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Patient-Reported Outcomes of Surgery of Non-Small Cell Lung Cancer: Evaluation Based on the Questionnaires of Anti-Aging Quality of Life and the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire

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Abstract

Background: Patient-reported outcomes of the quality of life (QOL) after an open thoracotomy have not been studied. To determine the physical and mental changes in surgical patients is very important for medical staffs. The surgical patient's satisfaction and overall healthy changes were evaluated by the patient-self assessment questionnaires. Materials and Methods: From July 2007 to April 2008, 26 patients with non-small cell lung cancer (NSCLC) underwent surgical resection. The outcome of the QOL was evaluated by using two kinds of questionnaire surveys from the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and the anti-aging QOL assessment (AA-QOL). The EORTC QLQ-C30 consisted of five domains (physical, role, cognitive, emotional, and social functionings) and global QOL. The AA-QOL contained 51 items; 30 physical and 21 mental symptoms regarding the elderly and the aging population. The patients replied to the two questionnaires at two different times, *i.e.*, at pre-surgery (baseline) and at post-surgery (2 weeks after the operation). The obtained data of these scores were averaged and compared between the two points of the pre-surgery and post-surgery. Results: Regarding the outcomes of the EORTC QLQ-C30, the physical and social functioning became significantly worse after the surgery. In contrast, the global QOL significantly became better after the surgery. For the symptom at post-surgery, three of which were "nausea and vomiting", "pain", and "appetite loss", became significantly worse compared to those at pre-surgery. Regarding the outcomes of

the AA-QOL, the physical symptoms (muscular pain/stiffness, palpitations, dyspnea, no feeling of good health, anorexia, and coughing and sputum) became significantly worse after the surgery. Regarding the mental symptoms, there were no significant differences. Conclusions: Regarding the outcomes based on the changes in the QOL after surgery, the physical symptoms became worse compared to the mental symptoms. To clarify the perioperative healthy changes of the QOL reported by patients with lung cancers is very important for multidisciplinary teamwork, which should play a role in providing the appropriate care and treatment and useful information for a preoperative patient's decision making of receiving surgical treatment.

Keywords

Patient-Reported Outcome, Surgery, Quality of Life, Non-Small Cell Lung Cancer

1. Introduction

The Japanese society is aging and consists of a higher elderly population. Therefore, the patients undergoing chest surgery are often elderly and often suffer from complications such as diabetes mellitus, hypertension, ischemic heart disease, and chronic obstructive pulmonary diseases.

Surgery is the only treatment modality that can consistently cure the early-staged patients with non-small cell lung cancer (NSCLC). On the other hand, radiotherapy and chemotherapy, often than surgery, may contribute in an adjuvant and neoadjuvant method, especially for the advanced unresectable lung cancers. Regarding the surgical outcome of lung cancer in Japan, the mean of the 30-day mortality and in-hospital mortality over a period of 16 years for the patients with lung cancer was 0.6 and 1.20, respectively [1]. The overall postoperative mortality rates for lung cancer in the USA and Norway were 4.1 (n = 11,668) [2], and 4.4% (n = 26,665) [3]. Thoracic surgery in Japan is considered to be relatively safe.

Regarding the outcomes of the surgical treatment of NSCLC, for example, it is usually used for comparison as a clinical indicator of the surgical invasive degree based on surgical procedures, factors of the preoperative patient's background, preoperative complications, postoperative adverse event, and overall survival outcomes, the factors of which have been evaluated and compared such as between two groups of open thoracotomic surgery and video-assisted thoracic surgery (VATS). Although there is the impact of surgical treatment, the survival outcomes and the postoperative complications, there has been an increased awareness to recognize the need of complement surgical treatment and assessment of the quality of life (QOL). The collected data of the postoperative QOL has been advocated in the follow-up of patients with cancer [4]. When evaluating the outcome of the surgical treatment, the assessment of the QOL became important [5] [6].

