affect RTW in cancer patients [5, 20]. Due to our small sample size, we did not adjust for factors other than age and sex. On the contrary, the subgroup analysis excluding patients who received adjuvant therapy showed that KES was significantly associated with early RTW. Further studies with larger sample sizes are needed to clarify the relationship between physical performance and RTW.

Strengths and limitations

This is the first study to comprehensively investigate not only inherent patient factors but also fam-

ily and occupational factors associated with RTW in patients with peri-operative LC. There are no prior reports on RTW in patients who have undergone the latest minimally invasive surgery and peri-operative management techniques, such as video- and robot-assisted thoracic surgeries. In addition, most previous reports on RTW and physical performance were based on questionnaires or self-reports [26]; no prior studies have directly assessed physical performance, which we performed in our study. In patients with peri-operative LC, better pre-operative QOL, mild dyspnea, and greater lower limb muscle strength tended to be associated with early RTW. We believe that the results of our study provide new possibilities for rehabilitation in the field of occupational health.

We acknowledge some limitations in this study. Due to the small sample size, only age and sex were adjusted for when investigating factors associated with early RTW. Originally, employment status should be adjusted for as a potential confounding factor in multivariate analyses, but the number of patients was so small that it was not possible to include employment status for analysis. We did not investigate income and education level, either, which are risk factors for job loss [20]. In the future, long-term studies with larger sample sizes are needed to adjust for a wide range of medical, occupational, and social factors. It is also necessary to investigate whether or not WAI could be improved through interventions provided by the Department of Occupational Medicine.

This study was conducted before the outbreak of the coronavirus disease 2019 (COVID-19) and does not reflect the current context of this pandemic. Economic recession due to COVID-19 has made it more difficult for individuals with disabilities to work [27]. Additional studies are required to investigate the RTW status in patients with peri-operative LC during the COVID-19 recession.

Conclusion

Thanks to the latest minimally invasive surgery and peri-operative management techniques, more than half of our patients were able to resume work within 14 days. In addition, better pre-operative QOL, mild dyspnea, and greater lower limb muscle strength tended to be associated with early RTW. For a smooth RTW in patients with peri-operative employed LC, we recommend that those who are expected to have difficulty in resuming work should be identified early using pre-operative physical performance assessments. Interventions conducted by the Department of Occupational Medicine should also be considered in addition to pre-operative rehabilitation to strengthen lower limb muscles and reduce dyspnea.

Acknowledgment

We would like to thank the staff at the University of Occupational and Environmental Health who cooperated in this study.

Funding

The study received no funding.

Conflict of Interest

None

References

1. World Health Organization (2012): World's health ministers renew commitment to cancer prevention and control. http://www.who.int/cancer/media/news/cancer-prevention-resolution/en/ (accessed June 1, 2021)
2. Xia W, Yu X, Mao Q *et al* (2017): Improvement of survival for non-small cell lung cancer over time. Onco Targets Ther 10: 4295–4303
3. Short PF, Vasey J J & Tunceli K (2005): Employment pathways in a large cohort of adult cancer survivors. Cancer 103(6): 1292–1301
4. Rottenberg Y, Amir Z & De Boer, A G E M (2019): Work cessation after cancer diagnosis: a population-based study. Occup Med (Lond) 69(2): 126–132
5. Paltrinieri S, Fugazzaro S, Bertozzi L *et al* (2018): Return to work in European cancer survivors: a systematic review. Support Care Cancer 26(9): 2983–2994
6. Jemal A, Bray F, Center M M *et al* (2011): Global cancer statistics. CA Cancer J Clin 61(2): 69–90
7. Ng CSH, MacDonald J K, Gilbert S *et al* (2019): Optimal approach to lobectomy for non-small cell lung can-

