ORIGINAL

Assessment of dyspnea, ADL, and QOL in the perioperative period in lung cancer patients treated with minimally invasive surgery

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Abstract : Objective : Patients with lung cancer generally undergo minimally invasive surgery, such as video-assisted thoracoscopic surgery (VATS). This study examined the changes in health conditions and symptoms of patients with lung cancer using the European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire (EORTC QLQ) C-30 questionnaires after surgery. Methods : This was a longitudinal descriptive study. One hundred and three patients with lung cancer who underwent lung resection at Tokushima University Hospital between 2012 and 2021 were eligible. They completed EORTC QLQ-C30, QLQ-LC13, the Cancer Dyspnea scale (CDS), and pulmonary-ADL (P-ADL) before and 1, 3, and 6 months after surgery. Results : Regarding functional scale scores, impairments in physical and role functions persisted for 6 months after surgery. In symptom scale scores, fatigue, pain, dyspnea, and appetite loss continued for 6 months after surgery. In CDS, sense of effort, discomfort, and total dyspnea scale scores were elevated for 6 months after surgery. In P-ADL, most ADL were impaired 1 month after surgery, but recovered by 3 months. The dyspnea index of ADL was lower for 6 months after surgery. Conclusions : Impairments in health conditions and symptoms persisted for 6 months after surgery despite its minimally invasive nature. J. Med. Invest. 70 : 388-402, August, 2023

Keywords **:** *ADL dyspnea, lung cancer, minimally invasive surgery, patient-reported outcome, QOL*

INTRODUCTION

Lung cancer is the most common cancer and the leading cause of death in Japan and worldwide (1, 2). Available treatments include surgery, radiotherapy, chemotherapy, targeted therapy, and immunotherapy, and patients with early-stage (stages I and II) lung cancer generally undergo surgery, while those with advanced or metastatic disease receive chemotherapy (3). The 5-year survival rate of early-stage lung cancer was previously reported to be 92% in patients with resected stage IA1 disease and 53% in those with stage IIB disease (4). However, despite improvements in treatment, patients with advanced lung cancer still have a poor prognosis (3). Lung resection is the mainstay of therapy for early-stage lung cancer. Treatment methods have shifted over the last few decades. Although resection is traditionally performed using thoracotomy, in the past two decades, video-assisted thoracoscopic surgery (VATS) and, more recently, robot-assisted thoracoscopic surgery (RATS) have emerged as a minimally invasive alternative method (5-7). Previous studies demonstrated that VATS was less invasive than thoracotomy, resulting in less postoperative pain, less perioperative bleeding, and shorter hospital stays (8, 9).

In patient-reported outcomes (PROs), patients directly report the status of their health condition and symptoms without interpretation by medical staff (10). The PRO questionnaire is an effective and accurate assessment of symptoms in patients treated with surgery, radiotherapy, and chemotherapy (11). Frequently used QOL questionnaires for cancer patients are the European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire (EORTC QLQ), QLQ-Lung Cancer-13 (QLQ-LC13), Functional Assessment of Cancer Therapy, and Medical Outcome Study Short Form-36 (12-14). EORTC QLQ-C30 and QLQ-LC13 are mostly used for patients with lung cancer. QLQ-LC13 consists of 13 items that assess specific symptoms of lung cancer and, based on the use of QLQ-C30, the findings of an extensive field study confirmed the reliability of LC13 to assess respiratory function (14).

Quality of life (QOL) after lung cancer surgery is currently attracting increasing attention. In the Akezaki study, QOL, pain, and fatigue did not sufficiently improve within the first week after minimally invasive surgery from those before surgery (15). However, the findings of a randomized study on VATS and open thoracotomy showed a better QOL in the VATS group one month after surgery (16).

We herein used EORTC QLQ-C30, QLQ-LC13, the Hospital Anxiety and Depression Scale (HADS), and Mental Adjustment to Cancer (MAC scale) to examine perioperative QOL, anxiety, depression, and mental adjustments in patients with lung cancer

Abbreviations : video-assisted thoracoscopic surgery (VATS), robot-assisted thoracoscopic surgery (RATS), Patient-reported outcomes (PROs), European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire (EORTC QLQ), QLQ-Lung Cancer-13 (QLQ-LC13), Quality of life (QOL), global health status (GHS), Hospital Anxiety and Depression Scale (HADS), Mental adjustment to cancer (MAC), Activities of Daily Living (ADL), Cancer Dyspnea scale (CDS), index pulmonary-ADL (P-ADL), standard deviation (SD), randomized controlled trials (RCT), chronic obstructive pulmonary disease (COPD).

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treated with minimally invasive surgery (14, 17, 18). Our preliminary study showed impairments in physical and role functions and several symptoms, such as coughing, dyspnea, and chest pain, persisted for up to 6 months after surgery. Shortness of breath in patients limits ADL and affects health-related QOL (19). Therefore, this study confirms impairments in physical and role functions and several symptoms persisted for up to 6 months after surgery by increasing the number of case, and clarifies whether dyspnea impair activities of daily living (ADL) or not using the Cancer Dyspnea Scale (CDS), a more detailed tool for assessing dyspnea, and the index pulmonary-ADL (P-ADL), an assessment of impaired ADL specific to respiratory disease in lung cancer patients (20, 21).

METHODS

Design

A longitudinal descriptive study

Patients

A flowchart summarizing the number of patients in 2 projects is shown in Supplementary Figure 1. Forty-nine patients with lung cancer who underwent lung resection at Tokushima University Hospital between 2012 and 2015 were eligible for inclusion in the present study (Project A). They completed EORTC QLQ-C30, QLQ-LC13, HADS, and MAC before and 1, 3, 6 months after surgery. Fifty-four lung cancer patients who underwent lung resection at Tokushima University Hospital between 2019 and 2021 were also eligible for inclusion in the present study (Project B). They completed EORTC QLQ-C30, QLQ-LC13, CDS, and P-ADL before and 1, 3, 6 months after surgery. The following patients were excluded from this study : patients with mental instability before surgery, patients with an inability to communicate or those with impaired cognitive function, and patients with mental illness.

Ethical considerations

The present study was approved by the Clinical Research Ethical Review Board of Tokushima University Hospital (approval no. 1460 for project A, approval no. 3543 for project B). Prior to the initiation of the study, subjects were informed of all necessary information regarding the publication of the study data, both verbally and in writing. They were also provided with the following details : the privacy of study subjects will be protected, there will be no treatment-related disadvantages regardless of whether they participate in the study, they will not be identifiable from the study data, and they may discontinue at any time. Patients who consented to these conditions were included in the present study. This study was conducted on patients who were recovering from invasive treatment associated with significant mental and physical burdens. Therefore, investigators conducted each interview after discussing the physical and mental conditions of the patient with the attending nurses, while carefully considering the mental and physical stress of the interview on the patient and the patient's physical condition.

Research tools

1. EORTC QLQ-C30 (version 3.0) and LC-13

EORTC QLQ-C30 (version 3.0) and LC-13 were used (14, 22). Version 3.0 is currently the standard version of QLQ-C30. It is a core cancer-specific questionnaire containing 30 items on patients' functioning, global QOL, and disease- and treatment-related symptoms. It includes five functional scales (physical, role, emotional, social, and cognitive functioning), three symptom scales (fatigue, pain, and nausea/vomiting), a Global Health Status/QoL scale, a number of single items assessing additional common symptoms of cancer (dyspnea, loss of appetite, insomnia, constipation, and diarrhea), and a single item measuring the financial impact of disease. QLQ-LC13 is a site-specific questionnaire consisting of 13 items on lung cancer symptoms (cough, hemoptysis, dyspnea, and site-specific pain) and its treatment-related side effects (sore mouth, dysphagia, peripheral neuropathy, and alopecia). Scores for all of the multi-item scales and single-item measures ranged between 0 to 100, with a high score for a functional scale indicating a healthy level of functioning and that for a symptom scale representing worse symptoms.

EORTC QLQ-C30 has been translated into more than 110 languages and validated in different samples of cancer patients in many countries (23, 24). The Japanese version was confirmed to be a reliable and valid questionnaire for assessing lung cancer patients in Japan (25). The EORTC QLQ-C30 summary score was previously shown to be more sensitive for detecting changes in QOL after lung cancer surgery than each QOL-C30 GHS (26-28). We also used the EORTC QLQ-C30 summary score in the present study. QLQ-C30 Summary Score = { Physical Functioning + Role Functioning + Social Functioning + Emotional Functioning + Cognitive Functioning + (100-Fatigue) + (100-Pain) + (100-Nausea/Vomiting) + (100-Dyspnea) + (100-Sleeping Disturbances) + (100-Appetite Loss) + (100-Constipation) + (100-Diarrhea) }/13.

2. HADS (17)

The purpose of HADS was to screen for clinically significant anxiety and depressive symptoms in medically ill patients. This is an individually administered questionnaire and may be given via a self-report or by an interviewer. There are 7 items for anxiety and 7 items for depression. Responses are rated on a 4-point Likert scale and range between 0 and 3. The total score for HADS ranges between 0 and 21 : 0–7 for normal or no anxiety or depression, 8–10 for mild anxiety or depression, 11–14 for moderate anxiety or depression, and 12–21 for severe anxiety or depression. In adults, this measure typically requires <5 minutes to complete.

3. MAC

The MAC scale was developed in England by Watson *et al*. (18). This is a unique scale that was developed in an attempt to measure the specific mental adjustments of cancer patients. The MAC scale is a 40-item self-rating scale. It consists of five subscales : fighting spirit (16 items), anxious preoccupation (nine items), fatalism (eight items), helplessness : hopelessness (six items), and avoidance (one item). Possible responses to each statement are : (1) 'definitely does not apply to me', (2) 'does not apply to me', (3) 'applies to me', and (4) 'definitely applies to me'. The MAC scale has adequate validity and reliability (18, 29, 30). The Japanese version, similar to the original MAC scale, is a reliable and valid clinical research tool in Japan (31).

4. CDS (20)

CDS is the first scale that evaluates the multidimensional nature of dyspnea. It is a brief self-rating questionnaire composed of 3 factors and 12 items ('sense of effort' for 5 items, 'sense of anxiety' for 3 items, and 'sense of discomfort' for 4 items). Its feasibility, reliability, and validity are satisfactory for clinical use. The average time required to complete CDS is 140 seconds. The English version of CDS is currently used worldwide.