In a clinical study of lung cancer, the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ) has been validated and widely used [7]. The EORTC-QLQ questionnaire is the most commonly used QOL assessment tool for cancer patients in European countries [8] [9].

However, there has not been developed an appropriate tool of a health-related QOL (HR-QOL) for the Japanese patients and there are many issues and concerns about the evaluation method. It is difficult for doctors to evaluate the patients' QOL as comprehensive and objective indicators. The interesting point of the present study is to clarify the degree of changes in the subjective symptoms of physical and mental issues as a HR-QOL of the surgical patients with lung cancer, which is an evaluation to be performed by the patient's self-assessment that is based on the patient-reported outcome (PRO).

The aim of the present study is to clarify the patient's satisfaction and healthy changes of those receiving surgery for lung cancer. The evaluation is to be performed by the patient's self-assessment, that is, to be patient-centered and also the PRO.

We used two questionnaire surveys of the QOL. One is the famous EORTC QLQ questionnaire survey [8] [9], which has been widely used in the world as a cancer-specific scale. The other is a "common questionnaire survey of anti-aging QOL assessment (AA-QOL)" [10], which is a tool specified for physical and mental symptoms of the Japanese elderly population. The obtained results from the above PROs would become useful information for the preoperative patients in the decision-making of receiving a surgical treatment and for the multidisciplinary staffs.

2. Materials and Methods

2.1. Patients

This study was approved by the University of Miyazaki Hospital Clinical Research Ethics Board. The procedures used in this study were in accordance with the Helsinki Declaration. From July 2007 to April 2008, a total of 26 patients with primary NSCLC underwent surgery at our University Hospital. The patients were preoperatively enrolled and surgical treatment was performed as a resectable NSCLC.

The background of the 26 patients entered in this study is shown in **Table 1**. The TNM classification and the histological analysis were based on the Union for International Cancer Control (UICC) [11] and the World Health Organization classification for cell types [12]. Patients were histologically diagnosed with NSCLC and were pathologically staged.

A pulmonary function test was performed. Patients currently smoking had stopped smoking for more than 1 month before the operation. The patients were appropriately selected by the attending physicians. All patients provided informed consent of this study and surgery.

Table 1. Patient characteristics (n = 26).

Gender	Male	8
	Female	18
Age	Mean ± SD	68.9 ± 8.5
	range	53 - 82
ECOG-PS	0	25
	1	1
Operative procedure	Lobectomy	25
	Segmentectomy	1
Histology	Adenocarcinoma	20
	Squamous cell carcinoma	5
	Atypical carcinoid	1
Pathological stage	IA	14
	IB	5
	IIB	2
	IIIA	3
	IIIB	1
	IV	1
Somatometry	Body weight (kg)	55.5 ± 7.4
	Body height (cm)	160.0 ± 6.0
	Body surface area (m^2)	1.57 ± 0.12
Preoperative lung function	VC (L)	3.32 ± 0.61
	%VC% (%)	114.2 ± 17.0
	FEV_1 (L)	2.30 ± 0.55
	$\%FEV_1$ (%)	69.7 ± 10.7
Postoperative lung function	VC (L)	2.39 ± 0.52
	%VC (%)	82.2 ± 13.9
	FEV_1 (L)	1.79 ± 0.48
	$\%FEV_1$ (%)	74.7 ± 10.6

2.2. Selection Criteria of the Patients

The Eastern Cooperative Oncology Group Performance Status of 0 or 1, able to climb up stairs, total leukocyte count ≥ 3.0×10^9/L, hemoglobin concentration ≥ 8.0 g/dl, platelet count ≥ 80×10^9/L, adequate liver and renal function (serum transaminase ≤ 2 times normal value; serum creatinine ≤ 1.5 times normal value), partial pressure of arterial oxygen (paO_2) ≥ 60 torr, past history of severe allergic reaction to drugs, or other serious preoperative complications, such as uncontrolled angina pectoris, myocardial infarction within 3 months, heart failure, uncontrolled diabetes mellitus or hypertension was evaluated. There were no intraoperative and postoperative complications. All patients provided informed consent before the surgery.