cer: systemic review and meta-analysis. Innovations (Phila) 14(2): 90–116
8. Vayr F, Savall F, Bigay-Game L *et al* (2019): Lung cancer survivors and employment: A systematic review. Lung Cancer 131: 31–39
9. Yatera K, Morimoto Y, Ueno S *et al* (2018): Cancer risks of hexavalent chromium in the respiratory tract. J UOEH 40(2): 157–172
10. Irie M, Nakanishi R, Yasuda M *et al* (2016): Risk factors for short-term outcomes after thoracoscopic lobectomy for lung cancer. Eur Respir J 48(2): 495–503
11. Tuomi K, Ilmarinen J, Eskelinen L *et al* (1991): Prevalence and incidence rates of diseases and work ability in different work categories of municipal occupations. Scand J Work Environ Health 17 Suppl 1: 67–74
12. Celli BR, MacN & ATS/ERS Task Force (2004): Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. Eur Respir J 23(6): 932–946
13. Oken MM, Creech R H, Tormey D C *et al* (1982): Toxicity and response criteria of the Eastern cooperative oncology group. Am J Clin Oncol 5(6): 649–655
14. Teramatsu H, Shiraishi J, Matsushima Y *et al* (2019): Using physical function to predict hospital readmission within 1 year in patients with heart failure. Prog Rehabil Med 4: 20190018
15. Guralnik JM, Simonsick E M, Ferrucci L *et al* (1994): A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 49(2): M85–M94
16. ATS Committee on proficiency standards for clinical pulmonary function laboratories (2002): ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 166(1): 111–117
17. Tsuchiya A, Ikeda S, Ikegami N *et al* (2002): Estimating an EQ-5D population value set: the case of Japan. Health Econ 11(4): 341–353
18. Harada A, Tateishi S, Hashimoto H *et al* (2021): Achievements and future challenges in the support of the balance of work and medical treatment at the hospital of the university of occupational and environmental health, Japan, in 2018–2020. J UOEH 43(4): 445–453
19. Endo M, Haruyama Y, Takahashi M *et al* (2016): Returning to work after sick leave due to cancer: a 365-day cohort study of Japanese cancer survivors. J Cancer Surviv 10(2): 320–329
20. Butow P, Laidsaar-Powell R, Konings S, Lim C Y S & Koczwara B (2020): Return to work after a cancer diagnosis: a meta-review of reviews and a meta-synthesis of recent qualitative studies. J Cancer Surviv 14(2): 114–134
21. Bae KR & Cho J (2021): Changes after cancer diagnosis and return to work: experience of Korean cancer patients. BMC Cancer 21(1): 86
22. Koide R, Kikuchi A, Miyajima M *et al* (2019): Quality assessment using EQ-5D-5L after lung surgery for non-small cell lung cancer (NSCLC) patients. Gen Thorac Cardiovasc Surg 67(12): 1056–1061
23. Hegendorfer E, Vaes B, Mathei C, Van Pottelbergh G & Degryse J M (2017): Correlates of dyspnoea and its association with adverse outcomes in a cohort of adults aged 80 and over. Age Ageing 46(6): 994–1000
24. Natori H, Kawayama T, Suetomo M *et al* (2016): Evaluation of the modified medical research council dyspnea scale for predicting hospitalization and exacerbation in Japanese patients with chronic obstructive pulmonary disease. Intern Med 55(1): 15–24
25. Garcia-Hermoso A, Ramirez-Velez R, Peterson M D *et al* (2018): Handgrip and knee extension strength as predictors of cancer mortality: A systematic review and meta-analysis. Scand J Med Sci Sports 28(8): 1852–1858
26. Rosbjerg R, Zachariae R, Hansen D G *et al* (2021): Physical activity, return to work self-efficacy, and work status among employees undergoing chemotherapy for cancer - a prospective study with 12 months follow-up. BMC Cancer 21(1): 169
27. Houtenville AJ, Paul S & Brucker D L (2021): Changes in the employment status of people with and without disabilities in the united states during the covid-19 pandemic. Arch Phys Med Rehabil 102(7): 1420–1423