5. P-ADL

Some of the ADL measurements introduced for patients with respiratory disorder are not the golden standard (32, 33). Goto *et al*. reported a new ADL measurement, Pulmonary emphysema

ADL (P-ADL, version 1.0), and revised it to P-ADL, version 2.0 (19, 21). P-ADL calculates scores by categories (Meals, Toileting, Bathing, Washing one's hair, Cosmetic, Gowning, Walking around indoors, Staircase, and Walking outdoors) or by an index (Distance, Accomplishment, Frequency, Velocity, Dyspnea and Oxygen content). It is possible to identify actions in ADL that are affected by respiratory disturbance. P-ADL is associated with respiratory function (such as vital capacity and forced vital capacity), the 6-minute walking distance test, and the functional independent measure, which measures ADL scores (19, 34). P-ADL is a reliable and valid clinical research tool for ADL by respiratory disturbance in Japan.

6. Statistical analysis

Data from EORTC QLQ-C30 and QLQ-LC13 were combined from project A (n=49) and project B (n=54) and analyzed. Data on HADS (n=49), MAC (n=49), CDS (n=54), and P-ADL (n=54) were analyzed separately. The Shapiro-Wilk test was used to examine whether numerical datasets were normally distributed. Statistical analyses were performed using the Friedman test and Scheffé's test (post-hoc), which calculated the p-value in multiple comparisons with a significance level of $p < 0.05$. The Friedman test is a non-parametric statistical test that was developed by Milton Friedman (35). It is used for a one-way repeated measure analysis of variance by ranks. Scheffé's test is a type of post-hoc statistical analysis that is used for unplanned comparisons. Statistical analyses were performed using Excel statistics version 3.21 (BellCurve, Inc.).

RESULTS

Participants

The clinicopathological characteristics of 103 patients are summarized in Table 1. There were 61 men (59%) with a mean age of 69 (46–88) years. There were 57 smokers with a mean Brinkman index of 900. Tumors were classified according to the predominant histological subtype, as proposed by the 2015 WHO classification (36). There were 83 cases (81%) of adenocarcinoma and 15 (15%) of squamous cell carcinoma. Tumor staging was selected based on the seventh edition of the tumor node metastasis classification for lung cancer (37). The numbers of

Table 1. Patient characteristics in the present study

Age	68.6		(46 - 88)
Gender (male/female)	61/42		
Smoker	57	55%	
Brinkman index (mean)	900		(200 - 2250)
Pathology*			
adenocarcinoma	83	81%	
squamous cell carcinoma	15	15%	
large-cell lung carcinoma	1	1%	
small cell lung cancer	2	2%	
others	2	2%	
Pathological stage*			
IA	65	63%	
IB	13	13%	
IIA	8	8%	
IIB	4	4%	
IIIA	9	9%	
IIIB	1	1%	
IVA	2	2%	
Respiratory function			
restrictive dysfunction (VC)	3	3%	
obstructive dysfunction ($FEV_{1.0}$)	31	30%	
diffusion dysfunction (DLco)	19	18%	
Surgery			
lobectomy	79	77%	
segmentectomy or wedge resection	24	23%	
Surgical approach			
video-assisted thoracic surgery (VATS)	91	88%	
robot-assisted thoracic surgery (RATS)	9	9%	
thoracotomy	3	3%	
Surgery time (min)	248.6		(89 - 521)

VC ; vital capacity, $FEV_{1.0}$; forced expiratory volume in 1 second, DLco ; diffusing capacity of the lungs for carbon monoxide

pStage IA, IB, IIA, IIB, and IIIA cases were 65 (63%), 13 (13%), 8 (8%), 4 (4%), and 9 (9%), respectively. Three cases (3%) showed a disorder in preoperative restrictive respiratory function, 31 (30%) in obstructive function, and 19 (18%) in diffusion function. Lobectomy was performed on 79 patients (77%) and segmentectomy or wedge resection on 24 (23%). Ninety-one patients (88%) underwent surgery using the VATS method and 9 (9%) using the RATS method. The mean operation time was 249 (89-521) min.

Perioperative changes in EORTC-QLQ-C30, QLQ-LC13, HADS, and MAC scale scores of lung cancer patients treated with surgery

1. Functional scales in EORTC-QLQ-C30 (Figure 1, Table 2)

Perioperative changes in QOL is shown in Figure 1. The mean, standard deviation (SD), and Scheffé's paired comparisons for each scale are shown in Table 2. In 5 functional (physical, role, emotional, social, and cognitive) scale scores, physical and role function scale scores were significantly lower 1, 3, and 6 months after surgery than before surgery (Fig. 1-b, 1-c). The emotional functioning score was higher 3 and 6 months after surgery than before surgery (Fig. 1-d). Although the GHS score was significantly lower 1 month after surgery than before surgery, it recovered to the pre-surgery value after 3 months (Fig. 2-a).

2. Symptom scales in EORTC-QLQ-C30 (Figure 1, Table 2)

In 9 symptom (fatigue, nausea and vomiting, pain, dyspnea, insomnia, anorexia, constipation, diarrhea, and financial difficulties) scale scores, fatigue, pain, dyspnea, and appetite loss scores were significantly higher 1, 3, and 6 months after surgery than before surgery (Fig. 1-e, f, g, and h).

3. EORTC QLQ-C30 summary score

EORTC QLQ-C30 summary scores were significantly lower 1 and 3 months after surgery than before surgery (Fig. 1-i).

4. Symptom scales in EORTC-LC-13 (Figure 1, Table 2)

Among 13 lung cancer-specific symptoms (cough, hemoptysis, severity of shortness of breath, chest/body pain, and chemotherapy/radiotherapy side effects, such as a sore mouth, dysphagia, peripheral neuropathy, and hair loss), dyspnea, cough, and pain in the chest scores were significantly higher 1, 3, and 6 months after surgery than before surgery (Fig. 1-j, k, l).

5. Symptom scales in HADS (Supplementary Figure 2-a and b, Table 2)

HADS is used to screen for clinically significant anxiety and depressive symptoms in medically ill patients. The anxiety score gradually decreased over time after surgery (Supplementary Figure 2-a, Table 2). No significant differences were observed perioperatively in depressive symptoms (Supplementary Figure 2-b, Table 2).

6. Symptom scales in MAC (Supplementary Figure 3-a, b, c, d, e, and g, Table 2)

The MAC scale consists of five subscales : fighting spirit, anxious preoccupation, fatalism, helplessness : hopelessness, and avoidance. No significant differences were observed in any of the subscales perioperatively.

CDS of lung cancer patients treated with surgery perioperatively (Figure 2 and Table 2)

Perioperative changes in CDS are shown in Figure 2. The mean, SD, and Scheffé's paired comparisons for each scale are shown in Table 2. Sense of effort and discomfort scale scores were significantly higher 1, 3, and 6 months after surgery than before surgery (Fig. 2-a, 2-b). The sense of anxiety score was significantly higher 3 months after surgery than before surgery (Fig. 2-c). The total dyspnea score was significantly higher 1, 3, and 6 months after surgery than before surgery (Fig. 2-d).

P-ADL of lung cancer patients treated with surgery perioperatively (Figure 3 and Table 2)

Perioperative changes in P-ADL are shown in Figure 3. The mean, SD, and Scheffé's paired comparisons for each scale are shown in Table 2. Most ADL (Meals, Excretion, Bathing, Cosmetic, Gowning, Walking around indoors, and Staircase) were significantly more impaired 1 month after surgery than before surgery. All ADL, except for Cosmetic, recovered 3 months after surgery. The total ADL score was significantly lower 1 month after surgery than before surgery. The frequency and velocity index of ADL were significantly lower 1 month after surgery than before surgery. The dyspnea index of ADL was significantly lower 1, 3, and 6 months after surgery than before surgery.

DISCUSSION

Minimally invasive surgery, such as VATS, is increasingly used to surgically treat early-stage lung cancer (5-7). A general assumption among surgeons is that VATS is less traumatic than thoracotomy and is associated with less postoperative pain, less operative bleeding, and shorter hospital stays (8, 9). The PRO questionnaire was recently shown to be an effective and accurate assessment of symptoms in patients treated with surgery, radiotherapy, and chemotherapy (11). However, limited information is currently available on the impact of minimally invasive surgery on lung cancer using PRO. Surgery studies use PRO-QOL less than chemotherapy studies. Koller *et al*. reviewed the use of EORTC QLQ C30 and LC13 in 109 randomized controlled trials (RCT) on lung cancer patients, and showed that chemotherapy was the most frequently applied treatment (79%), followed by radiotherapy (16%), and targeted therapy (16%). RTC included only 2 surgery studies (1.8%) (38).

Previous studies that measured PRO-QOL after thoracotomy or VATS have been retrospective or cross-sectional in design and with a small sample size (39-42). A few recent studies on PRO-QOL have been prospective, longitudinal descriptive-before and after VATS 6-12 months and with a moderate sample size, which is similar to the present study (43-45). We prospectively measured EORTC-QLQ C30 and LC-13 before and 6 months after VATS. The surgery modality was mostly minimally invasive surgery, namely, VATS (88%) and RATS (9%). However, impairments in physical and role functions persisted until 6 months after surgery, as did symptoms such as fatigue, pain, dyspnea, and cough. Bendixen *et al*. compared pain and QOL between lung cancer patients treated with VATS and those treated with thoracotomy using RCT, and reported that VATS was associated with less postoperative pain and better QOL than thoracotomy in the first year after surgery (43). Avery *et al*. examined EORTC-QLQ-C30 for lung cancer patients who underwent VATS (84%), and reported that PRO QOL had not fully recovered 12 months post-surgery, with reduced physical, role, and social functions and increased fatigue and dyspnea (44). Pompili *et al*. examined PRO-QOL in lung cancer patients treated with VATS, and reported a deterioration in role, physical, and social functions and global health, fatigue, dyspnea, pain, appetite loss, and constipation 6 weeks after surgery. These scores improved by 12 months, but did not reach preoperative values (45). Collectively, these findings and the present results revealed impairments in physical and role functions and the worsening of fatigue, dyspnea, and pain symptoms immediately after surgery without full recovery after 6-12 months ; however, VATS was associated with less postoperative pain and better QOL than thoracotomy.