2.3. Surgery

All of the patients were preoperatively diagnosed with resectable NSCLC and a lobectomy with an open thoracotomy was surgerically performed.

Under general and epidural anesthesia with double-lumen endobronchial tube and single-lung ventilation, the patient was flexed in the lateral decubitus position. An open thoracotomy with a posterolateral skin incision was performed at the fifth intercostal space.

Anatomic resection was performed with an endoscopic stapler (Ethicon, Tokyo, Japan, Covidien, Tokyo, Japan) to divide the lung parenchyma and incomplete fissures, and excise the bronchi. The pulmonary arteries and veins were also divided with an endoscopic stapler. A mediastinal lymphadenectomy was performed and a water-seal test was done to ensure pneumostasis. Air leak from suture-lines were closed with sutures and sealed with fibrin glue. A 24-F chest tube was inserted in the iontrathorax. The open thoracotomic wound was closed. Patients started to drink water 6 hours after extubation. Eating, standing and walking were allowed during the next morning after surgery. As postoperative pain management, epidural anesthesia was maintained until the 3rd to 7th postoperative days. They were started on oral analgesia from the first postoperative day. The chest drainage tubes were removed after confirmation of no air leakage and the level of discharge volume was less than 200 ml per day. A postoperative pulmonary function test was performed 3 weeks after the surgery.

2.4. Outcomes of Quality of Life

The patient-reported outcome of the QOL was evaluated by using the questionnaire survey from the EORTC QLQ-C30 and the anti-aging QOL assessment (AA-QOL). The questionnaires of the EORTC QLQ-C30 and the AA-QOL were used to obtain the patient-centered QOL of the surgical treatment period. The patients answered the questions at two different times during the perioperative period, which were at pre-surgery (baseline) and at post-surgery (2 weeks after the operation). The obtained data of these scores at the pre-surgery and post-surgery times were averaged and compared, and the changes were represented as the second evaluation of the QOL.

2.4.1. Health-Related Quality of Life (HR-QOL) Assessment

The outcome of the QOL was assessed by the EORTC QLQ-C30, a well-validated and widely used QOL tool [8] [9]. The EORTC QLQ-C30 is a standardized, self-administered disease-specific HR-QOL instrument designed for use in estimation of the HR-QOL of oncologic patients. The EORTC QLQ-C30 is composed of 5 functional scales, 3 symptom scales, a global QOL scale, and 6 single-item symptom measures. All the items are scored on a scale of 0 to 100 and a higher score represents a more favorable functional level of the QOL. The global QOL scale represents a higher favorable level of the QOL in case of a higher score. A high score on a symptom scale represents a high level of symptoms.

2.4.2. Anti-Aging Quality of Life Assessment (AA-QOL)

Observation of improvement in the QOL was done using a common interview sheet. At the baseline and after surgery, any improvement in the QOL, "physical symptoms" and "mental symptoms" as subjective symptoms were evaluated using a five-point scale (1-point: absolutely none; 2-point: almost not; 3-point: mild; 4-point: moderate; 5-point:severe) by the (AA-QOL) [10].

The symptomatic evaluated items are 30 physical symptoms and 21 mental ones. The 30 physical symptoms are listed in Table 2 and the 21 mental symptoms are listed in Table 3.

Table 2. Outcomes for anti-aging quality of life assessment (30 items, physical symptoms).