Dyspnea predominantly affects physical activities, such as

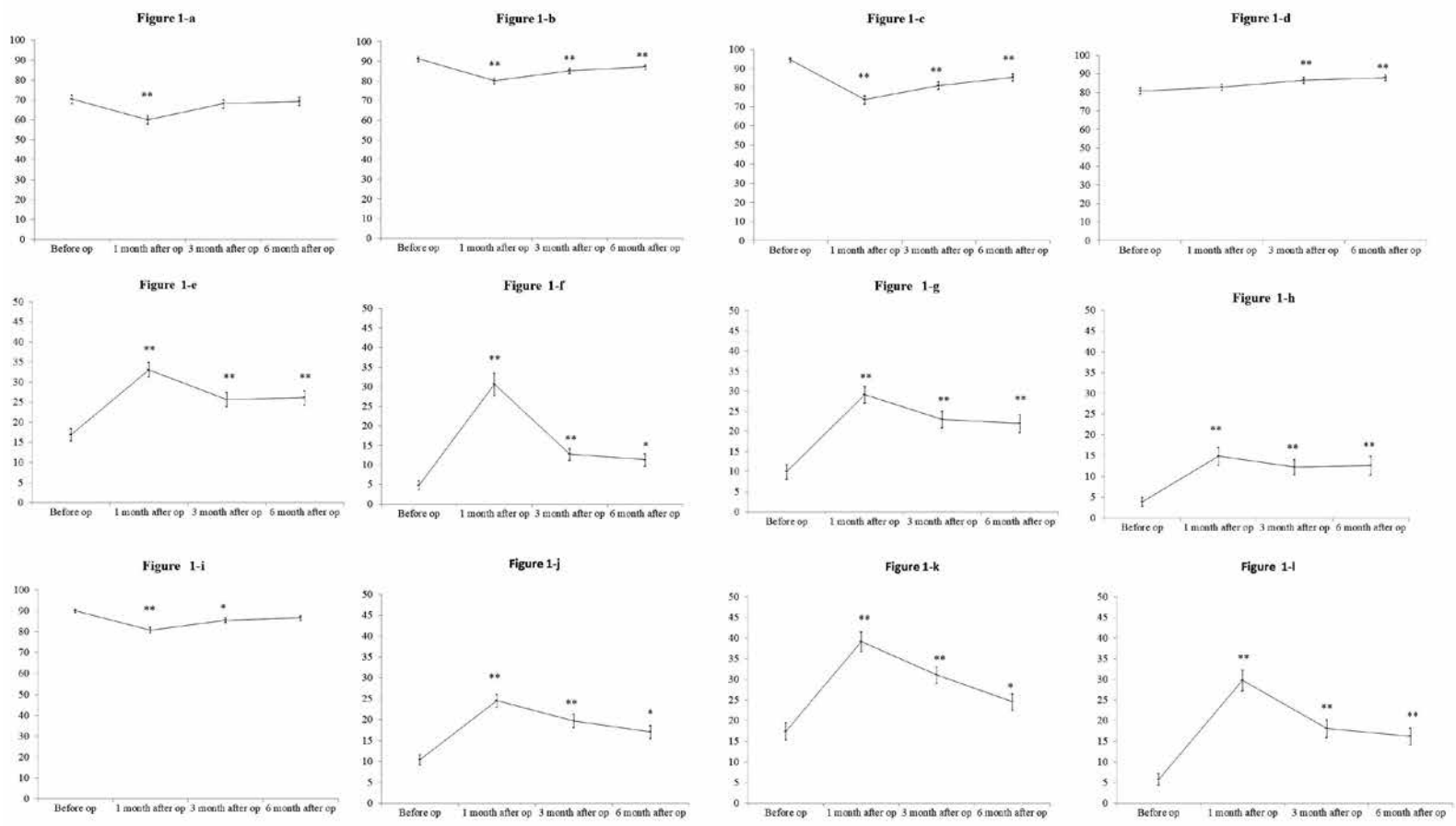


Figure 1. Perioperative time-dependent changes in EORTC-QLQ-C30 and LC-13 in lung cancer patients treated with surgery
Statistical analyses were performed using the Freidman test and Scheffé's test (post-hoc).
(a) Global health status (Freidman : $P < 0.001$). GHS scores were significantly lower 1 month after surgery than before surgery.
(b) Physical function (Freidman : $P < 0.001$). Physical function scores were significantly lower 1 ($P < 0.001$), 3 ($P < 0.001$), and 6 months ($P = 0.0014$) after surgery than before surgery.
(c) Role function (Freidman : $P < 0.001$). Role function scores were significantly lower 1 ($P < 0.001$), 3 ($P < 0.001$), and 6 months ($P < 0.001$) after surgery than before surgery.
(d) Emotional function. (Freidman : $P < 0.001$). Emotional function scores were significantly lower 3 ($P = 0.0034$) and 6 months ($P < 0.001$) after surgery than before surgery.
(e) Fatigue (Freidman : $P < 0.001$). Fatigue scores were significantly higher 1 ($P < 0.001$), 3 ($P = 0.0011$), and 6 months ($P = 0.0014$) after surgery than before surgery.
(f) Pain (Freidman : $P < 0.001$). Pain scores were significantly higher 1 ($P < 0.001$), 3 ($P = 0.0041$), and 6 months ($P = 0.0198$) after surgery than before surgery.
(g) Dyspnea (Freidman : $P < 0.001$). Dyspnea scores were significantly higher 1 ($P < 0.001$), 3 ($P < 0.001$), and 6 months ($P < 0.001$) after surgery than before surgery.
(h) Appetite loss (Freidman : $P < 0.001$). Appetite loss scores were significantly higher 1 ($P < 0.001$), 3 ($P < 0.001$), and 6 months ($P = 0.0068$) after surgery than before surgery.
(i) QLQ-C30 Summary Score = (Physical Functioning + Role Functioning + Social Functioning + Emotional Functioning + Cognitive Functioning + 100-Fatigue + 100-Pain + 100-Nausea_Vomiting + 100-Dyspnea + 100-Sleeping Disturbances + 100-Appetite Loss + 100-Constipation + 100-Diarrhea)/13. (Freidman : $P < 0.001$). QLQ-C30 Summary Scores were significantly higher 1 ($P < 0.001$) and 3 months ($P = 0.011$) after surgery than before surgery.
(j) Dyspnea (Freidman : $P < 0.001$). Dyspnea scores were significantly higher 1 ($P < 0.001$), 3 ($P < 0.001$), and 6 months ($P = 0.02$) after surgery than before surgery.
(k) Cough (Freidman : $P < 0.001$). Cough scores were significantly higher 1 ($P < 0.001$), 3 ($P < 0.001$), and 6 months ($P = 0.0361$) after surgery than before surgery.
(l) Pain in chest (Freidman : $P < 0.001$). Pain in chest scores were significantly higher 1 ($P < 0.001$), 3 ($P < 0.001$), and 6 months ($P < 0.001$) after surgery than before surgery.

Table 2. Results of Scheffé's paired comparisons for each scale

Scales	Before op (Mean ± SD)	1 month after op (Mean ± SD)	P	3 months after op (Mean±SD)	P	6 months after op (Mean ± SD)	P
QLQ-C30							
Global health status · QOL	70.4 ± 21.1	60.0 ± 21.3	**< 0.001**	68.1 ± 21.8		69.3 ± 20.9	
Physical functioning	91.3 ± 12.2	80.1 ± 14.5	**< 0.001**	85.2 ± 12.4	**< 0.001**	87.1 ± 11.1	**0.001**
Role functioning	94.5 ± 11.5	73.8 ± 22.8	**< 0.001**	81.2 ± 20.3	**< 0.001**	85.6 ± 17.8	**< 0.001**
Emotional functioning	80.8 ± 18.0	82.9 ± 16.1		86.7 ± 16.1	**0.003**	87.9 ± 13.8	**< 0.001**
Cognitive functioning	85.0 ± 15.0	85.8 ± 16.6		84.6 ± 17.4		84.1 ± 19.2	
Social functioning	84.8 ± 17.6	81.4 ± 21.3		87.7 ± 15.6		89.2 ± 15.8	
Fatigue	16.9 ± 15.5	33.1 ± 18.2	**< 0.001**	25.7 ± 18.1	**0.001**	26.1 ± 18.4	**< 0.001**
Nausea and vomiting	1.5 ± 7.8	3.0 ± 9.3		3.7 ± 8.1	**0.019**	2.3 ± 8.1	
Pain	4.9 ± 10.9	30.7 ± 29.9	**< 0.001**	12.8 ± 15.9	**0.004**	11.3 ± 15.5	**0.020**
Dyspnea	10.0 ± 18.0	29.1 ± 21.2	**< 0.001**	23.0 ± 21.4	**< 0.001**	22.0 ± 22.7	**< 0.001**
Insomnia	9.7 ± 16.6	20.1 ± 26.5	**0.003**	10.5 ± 19.3		11.7 ± 17.9	
Appetite loss	3.9 ± 10.7	14.9 ± 21.8	**< 0.001**	12.3 ± 18.1	**< 0.001**	12.6 ± 23.4	**0.007**
Constipation	14.6 ± 19.1	16.2 ± 24.6		15.9 ± 20.3		12.3 ± 18.7	
Diarrhea	5.5 ± 14.1	5.5 ± 14.1		9.1 ± 18.8		8.7 ± 17.4	
Financial difficulties	16.8 ± 21.3	18.4 ± 21.8		12.9 ± 20.5		10.8 ± 19.4	**0.033**
C30 summary score	90.0 ± 7.6	80.9 ± 12.6	**< 0.001**	85.6 ± 10.5	**0.011**	86.7 ± 11.0	
QLQ-LC13							
Dyspnea	10.4 ± 11.7	24.6 ± 15.5	**< 0.001**	19.7 ± 16.5	**< 0.001**	17.0 ± 15.5	**0.020**
Coughing	17.5 ± 21.8	39.2 ± 24.9	**< 0.001**	31.1 ± 20.5	**< 0.001**	24.6 ± 20.3	**0.036**
Hemoptysis	1.9 ± 9.1	0.6 ± 4.6		0.0 ± 0.0		0.3 ± 3.3	
Sore mouth	6.1 ± 14.6	8.1 ± 17.1		9.4 ± 18.3		8.1 ± 15.1	
Dysphagia	3.2 ± 9.9	7.8 ± 17.0		7.8 ± 17.0		9.4 ± 19.5	
Peripheral neuropathy	8.7 ± 18.6	7.8 ± 16.3		8.7 ± 19.8		11.3 ± 21.7	
Alopecia	2.6 ± 12.1	2.3 ± 8.4		5.9 ± 19.0		5.8 ± 18.9	
Pain in the chest	5.8 ± 14.3	29.8 ± 26.0	**< 0.001**	18.1 ± 22.3	**< 0.001**	16.2 ± 20.8	**< 0.001**
Pain in an arm or shoulder	12.0 ± 21.8	14.6 ± 21.7		10.7 ± 19.9		11.0 ± 17.7	
Pain in other parts	8.4 ± 19.1	15.9 ± 24.6		10.4 ± 19.3		13.3 ± 23.0	
MAC							
Fighting spirit	50.6 ± 7.2	45.6 ± 12.7		47.4 ± 8.6		44.7 ± 13.1	
Helplessness	10.2 ± 3.6	9.1 ± 3.3		10.3 ± 4.0		9.2 ± 3.4	
Anxious preoccupation	22.5 ± 4.1	20.7 ± 5.5		22.0 ± 4.9		19.9 ± 5.9	
Fatalism	20.8 ± 4.9	20.4 ± 6.2		20.8 ± 5.0		19.7 ± 6.5	
Avoidance	2.3 ± 1.1	1.7 ± 1.1		1.8 ± 0.9		2.0 ± 1.2	
HADS							
Anxiety	5.1 ± 4.0	3.6 ± 3.5		3.2 ± 4.0		3.1 ± 3.3	
Depression	4.8 ± 3.8	4.9 ± 4.3		4.3 ± 4.6		4.0 ± 3.8	
CDS							
sense of effort	1.5 ± 2.6	3.5 ± 3.0	**< 0.001**	2.7 ± 2.8	**0.029**	2.9 ± 3.4	**0.007**
sense of discomfort	1.2 ± 2.0	3.8 ± 2.7	**< 0.001**	2.7 ± 2.6	**0.013**	2.4 ± 2.2	**0.044**
sense of anxiety	0.2 ± 1.1	0.6 ± 1.6		0.6 ± 1.4	**0.018**	0.4 ± 1.2	
total dyspnea	2.8 ± 4.6	7.9 ± 6.1	**< 0.001**	6.0 ± 5.5	**0.004**	5.6 ± 5.6	**0.006**
PADL							
Meals	99.0 ± 2.7	97.2 ± 4.8	**0.020**	97.5 ± 5.6		99.0 ± 2.9	
Excretion	100.0 ± 0.0	98.2 ± 3.9	**< 0.001**	98.5 ± 4.3		99.3 ± 2.5	
Bathing	98.7 ± 3.2	95.3 ± 6.9	**< 0.001**	97.4 ± 4.6		98.1 ± 4.6	
Washing one's hair	99.5 ± 2.6	98.7 ± 3.4		98.1 ± 4.4	**0.021**	99.0 ± 3.0	
Cosmetic	99.9 ± 0.6	98.4 ± 4.4	**0.007**	98.3 ± 5.0	**0.032**	99.4 ± 2.9	
Gowning	99.7 ± 1.2	98.2 ± 4.3	**0.024**	98.2 ± 5.1		99.0 ± 3.6	

Scales	Before op (Mean ± SD)	1 month after op (Mean ± SD)	P	3 months after op (Mean ± SD)	P	6 months after op (Mean ± SD)	P
Walking around indoors	99.5 ± 2.0	97.5 ± 4.8	**0.005**	98.2 ± 4.3		98.7 ± 3.4	
Staircases	94.8 ± 7.7	89.6 ± 11.3	**< 0.001**	92.1 ± 9.1		93.4 ± 7.7	
Walking outdoors	96.7 ± 6.1	93.8 ± 7.7		94.5 ± 7.3		95.3 ± 6.7	
Total score	98.7 ± 2.0	96.3 ± 4.5	**< 0.001**	97.0 ± 4.8		97.9 ± 3.2	
Distance	98.0 ± 3.6	96.8 ± 4.1		97.4 ± 3.7		98.1 ± 3.0	
Accomplishment	99.8 ± 1.1	99.3 ± 2.2		99.8 ± 0.9		99.8 ± 0.8	
Frequency	98.7 ± 3.0	97.2 ± 3.9	**0.030**	99.0 ± 2.9		99.1 ± 2.1	
Velocity	97.2 ± 4.7	93.8 ± 8.2	**0.005**	95.6 ± 6.0		96.3 ± 5.5	
Dyspnea	98.1 ± 3.5	95.3 ± 6.6	**< 0.001**	95.9 ± 6.3	**0.015**	96.3 ± 5.5	**0.026**
Oxygen content	100.0 ± 0.0	96.7 ± 15.2		94.6 ± 19.7		98.0 ± 12.0	

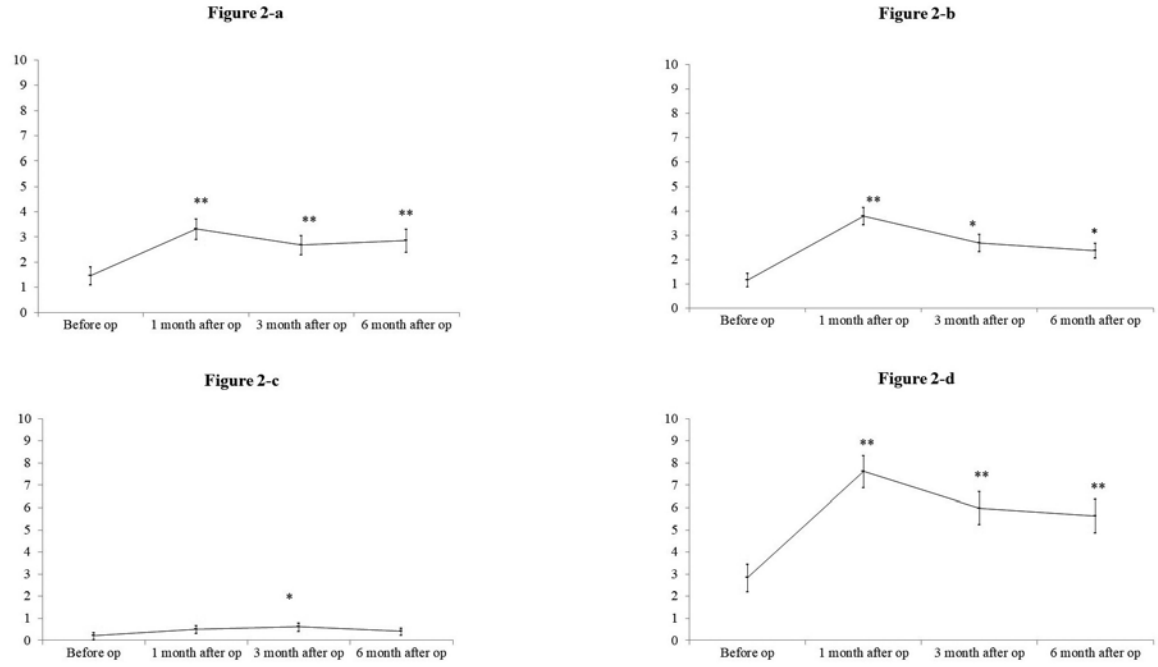


Figure 2. Perioperative time-dependent changes in CDS in lung cancer patients treated with surgery
Statistical analyses were performed using the Freidman test and Scheffé's test (post-hoc).
(a) Sense of effort score (Freidman : P < 0.001). Sense of effort scores were significantly higher 1 (P < 0.001), 3 (P = 0.029), and 6 months (P = 0.007) after surgery than before surgery.
(b) The discomfort scale score (Freidman : P < 0.001). Discomfort scores were significantly higher 1 (P < 0.001), 3 (P = 0.013), and 6 months (P = 0.044) after surgery than before surgery.
(c) Sense of anxiety score (Freidman : P < 0.001). Sense of anxiety scores were significantly higher 3 months (0.018) after surgery than before surgery.
(d) Total dyspnea score (Freidman : P < 0.001). Total dyspnea score scores were significantly higher 1 (P < 0.001), 3 (P = 0.004), and 6 months (P = 0.006) after surgery than before surgery.