Physical symptoms (30 items)	Pre-surgery	Post-surgery	p value	change	2nd evaluation of QOL
	Scores at baseline	Scores at 2 weeks		(%)	
Tired eyes	1.8 ± 1.0	1.9 ± 0.9	0.365	4.4	→
Blurry eyes	1.6 ± 0.8	1.7 ± 0.9	0.200	11.6	↑
Eye pain	1.4 ± 0.7	1.4 ± 0.7	0.484	−0.5	→
Stiff shoulders	2.1 ± 1.2	2.5 ± 1.3	0.081	20.5	↑
Muscular pain/stiffness	1.9 ± 0.9	2.7 ± 1.4	0.001	45.2	↑
Palpitations	1.6 ± 0.8	2.1 ± 1.2	0.022	31.4	↑
Dyspnea	1.7 ± 0.9	2.5 ± 1.2	0.002	45.0	↑
Tendency to gain weight	2.1 ± 1.2	1.9 ± 0.9	0.245	−8.3	→
Weight loss; thin	1.8 ± 1.2	2.0 ± 1.1	0.238	11.2	↑
Lethargy	1.8 ± 1.0	1.9 ± 0.9	0.313	6.0	→
No feeling of good health	1.7 ± 0.9	2.3 ± 1.0	0.005	37.1	↑
Thirst	1.7 ± 0.9	1.9 ± 1.1	0.129	16.6	↑
Skin problems	1.6 ± 1.0	1.9 ± 1.1	0.114	18.3	↑
Anorexia	1.6 ± 0.8	2.1 ± 1.0	0.022	27.8	↑
Early satiety	1.3 ± 0.5	1.5 ± 0.7	0.116	13.6	↑
Epigastralgia	1.4 ± 0.6	1.5 ± 0.6	0.328	4.7	→
Liable to catch colds	1.7 ± 1.0	1.8 ± 0.9	0.319	6.2	→
Coughing and sputum	2.0 ± 1.2	2.6 ± 1.1	0.012	31.8	↑
Diarrhea	1.7 ± 1.0	1.6 ± 0.9	0.219	−9.8	→
Constipation	2.0 ± 1.3	2.0 ± 1.3	0.464	−1.4	→
Headaches	2.1 ± 1.3	2.3 ± 1.2	0.419	5.9	→
Dizziness	2.0 ± 1.2	1.9 ± 1.0	0.412	−6.3	→
Tinnitus	1.6 ± 1.0	1.7 ± 0.9	0.369	4.6	→
Lumbago	1.4 ± 0.7	1.5 ± 0.8	0.288	6.8	→
Arthralgia	1.7 ± 1.2	1.7 ± 1.2	0.473	1.1	→
Edematous	2.1 ± 1.2	1.9 ± 0.9	0.215	−9.6	→
Easily breaking into a sweat	1.7 ± 0.9	1.8 ± 0.8	0.293	6.2	→
Frequent urination	1.5 ± 0.8	1.5 ± 1.0	0.366	4.8	→
Hot flash	2.1 ± 1.1	2.2 ± 1.3	0.339	5.9	→
Cold skin	1.7 ± 1.0	1.8 ± 1.0	0.366	4.6	→

a five-point scale (1-point: absolutely none; 2-point: almost not; 3-point: mild, 4-point: moderate; 5-point: severe). Mean ± SD, Wilcoxo's signed rank test.

Table 3. Outcomes for anti-aging quality of life assessment (21 items, mental symptoms).