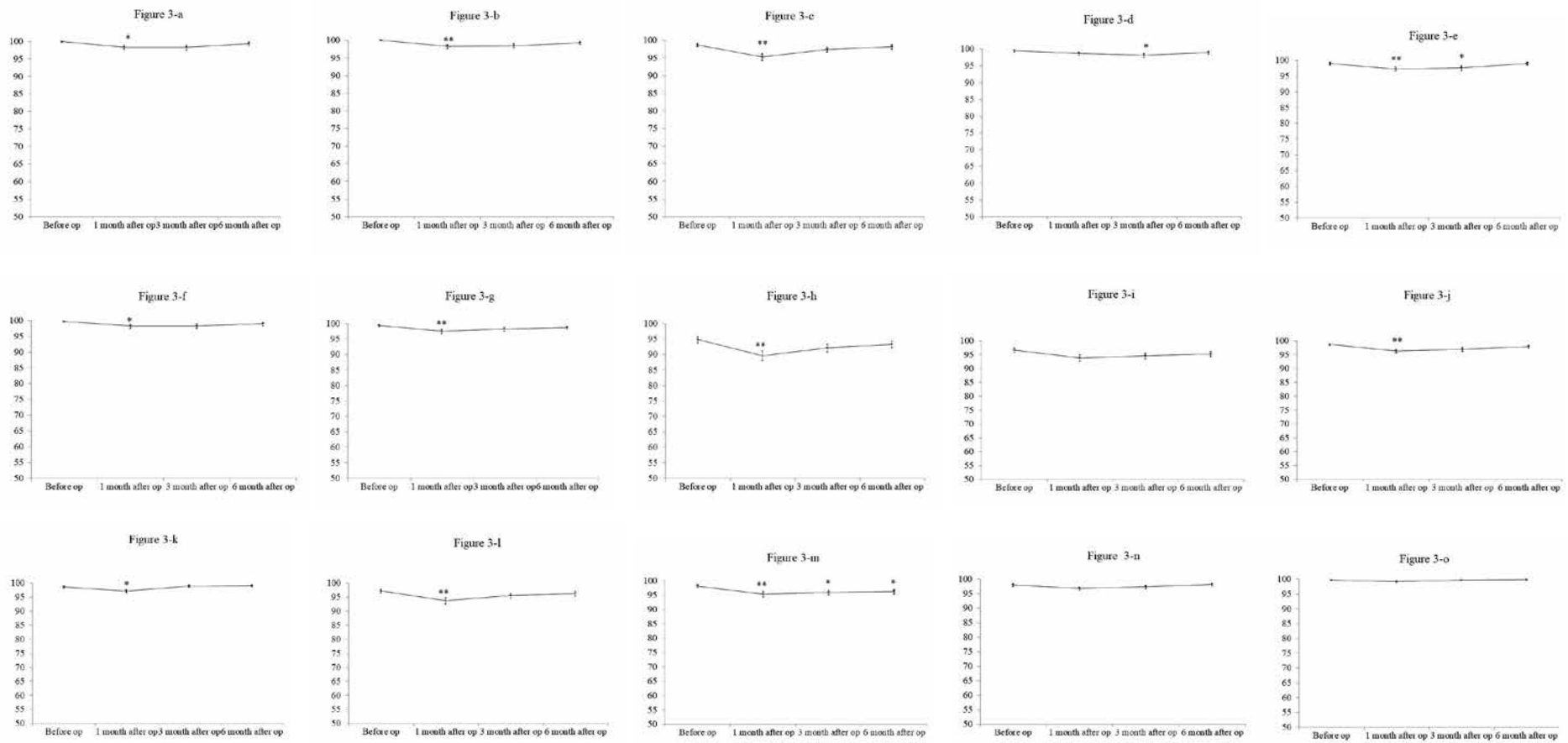


Figure 3. Perioperative time-dependent changes in P-ADL in lung cancer patients treated with surgery
Statistical analyses were performed using the Freidman test and Scheffé's test (post-hoc).
(a) Meals (Freidman : P = 0.006). Meals scores were significantly higher 1 month (P = 0.020) after surgery than before surgery. They recovered after 3 months.
(b) Excretion (Freidman : P < 0.001). Excretion scores were significantly higher 1 month (P < 0.001) after surgery than before surgery. They recovered after 3 months.
(c) Bathing (Freidman : P < 0.001). Bathing scores were significantly higher 1 month (P < 0.001) after surgery than before surgery. They recovered after 3 months.
(d) Washing one's hair (Freidman : P = 0.0071). Washing one's hair scores were significantly higher 3 months (P < 0.021) after surgery than before surgery.
(e) Cosmetic (Freidman : P < 0.001). Cosmetic scores were significantly higher 1 (P = 0.007) and 3 months (P = 0.0032) after surgery than before surgery.
(f) Gowning (Freidman : P = 0.0168). Gowning scores were significantly higher 1 month (P = 0.024) after surgery than before surgery. They recovered after 3 months.
(g) Walking around indoors (Freidman : P = 0.0052). Walking around indoors scores were significantly higher 1 month (P = 0.005) after surgery than before surgery. They recovered after 3 months.
(h) Staircase (Freidman : P < 0.001). Staircase scores were significantly higher 1 month (P < 0.001) after surgery than before surgery. They recovered after 3 months.
(i) Walking outdoors. Walking outdoors scores remained unchanged after surgery.
(j) Total score (Freidman : P < 0.001). Total scores were significantly higher 1 month (P < 0.001) after surgery than before surgery. They recovered after 3 months.
(k) Frequency (Freidman : P < 0.001). Frequency scores were significantly higher 1 month (P = 0.030) after surgery than before surgery. They recovered after 3 months.
(l) Velocity (Freidman : P = 0.0028). Velocity scores were significantly higher 1 month (P = 0.005) after surgery than before surgery. They recovered after 3 months.
(m) Dyspnea (Freidman : P < 0.001). Dyspnea scores were significantly higher 1 (P< 0.001), 3 (P< 0.001), and 6 months (P< 0.001) after surgery than before surgery.
(n) Distance. Then is no significance
(o) Accomplishment

walking, taking meals, and climbing staircases, because it causes an imbalance between oxygen demand and supply. On the other hand, pain affects psychological conditions and physical activities to the same degree (46). In the present study, we focused on the relationship between "dyspnea" and "ADL" using CDS and P-ADL questionnaires. To the best of our knowledge, CDS developed by Tanaka *et al*. (20) is the first scale to evaluate the multidimensional nature of dyspnea in cancer patients. It comprises 3 factors (sense of effort, sense of discomfort, and sense of anxiety) and 12 items. Tanaka *et al*. reported that 'sense of effort' correlated with the performance status, which represents physical status, and reflected impairments in physical activity aspects because of dyspnea. They reported that 'sense of discomfort' correlated with the saturation of percutaneous oxygen measured at rest, which reflected an uncomfortable feeling at rest rather than shortness of breath during exercise. They also demonstrated that 'sense of anxiety' correlated with the psychological status measured by the State-Trait Anxiety Inventory questionnaire (47), which reflected the psychological nature of dyspnea amplified by anxiety rather than a patient's physical condition (20, 48). The present study showed that sense of effort, discomfort scale, and total dyspnea scores were significantly higher 1, 3, and 6 months after surgery than before surgery, whereas no significant differences were observed in the sense of anxiety. These results revealed that the psychological nature of dyspnea remained stable over time after surgery, whereas dyspnea on exercise and at rest continued until 6 months after surgery.

Patients with respiratory disorders, such as chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis, have restricted ADL and impaired QOL (48). Difficulties are associated with accurately measuring ADL in these patients using a standard ADL scale because of dyspnea. Goto *et al*. produced and developed the P-ADL questionnaire (versions 1 and 2), which is a specific ADL scale for patients with respiratory disorders (21, 49, 50). Dyspnea is classified not only by the categories of the action, but also by the index of the action. P-ADL consists of 9 categories (Meals, Excretion, Bathing, Washing one's hair, Cosmetic, Gowning, Walking around indoors, Walking outdoors, and Staircase) and estimates 6 indexes (Distance, Accomplishment, Frequency, Velocity, Dyspnea, and Oxygen content). We used P-ADL to perioperatively estimate ADL in lung cancer patients treated with surgery ; however, it is frequently used for patients with COPD. The present study showed that most of the categories of ADL were impaired 1 month after surgery, but recovered by 3 months after surgery. Blackwood reported that lung cancer survivors showed the greatest impairments in five ADL categories : transferring, bathing, dressing, toileting, and feeding (51). This is consistent with the present results. In P-ADL, the frequency and velocity of performing ADL were reduced at 1 month, but were not observed at 3 months.

However, only dyspnea when performing ADL persisted until 6 months. Patients with lung cancer need advice regarding QOL-dyspnea, pain and fatigue, and ADL from medical doctors and nurses in the 3 months after surgery, particularly within 1 month. They may perform most ADL without any restrictions at 3 months. However, medical staff need to consider the impact of dyspnea 6 months after surgery despite the minimally invasive nature of surgery.

Since dyspnea is an uncontrollable symptom that occurs at an indeterminate time, it is not possible to plan for timely treatment (52). Comprehensive breathlessness services that integrate self-management support are ideal for improving breathlessness and QOL (53). Breathing exercises for pulmonary expansion, such as pursed-lip breathing, abdominal breathing, thoracic breathing, incentive spirometry, inspiratory and muscle training, bronchial hygiene, early mobilization, deambulation, postural correction, and shoulder range of motion activities during the perioperative period, improve dyspnea in lung cancer patients (54, 55). Nursing interventions are needed for patients to understand the multiple benefits of perioperative exercise training for physical function, the prevention of postoperative complications, and reductions in hospitalization. Nurses may assist a patient's family to help the patient get out of bed for walking as early as possible after surgery and provide appropriate assistance with ADL.

We used the MAC scale and HADS to examine whether surgery affected the psychological status perioperatively. The MAC scale measures the specific mental adjustment of cancer patients using 5 subscales : helpless/hopeless, anxious preoccupation, fighting spirit, cognitive avoidance, and fatalism. All 5 subscales were stable 6 months after surgery. Surgery did not affect mental adjustment. However, although it was not significant, anxiety gradually decreased after surgery. Khullar *et al*. reported that anxiety-fear and depression both significantly improved after surgery (56). Therefore, patients may become comfortable after successful surgery.

STUDY LIMITATIONS

There are several limitations that need to be addressed. 1) This was a single-center study with a moderate sample size (n = 103). 2) There was an interval of 4 years between Projects A (n = 49) and B (n = 54). We simultaneously analyzed EORTC QLQ C30 and QLQ C-13 data from the two projects. However, the patient population was almost homologous for early-stage lung cancer (pStage I or II), lobectomy, minimally invasive surgery (VATS or RATS), and adenocarcinoma. This was a prospective longitudinal descriptive study. 3) P-ADL may be used to clarify which actions in ADL are affected by respiratory disturbance. However, since there is currently no English version of P-ADL, researchers outside of Japan cannot use it.

CONCLUSIONS

Impairments in physical and role functions and the symptoms of pain and dyspnea persisted until 6 months after surgery despite the minimally invasive nature of surgery. Dyspnea after surgery was physiological, not psychological. Impairments in ADL were related to dyspnea. Breathing exercises are necessary to improve dyspnea in lung cancer patients.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Zhang Linwan : Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing-original draft, Writing-review and editing. Kazuya Kondo : Conceptualization, Methodology, Formal analysis, Data curation, Writing-original draft, Writing-review and editing, Project administration. Takae Bando : Conceptualization, Methodology, Validation, Formal analysis, Data curation, Writing-review and editing. Yoshie Imai : Conceptualization, Investigation, Data curation, Writing-review and editing. Naoya Kawakita : Conceptualization, Investigation, Data curation. Hiroaki Toba : Conceptualization, Investigation, Data curation. Hiromitsu Takizawa : Conceptualization, Methodology, Formal analysis, Supervision, Writing-review and editing.