Mental symptoms (21 items)	Pre-surgery	Post-surgery	p value	change	2nd evaluation of QOL
	Scores at baseline	Scores at 2 weeks		(%)	
Irritability	1.4 ± 0.6	1.5 ± 0.7	0.392	2.9	→
Easily angered	2.1 ± 1.3	2.0 ± 1.2	0.388	−4.1	→
Loss of motivation	1.9 ± 1.0	1.6 ± 0.7	0.105	−13.8	↓
No feeling of happiness	1.8 ± 1.1	1.5 ± 0.6	0.086	−16.1	↓
Nothing to look forward in life	1.7 ± 0.8	1.8 ± 0.9	0.195	10.3	↑
Daily life is not enjoyable	1.8 ± 1.0	1.6 ± 0.9	0.182	−12.0	↓
Loss of confidence	1.7 ± 1.0	1.6 ± 1.0	0.333	−6.1	→
Reluctance to talk with others	1.7 ± 0.9	1.6 ± 1.0	0.350	−5.2	→
Depressed	1.7 ± 1.0	1.7 ± 1.1	0.500	0.0	→
A sense of uselessness	1.6 ± 1.1	1.6 ± 0.9	0.483	−0.6	→
Shallow sleep	1.7 ± 1.0	1.6 ± 0.7	0.259	−8.0	→
Difficulty falling asleep	1.6 ± 1.0	1.5 ± 0.8	0.477	−0.8	→
Pessimism	2.3 ± 1.3	2.7 ± 1.3	0.124	15.2	↑
Lapse of memory	2.1 ± 1.3	2.6 ± 1.4	0.083	21.0	↑
Inability of concentrate	1.9 ± 1.2	1.8 ± 1.1	0.408	−3.3	→
Inability to solve problems	2.4 ± 1.1	2.3 ± 1.2	0.339	−4.8	→
Inability to make judgements readily	1.9 ± 1.0	1.8 ± 0.9	0.309	−6.1	→
Inability to sleep because of worries	1.7 ± 0.9	1.6 ± 0.7	0.264	−7.1	→
A sense of tension	1.8 ± 1.0	1.7 ± 0.8	0.241	−8.6	→
Feeling of anxiety for no special reason	2.1 ± 1.2	1.8 ± 1.0	0.081	−17.2	↓
A vague feeling of fear	2.4 ± 1.2	1.9 ± 1.1	0.064	−17.7	↓

a five-point scale (1-point: absolutely none; 2-point: almost not; 3-point: mild, 4-point: moderate; 5-point: severe). Mean ± SD, Wilcoxo's signed rank test.

To perform the second evaluation of the QOL scores using a five-point scale, we evaluated the transition of the QOL scores regarding each symptom before and after surgery. We determined a significant change as the second evaluation of the QOL score, that is, in case of which the values changed more than 10% from the baseline score. We allocated the changed rates of each symptom before and after surgery, *i.e.*, as three classified types, that is improved (" ↑ "; increased more than 10%), unchanged ("→"; changed less than ± 10%), and worse (" ↓ "; decreased more than −10%).

2.5. Statistical Analysis

A statistical analysis of the results was performed using the paired t-test. A value of $p < 0.05$ was considered to indicate a statistically significant change. A statistical analysis of the results was performed using the paired t-test for comparison of the values between the level at the baseline and that after 8 weeks of administration in each group.

3. Results

3.1. Background of Patients

The 26 patients (8 males and 18 females) are summarized in Table 1. The majority of patients were females (18/26, 69.2%), with a median age of 68.9 ± 8.5 years (range 53 - 82). The ECOG performance status was 0 in 25 patients (25/26, 96.2%). 25 lobectomies (25/26, 96.2%) and 1 segmentectomy (1/26, 3.8%) were performed. Tumor histology included 20 adenocarcinomas (76.9%), 5 squamous cell carcinomas (19.2%) and 1 atypical carcinoid. The stage classification was IA-staged (n = 14, 53.8%), IB-staged (n = 5, 19.2%), IIB-staged (n = 2, 7.7%), IIIA-staged (n = 3, 11.5%), IIIB-staged (n = 1, 3.2%), and IV-staged (n = 1, 3.2%).

Regarding the preoperative lung function test, the vital capacity (VC) was 3.32 ± 0.61 L, the predicted percentage of VC (%VC) was 114.2% ± 17.0%, the forced expiratory volume in one second (FEV_1) was 2.30 ± 0.55 L, and the percentage of FEV_1 (%FEV_1) was 69.7% ± 10.7%. On the other hand, for the postoperative lung function test, the VC was 2.39 ± 0.52 L, the %VC was 82.2% ± 13.9%, the FEV_1 was 1.79 ± 0.48 L, and the %FEV_1 was 74.7% ± 10.6%.