FUNDING

No funding was received.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the present study are available from the corresponding author upon reasonable request.

DECLARATION OF COMPETING INTERESTS

There is no conflict of interest.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Ethics Committee of the University of Tokushima approved the present study (Tokushima University Hospital, approval no. 4071), and all procedures were conducted according to the Declaration of Helsinki. All patients provided written informed consent.

PATIENT CONSENT FOR PUBLICATION

Not applicable.

ACKNOWLEDGMENTS

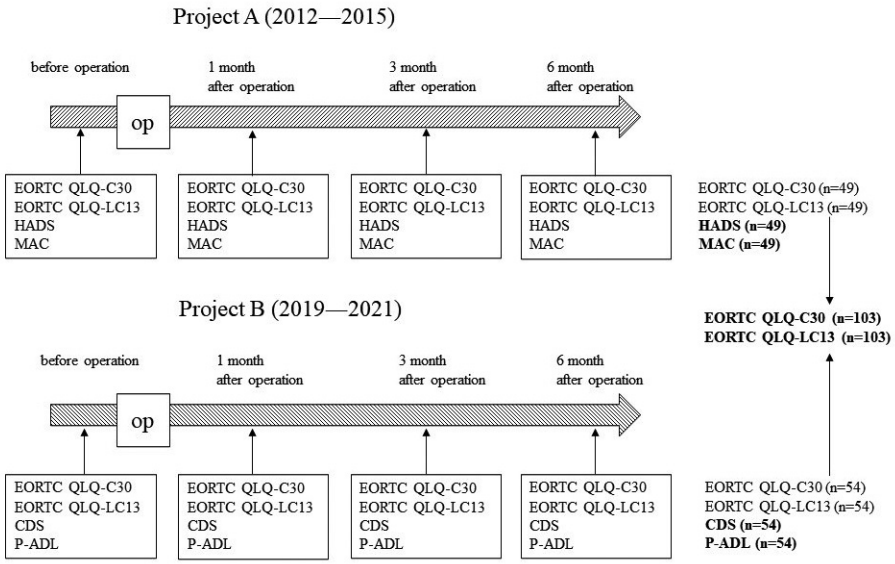
Not applicable.

REFERENCES

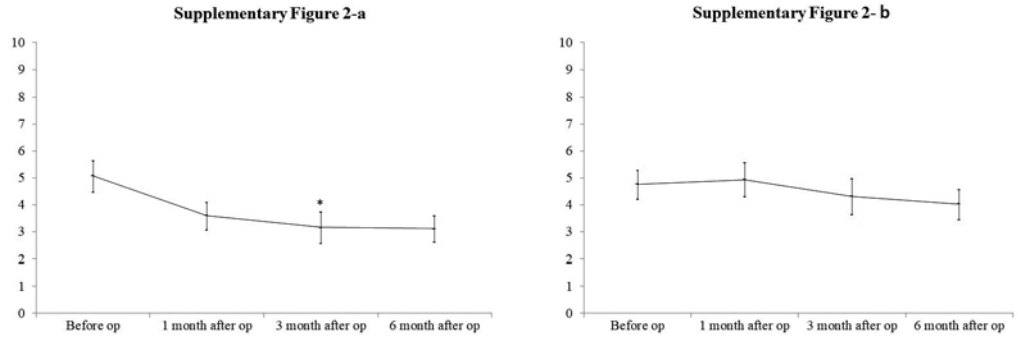
1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A : Global cancer statistics 2018 : GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68 : 394-424, 2018
2. Katanoda K, Hori M, Saito E, Shibata A, Ito Y, Minami T, Ikeda S, Suzuki T, Matsuda T : Updated Trends in Cancer in Japan : Incidence in 1985-2015 and Mortality in 1958-2018-A Sign of Decrease in Cancer Incidence. J Epidemiol 31 : 426-450, 2021
3. Lu T, Yang X, Huang Y, Zhao M, Li M, Ma K, Yin J, Zhan C, Wang Q : Trends in the incidence, treatment, and survival of patients with lung cancer in the last four decades. Cancer Management and Research 11 : 943-953, 2019
4. Goldstraw P, Chansky K, Crowley J, Rami-Porta R, Asamura H, Eberhardt WE, Nicholson AG, Groome P, Mitchell A, Bolejack V : The IASLC Lung Cancer Staging Project : proposals for revision of the TNM stage groupings in the forthcoming (eighth) edition of the TNM classification for lung cancer. J Thorac Oncol 11 : 39-51, 2016
5. Whitson BA, Andrade RS, Boettcher A, Bardales R, Kratzke RA, Dahlberg PS, Maddaus MA : Video-assisted thoracoscopic surgery is more favorable than thoracotomy for resection of clinical stage I non-small cell lung cancer. Ann Thorac Surg 83 : 1965-70, 2007
6. Hanna WC, de Valence M, Atenafu EG, Cypel M, Waddell TK, Yasufuku K, Pierre A, De Perrot M, Keshavjee S, Darling GE : Is video-assisted lobectomy for non-small cell lung cancer oncologically equivalent to open lobectomy? European Journal of Cardio-Thoracic Surgery 43 : 1121-1125, 2013
7. Zheng L, Song P, Jiang Y, Fan X, Yang C, Zhang L, Wang Q : Outcomes and quality of life after Robot-assisted lobectomy/segmentectomy for lung cancer compared to video-assisted thoracoscopic surgery : both three-port procedures performed by a single surgeon. J Thorac Dis 14 : 689-698, 2022
8. Yan TD, Black D, Bannon PG, McCaughan BC : Systematic review and meta-analysis of randomized and nonrandomized trials on safety and efficacy of video-assisted thoracic surgery lobectomy for early-stage non-small-cell lung cancer. J Clin Oncol 27 : 2553-62, 2009
9. Cao C, Manganas C, Ang SC, Peeceeyen S, Yan TD : Video-assisted thoracic surgery versus open thoracotomy for non-small cell lung cancer : a meta-analysis of propensity score-matched patients. Interactive Cardiovascular and Thoracic Surgery 16 : 244-9, 2013
10. Weldring T, Smith SM : Patient-Reported Outcomes (PROs) and Patient-Reported Outcome Measures (PROMs). Health Serv Insights 6 : 61-8, 2013
11. Singhal S, Dickerson J, Glover MJ, Roy M, Chiu M, Ellis-Caleo T, Hui G, Tamayo C, Loecher N, Wong HN, Heathcote LC, Schapira L : Patient-reported outcome measurement implementation in cancer survivors : a systematic review. Journal of Cancer Survivorship 5 : 23, 2022
12. Cella DF, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, Silberman M, Yellen SB, Winicour P, Brannon J : The Functional Assessment of Cancer Therapy Scale : Development and Validation of the General Measure. J Clin Oncol 11 : 570-9, 1993
13. Ware JE, Sherboune CD : The MOS 36-item Short-Form Health Survey (SF-36) : I. Conceptual framework and item selection. Med Care 30 : 473-89, 1992
14. Coon CD, Schlichting M, Zhang X : Interpreting Within-Patient Changes on the EORTC QLQ-C30 and EORTC QLQ-LC13. Patient 15 : 691-702, 2022
15. Akezaki Y, Nakata E, Tominaga R, Iwata O, Kawakami J, Tsuji T, Ueno T, Yamashita M, Sugihara S : Short-Term Impact of Video-Assisted Thoracoscopic Surgery on Lung Function, Physical Function, and Quality of Life. Healthcare 9 : 136, 2021
16. Bendixen M, Dan Jorgensen O, Kronborg C, Andersen C, Licht PB : Postoperative pain and quality of life after lobectomy via video-assisted thoracoscopic surgery or anterolateral thoracotomy for early stage lung cancer : a randomised controlled trial. The Lancet Oncology 17 : 836-844, 2016
17. Zigmond AS, Snaith RP : The hospital anxiety and depression scale. Acta Psychiatr Scand 67 : 361-70,1983
18. Watson M, Greer S, Young J, Inayat Q, Burgess C, Robertson B : Development of a questionnaire measure of adjustment to cancer : the MAC scale. Psychol Med 18 : 203-9, 1988
19. Goto Y, Sato Y, Kawabe T, Kashiwagi C, Kozuki M : Examination of a new ADL rating scale for patients with chronic obstructive pulmonary disease. Journal of the Japanese Society of Respiratory Care and Rehabilitation 25 : 423-8, 2015
20. Tanaka K, Akechi T, Okuyama T, Nishiwaki Y, Uchitomi Y : Development and validation of the Cancer Dyspnoea Scale : a multidimensional, brief, self-rating scale. British Journal of Cancer 82 : 800-805, 2000
21. Goto Y, Kozuki M, Watanabe M : Development of a new ADL measurement for patients with emphysema at home. SoGo Rehabilitation 28 : 863-8, 2000 (in Japanese)
22. Bergman B, Aaronson NK, Ahmedzai S, Kaasa S, Sullivan M : The EORTC QLQ-LC13 : a modular supplement to the