3.2. Outcomes of Quality of Life

3.2.1. Patient-Reported Outcomes of EORTC QLQ-C30

Table 4 shows the outcomes for the EORTC QLQ-C30 (5 functional scales and global QOL). Table 5 shows the outcomes for the EORTC QLQ-C30 (8 symptom scales and financial difficulties). All the items were scored on a scale of 0 to 100; a higher score represents a more favorable functional QOL level. The global QOL scale with a higher score represented a higher favorable level of the QOL. A high score on the symptom scale represented a high level of symptoms.

The level of five domains (physical, role, cognitive, emotional, and social functionings) and global QOL at the time of pre-surgery (scores at baseline) and at post-surgery (scores at 2 weeks) were evaluated and compared. Although surgical treatment involved general anesthesia in addition to the surgical physical load, the situation showed decreased score values.

Table 4. Outcomes for EORTC QLQ-C30 (5 functional scales and global QOL scale).

Functional scales	Pre-surgery (Scores at baseline) Mean score ± S.D.	Post-surgery (Scores at 2 weeks) Mean score ± S.D.	p value
Physical functioning	93.8 ± 13.9	63.1 ± 22.8	<0.001
Role functioning	98.9 ± 4.3	53.6 ± 36.5	0.432
Cognitive functioning	84.4 ± 29.2	78.9 ± 19.4	0.219
Emotional functioning	74.4 ± 27.2	73.3 ± 20.2	0.127
Social functioning	88.9 ± 25.7	78.9 ± 37.5	<0.001
Global QOL	30.0 ± 25.0	38.3 ± 29.8	<0.001

The point range between 0 to 100 and 100-point represents a favorable QOL. A higher score represents a better QOL and a lower score a worse QOL.

Table 5. Outcomes for EORTC QLQ-C30 (8 symptom scales and single items).

Symptom scales and single items	Pre-surgery (Scores at baseline) Mean score ± S.D.	Post-surgery (Scores at 2 weeks) Mean score ± S.D.	p value
Fatigue	12.6 ± 20.5	40.7 ± 26.4	0.076
Nausea and vomiting	1.1 ± 4.3	5.6 ± 8.1	<0.001
Pain	12.2 ± 24.8	56.7 ± 30.1	<0.001
Dyspnea	8.9 ± 19.8	48.9 ± 27.8	0.091
Appetite loss	24.4 ± 36.7	42.2 ± 34.4	0.010
Insomnia	11.1 ± 20.6	31.1 ± 23.5	0.276
Constipation	15.6 ± 30.5	22.2 ± 30.0	0.500
Diarrhea	4.4 ± 11.7	4.4 ± 11.7	0.336
Financial difficulties	13.3 ± 27.6	17.9 ± 29.2	0.336

The point range between 0 to 100 and 100-point represents a favorable QOL. A higher score represents a better QOL and a lower score a worse QOL.

In Table 4, for the functional scales at post-surgery, two scales (physical and social functional scales) showed significantly decreased values, which represented a significantly worse QOL level. The physical functioning scale changed from 93.8 ± 13.9 at pre-surgery to 63.1 ± 22.8 at post-surgery ($p < 0.001$), and the social functioning scale changed from 88.9 ± 25.7 at pre-surgery to 78.9 ± 37.5 at post-surgery ($p < 0.001$).

On the contrary, the global QOL scale significantly changed from 30.0 ± 25.0 at pre-surgery to 38.3 ± 29.8 at post-surgery ($p < 0.001$). The global QOL scale showed a significantly increased value, which meant a significantly better level of QOL compared to those at pre-surgery. Due to the open thoracotomy and anesthesia, the physical, social functioning scales significantly became worse, however, the global QOL became better after the surgical treatment.