EORTC Core Quality of Life Questionnaire (QLQ-C30) for use in lung cancer clinical trials. EORTC Study Group on Quality of Life. Eur J Cancer 30A : 635-42, 1994
23. Bjordal K, de Graeff A, Fayers PM, Hammerlid E, van Pottelsberghe C, Curran D, Ahlner-Elmqvist M, Maher EJ, Meyza JW, Brédart A, Söderholm AL, Arraras JJ, Feine JS, Abendstein H, Morton RP, Pignon T, Huguenin P, Bottomly A, Kaasa S : A 12 country field study of the EORTC QLQ-C30 (version 3.0) and the head and neck cancer specific module (EORTC QLQ-H&N35) in head and neck patients. EORTC Quality of Life Group. Eur J Cancer 36 : 1796-1807, 2000
24. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JC : The European Organization for Research and Treatment of Cancer QLQ-C30 : a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 85 : 365-76, 1993
25. Kobayashi K, Takeda F, Teramukai S, Gotoh I, Sakai H, Yoneda S, Noguchi Y, Ogasawara H, Yoshida K : A cross-validation of the European Organization for Research and Treatment of Cancer QLQ-C 30 (EORTC QLQ-C30) for Japanese with lung cancer. Eur J Cancer 34 : 810-815, 1998
26. Pompili C, Koller M, Velikova G, Franks K, Absolom K, Callister M, Robson J, Imperatori A, Brunelli A : EORTC QLQ-C30 summary score reliably detects changes in QOL three months after anatomic lung resection for non-small cell lung cancer (NSCLC). Lung cancer 123 : 149-154, 2018
27. Fayers P, Aaronson NK, Bjordal K, Groenvold M, Curran D, Bottomley : In : European Organisation for Research and Treatment of Cancer, editors. A. EORTC QLQ-C30 Scoring Manual. (3rd ed.). E-Publishing Inc, 2001
28. Husson O, de Rooij BH, Kieffer J, Oerlemans S, Mols F, Aaronson NK, van der Graaf WTA, van de Poll-Franse LV : The EORTC QLQ-C30 Summary Score as Prognostic Factor for Survival of Patients with Cancer in the "Real-World" : Results from the Population-Based PROFILES Registry. Oncologist 25 : e722-e732, 2020
29. Watson M, Greer S, Bliss JM : Mental Adjustment to Cancer Scale User's Manual. Cancer Research Campaign Medical Research Group, Royal Marsden Hospital : Sutton, Surrey, 1989
30. Greer S, Moorey S, Watson M : Patients' adjustment to cancer : the mental adjustment to cancer (MAC) scale vs clinical ratings. J Psychosom Res 33 : 373-377, 1989
31. Akechi T, Fukue-Saeki M, Kugaya A, Okamura H, Nishiwaki Y, Yamawaki S, Uchitomi Y : Psychometric properties of the Japanese version of the Mental Adjustment to Cancer (MAC) scale. Psychooncology 9 : 395-401, 2000
32. Lareau SC, Meek PM, Roos PJ : Development and testing of the modified version of the pulmonary functional status and dyspnea questionnaire (PFSDQ-M). Heart Lung 27 : 159-168, 1998
33. Garrod R, Bestall JC, Paul EA, Wedzicha JA, Jones PW : Development and validation of a standardized measure of activity of daily living in patients with severe COPD : the London Chest Activity of Daily Living scale (LCADL). Respir Med 94 : 589-96, 2000
34. Wakabayashi R, Motegi T, Yamada K, Ishii T, Gemma A, Kida K : Presence of in-home caregiver and health outcomes of older adults with chronic obstructive pulmonary disease. J Am Geriatr Soc 59 : 44-9, 2011
35. Friedman M : The use of ranks to avoid the assumption of normality implicit in the analysis of variance. Journal of the American Statistical Association 32 : 675-701, 1937
36. Travis WD, Brambilla E, Burke AP, Marx A, Nicholson AG : WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart. Lyon, 2015
37. Goldstraw P, Crowley J, Chansky K, Giroux DJ, Groome PA, Rami-Porta R, Postmus PE, Rusch V, Sobin L : The IASLC lung cancer staging project : proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM classifcation of malignant tumours. J Thorac Oncol 2 : 706-714, 2007
38. Koller M, Warncke S, Hjermstad MJ, Arraras J, Pompili C, Harle A, Johnson CD, Chie WC, Schulz C, Zeman F, van Meerbeeck JP, Kuliś D, Bottomley A : European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group ; EORTC Lung Cancer Group. Use of the lung cancer-specific Quality of Life Questionnaire EORTC QLQ-LC13 in clinical trials : A systematic review of the literature 20 years after its development. Cancer 121 : 4300-23, 2015
39. Pompili C, Absolom K, Franks K, Velikova G : Are quality of life outcomes comparable following stereotactic radiotherapy and minimally invasive surgery for stage I lung cancer patients? J Thorac Dis 10 : 7055-7063, 2018
40. Khullar OV, Rajaei MH, Force SD, Binongo JN, Lasanajak Y, Robertson S, Pickens A, Sancheti MS, Lipscomb J, Gillespie TW, Fernandez FG : Pilot Study to Integrate Patient Reported Outcomes After Lung Cancer Operations Into The Society of Thoracic Surgeons Database. Ann Thorac Surg 104 : 245-53, 2017
41. Rizk NP, Ghanie A, Hsu M, Bains MS, Downey RJ, Sarkaria IS, Finley DJ, Adusumilli PS, Huang J, Sima CS, Burkhalter JE, Park BJ, Rusch VW : A prospective trial comparing pain and quality of life measures after anatomic lung resection using thoracoscopy or thoracotomy. Ann Thorac Surg 98 : 1160-6, 2014
42. Fagundes CP, Shi Q, Vaporciyan AA, Rice DC, Popat KU, Cleeland CS, Wang XS : Symptom recovery after thoracic surgery : Measuring patient-reported outcomes with the MD Anderson Symptom Inventory. J Thorac Cardiovasc Surg 150 : 613-9, 2015
43. Bendixen M, Jørgensen OD, Kronborg C, Andersen C, Licht PB : Postoperative pain and quality of life after lobectomy via video-assisted thoracoscopic surgery or anterolateral thoracotomy for early stage lung cancer : a randomised controlled trial. Lancet Oncol 17 : 836-44, 2016
44. Avery KNL, Blazeby JM, Chalmers KA, Batchelor TJP, Casali G, Internullo E, Krishnadas R, Evans C, West D : Impact on Health-Related Quality of Life of Video-Assisted Thoracoscopic Surgery for Lung Cancer. Ann Surg Oncol 27 : 1259-1271, 2020
45. Pompili C, Rogers Z, Absolom K, Holch P, Clayton B, Callister M, Robson J, Brunelli A, Franks K, Velikova G : Quality of life after VATS lung resection and SABR for early-stage non-small cell lung cancer : A longitudinal study. Lung Cancer 162 : 71-78, 2021
46. Tanaka K, Akechi T, Okuyama T, Nishiwaki Y, Uchitomi Y : Impact of Dyspnea, Pain, and Fatigue on Daily Life Activities in Ambulatory Patients with Advanced Lung Cancer. J Pain Symptom Manage 23 : 417-423, 2002
47. Spielberger CD, Gorsuch RL, Lushene RE : STAI Manual for the State-Trait Anxiety Inventory. Consulting Psychologists Press : Palo Alto, 1970
48. Damani A, Ghoshal A, Salins N, Deodhar J, Muckaden M : Validation of "Cancer Dyspnea Scale" in Patients With Advanced Cancer in a Palliative Care Setting in India. J Pain Symptom Manage 54 : 715-720, 2017
49. Velloso M, Stella SG, Cendon S, Silva AC, Jardim JR : Metabolic and ventilatory parameters of four activities of daily

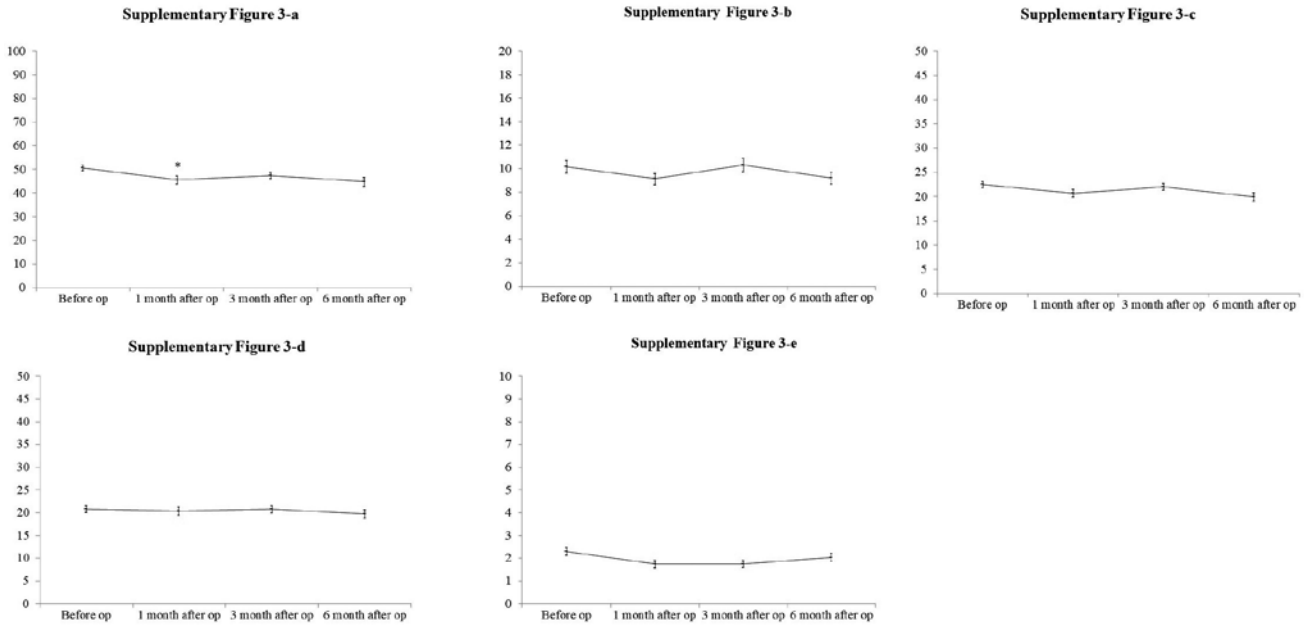
living accomplished with arms in COPD patients. Chest 123 : 1047-53, 2003
50. Japanese Society for Respiratory Care and Rehabilitation, Japanese Respiratory Society, Japanese Society of Rehabilitation Medicine, Japanese Physiotherapy Association, In : Shorinsha editors. Respiratory Rehabilitation Manual - Exercise Therapy. Edition 2. Tokyo, Japan : E-Publishing Inc, 2009, p.171
51. Blackwood J, Karczewski H, Huang MH, Pfalzer L : "Katz activities of daily living disability in older cancer survivors by age, stage, and cancer type". J Cancer Surviv 14 : 769-778, 2020
52. Saetan P, Chaiviboontham S, Pokpalagon P, Chansriwong P : The Effects of the Respiratory Rehabilitation Program on Perceived Self-Efficacy and Dyspnea in Patients with Lung Cancer. Korean Society of Nursing Science 14 : 277-285, 2020
53. Howell D : Enabling patients in effective self-management of breathlessness in lung cancer : the neglected pillar of personalized medicine. Lung Cancer Management 10 : LMT52, 2021
54. Kendall F, Abreu P, Pinho P, Oliveira J, Bastos P : The role of physiotherapy in patients undergoing pulmonary surgery for lung cancer. A literature review. Revista Portuguesa de Pneumologia (English Edition) 23 : 343-351, 2017
55. Cavalheri V, Granger CL : Exercise training as part of lung cancer therapy. Respirology 25 : 80-87, 2020
56. Khullar OV, Rajaei MH, Force SD, Binongo JN, Lasanajak Y, Robertson S, Pickens A, Sancheti MS, Lipscomb J, Gillespie TW, Fernandez FG : Pilot Study to Integrate Patient Reported Outcomes After Lung Cancer Operations Into The Society of Thoracic Surgeons Database. Ann Thorac Surg 104 : 245-253, 2017



Supplementary Figure 1. Flowchart summarizing the number of patients in 2 projects.
EORTC-QLQ : European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire, HADS : Hospital Anxiety and Depression Scale, MAC : Mental Adjustment to Cancer, CDS : Cancer Dyspnea Scale, P-ADL : Pulmonary Activities of Daily Living, op : operation



Supplementary Figure 2. Perioperative time-dependent changes in HADS in lung cancer patients treated with surgery
Statistical analyses were performed using the Friedman test and Scheffé's test (post-hoc).
(a) Anxiety. Anxiety scores gradually decreased after surgery.
(b) Depression. Depression scores remained constant perioperatively.



Supplementary Figure 3. Perioperative time-dependent changes in MAC in lung cancer patients treated with surgery
Statistical analyses were performed using the Friedman test and Scheffé's test (post-hoc).
(a) Fighting spirit. Fighting spirit scores remained constant perioperatively.
(b) Helplessness. Helplessness scores remained constant perioperatively.
(c) Anxious preoccupation. Anxious preoccupation scores remained constant perioperatively.
(d) Fatalism. Fatalism scores remained constant perioperatively.
(e) Avoidance. Avoidance scores remained constant perioperatively.

Supplementary Table 1

Pulmonary ADL : P-ADL evaluation table

Please describe your life at home. (If you are in hospital, please describe your situation immediately prior to admission)

Prescribed oxygen volume : 1) at rest ( ) L/min, 2) during movement ( ) L/min, 3) during sleep ( ) L/min
◇ Please indicate the activity that changes your oxygen level ( )

Please select and circle one number (0-4) for each item.

Meals

Accomplishment	0 Need assistance in eating	1	2 Eat without assistance (e.g. chopped food needs to be processed)	3	4 Eat without assistance (normal diet)
Distance	0 My own room (recumbent position)	1	2 My own room (on the bed)	3	4 Outside my own room (e.g. canteen)
Frequency	0 Every time I am fed	1	2 Eat without assistance depending on the situation	3	4 Eat without assistance every time
Velocity	0 Cannot eat at all	1 With a lot of rest	2 Take a break on the way	3 Slowly and without rest	4 Smoothly done
Dyspnea	0 Severe	1 Marked	2 Moderate	3 Slight	4 None
Oxygen content	0 Cancel by myself	1 Make changes myself	2 Mostly adhere to prescribed doses	3 Always adhere to prescribed doses	4 Not prescribed

Toileting

Accomplishment	0 Use a plug-in toilet	1 Use a urinal and portable toilet	2 Use a urinal and portable toilet at night only	3 Use a toilet with assistance	4 Use a toilet without assistance
Distance	0 In the bed	1	2 By the bed	3	4 Separate toilet
Frequency	0 Do not use the toileting to defecate	1 Defecate in the toilet	2 May go to the toileting during the day	3 Use the toilet every time during the day only	4 Use the toilet every time
Velocity	0 Do not use to the toilet at all	1 With a lot of rest	2 Take a break on the way	3 Slowly and without rest	4 Smoothly done
Dyspnea	0 Severe	1 Marked	2 Moderate	3 Slight	4 None
Oxygen content	0 Cancel by myself	1 Make changes myself	2 Mostly adhere to prescribed doses	3 Always adhere to prescribed doses	4 Not prescribed

Bathing

Accomplishment	0 Assisted bed bath	1 Bed bath by myself	2 Mostly assisted bathing	3 Occasionally assisted bathing	4 Self bathing
Distance	0 My own room	1	2 Shower only in bathrooms	3	4 Step into the bathtub
Frequency	0 No bathing at all	1	2 Occasional bathing	3	4 Bathe daily
Velocity	0 Cannot do it myself at all	1 With a lot of rest	2 Take a break on the way	3 Slowly and without rest	4 Smoothly done
Dyspnea	0 Severe	1 Marked	2 Moderate	3 Slight	4 None
Oxygen content	0 Cancel by myself	1 Make changes myself	2 Mostly adhere to prescribed doses	3 Always adhere to prescribed doses	4 Not prescribed

Washing one's hair

Accomplishment	0 I do not wash my hair	1	2 Get my hair washed (including barbershops and salons)	3	4 I do it myself
Distance	0 At the bed	1	2 Washing rooms	3	4 Bathroom
Frequency	0 Never wash my hair	1	2 Wash hair separately from bathing	3	4 Wash hair when bathing
Velocity	0 Cannot do it myself at all	1 With a lot of rest	2 Take a break on the way	3 Slowly and without rest	4 Smoothly done
Dyspnea	0 Severe	1 Marked	2 Moderate	3 Slight	4 None
Oxygen content	0 Cancel by myself	1 Make changes myself	2 Mostly adhere to prescribed doses	3 Always adhere to prescribed doses	4 Not prescribed

Hygiene

Accomplishment	0 Stay in bed and receive assistance	1 Sit down and receive assistance	2 Sit down and do it by myself if prepared	3 Sit down and do it by myself	4 Stand up and do it by myself
Distance	0 Above the bed	1	2 Other than washing rooms (my own room)	3	4 Washing rooms
Frequency	0 Do not brush my teeth in the washroom	1	2 Occasionally wash in the bathroom and brush my teeth	3	4 Wash and brush my teeth in the washroom every time
Velocity	0 Cannot do it myself at all	1 With a lot of rest	2 Take a break on the way	3 slowly and without rest	4 Smoothly done
Dyspnea	0 Severe	1 Marked	2 Moderate	3 Slight	4 None
Oxygen content	0 Cancel by myself	1 Make changes myself	2 Mostly adhere to prescribed doses	3 Always adhere to prescribed doses	4 Not prescribed

Dressing

Accomplishment	0 Getting help to change clothes	1	2 I can do it by myself if prepared	3	4 I can do it by myself
Distance					
Frequency	0 I cannot change clothes by myself	1	2 I can do it by myself depending on the situation	3	4 I can do it by myself each time
Velocity	0 Cannot do it myself at all	1 With a lot of rest	2 Take a break on the way	3 Slowly and without rest	4 Smoothly done
Dyspnea	0 Severe	1 Marked	2 Moderate	3 Slight	4 None
Oxygen content	0 Cancel by myself	1 Make changes myself	2 Mostly adhere to prescribed doses	3 Always adhere to prescribed doses	4 Not prescribed

Walking around indoors

Accomplishment	0 Cannot walk at all	1 Can walk with help	2	3 Can walk if looked after (supervised)	4 I can walk by myself
Distance	0 Cannot walk at all	1 Only around the bed	2 Only in my own room	3 Toilets and washrooms only	4 All inside the home
Frequency	0 Cannot walk at all	1	2 Can walk in some situations	3	4 Can walk anytime
Velocity	0 Cannot do it myself at all	1 With a lot of rest	2 Take a break on the way	3 Slowly and without rest	4 Smoothly done
Dyspnea	0 Severe	1 Marked	2 Moderate	3 Slight	4 None
Oxygen content	0 Cancel by myself	1 Make changes myself	2 Mostly adhere to prescribed doses	3 Always adhere to prescribed doses	4 Not prescribed

Ascending a staircase

Accomplishment	0 Cannot ascend by myself	1	2 Can ascend with assistance	3	4 I can ascend by myself
Distance	0 I cannot ascend at all	1 2~3 stairs	2 5~6 stairs	3 Up to the second floor	4 3rd floor and above
Frequency	0 Inaccessible	1	2 Ascend only when necessary	3	4 Can ascend at any time
Velocity	0 Cannot do it myself at all	1 With a lot of rest	2 Take a break on the way	3 Slowly and without rest	4 Smoothly done
Dyspnea	0 Severe	1 Marked	2 Moderate	3 Slight	4 None
Oxygen content	0 Cancel by myself	1 Make changes myself	2 Mostly adhere to prescribed doses	3 Always adhere to prescribed doses	4 Not prescribed

Walking outdoors

Accomplishment	0 Cannot walk at all	1 Can walk with help	2	3 Can walk if supervised	4 Can walk by myself
Distance	Maximum distance you can walk			( ) meters	
Frequency	0 Cannot walk at all	1	2 Can walk in some situations	3	4 Can walk anytime
Velocity	0 Cannot do it myself at all	1 With a lot of rest	2 Take a break on the way	3 Slowly and without rest	4 Smoothly done
Dyspnea	0 Severe	1 Marked	2 Moderate	3 Slight	4 None
Oxygen content	0 Cancel by myself	1 Make changes myself	2 Mostly adhere to prescribed doses	3 Always adhere to prescribed doses	4 Not prescribed

Conversation

Accomplishment	0 While in bed (on the bed)	1	2 Sitting in a wheelchair or easy chair	3	4 Can be done wherever I sit
Distance	Maximum time you can talk			( ) hours	
Frequency					
Velocity	0 Cannot do it myself at all	1 With a lot of rest	2 Take a break on the way	3 Slowly and without rest	4 Smoothly done
Dyspnea	0 Severe	1 Marked	2 Moderate	3 Slight	4 None
Oxygen content	0 Cancel by myself	1 Make changes myself	2 Mostly adhere to prescribed doses	3 Always adhere to prescribed doses	4 Not prescribed

Special mention

State of affairs as of the year/month

Date of entry : _____year_____month_____day