In contrast, due to the open thoracotomy and anesthesia, the functioning scales of role, cognitive, and emotional at post-surgery showed decreased values, which meant a worse level of QOL compared to those values at pre-surgery, however, there were no significant differences. The values of the cognitive and the emotional functionings at post-surgery showed similar values compared to those at pre-surgery.

In Table 5, regarding the symptom scales at post-surgery, three scales ("nausea and vomiting", "pain", and "appetite loss") became significantly severe compared to those at pre-surgery. The symptoms of "nausea and vomiting" changed from 1.1 ± 4.3 at pre-surgery to 5.6 ± 8.1 at post-surgery ($p < 0.001$) (increase of 5.1-fold magnitude). The symptom of "pain" changed from 12.2 ± 24.8 at pre-surgery to 56.7 ± 30.1 at post-surgery ($p < 0.001$) (increase of 4.6-fold magnitude). The symptom of "appetite loss" changed from 24.4 ± 36.7 at pre-surgery value to 42.2 ± 34.4 at post-surgery ($p < 0.001$) (increase of 1.7-fold magnitude). Due to the open thoracotomy and anesthesia, symptoms of nausea

and vomiting, pain, and appetite loss became significantly stronger.

On the other hand, due to the open thoracotomy and anesthesia, the symptoms of fatigue (increase of 3.2-fold magnitude), dyspnea (increase of 5.4-fold one), and insomnia (increase of 2.8-fold one) at post-surgery became worse compared to those values at pre-surgery, however, there were no significant differences. The symptoms of constipation, diarrhea, and financial difficulties at post-surgery appeared to be similar compared to these values at pre-surgery.

3.2.2. Patient-Reported Outcomes of AA-QOL

Table 2 shows the values of 30 items regarding the physical symptoms. The 6 symptom items, which are the "muscular pain/stiffness", "palpitations", "dyspnea", "no feeling of good health", "anorexia", and "coughing and sputum", became significantly worse compared to those at pre-surgery.

The symptom of "muscular pain/stiffness" changed from 1.9 ± 0.9 as the pre-surgery value to 2.7 ± 1.4 as the post-surgery ($p = 0.001$) (increase of 1.4-fold magnitude). The symptom of "palpitations" changed from 1.6 ± 0.8 at pre-surgery to 2.1 ± 1.2 at post-surgery ($p = 0.022$) (increase of 1.3-fold magnitude). The symptom of "dyspnea" changed from 1.7 ± 0.9 at pre-surgery to 2.5 ± 1.2 at post-surgery ($p = 0.002$) (increase of 1.5-fold magnitude). The symptom of "no feeling of good health" changed from 1.7 ± 0.9 at pre-surgery to 2.3 ± 1.0 at post-surgery ($p = 0.005$) (increase of 1.4-fold magnitude). The symptom of "anorexia" changed from 1.6 ± 0.8 at pre-surgery to 2.1 ± 1.0 at post-surgery ($p = 0.022$) (increase of 1.3-fold magnitude). The symptom of "coughing and sputum" changed from 2.0 ± 1.2 at pre-surgery to 2.6 ± 1.1 at post-surgery ($p = 0.012$) (increase of 1.3-fold magnitude).

Regarding the second evaluation of the QOL, 12 items, that were "blurry eyes", "stiff shoulders", "muscular pain/stiffness", "palpitations", "dyspnea", "weight loss; thin", "no feeling of good health", "thirst", "skin problems", "anorexia", "early satiety", and "coughing and sputum", which were evaluated to become worse (40%, 12/30), that is, these symptoms become worse due to the open thoracotomy and anesthesia, and 18 items were evaluated to be unchanged (60%, 18/30), that is, these symptoms appeared to be changes similar between the pre- and post-surgeries. There were no symptoms that became better after the surgical treatment.

Table 3 shows the values of 21 items regarding the mental symptoms in which there were no significant differences. For the second evaluation of the QOL, the 3 items, *i.e.*, "nothing to look forward in life", "difficulty falling asleep", and "pessimism", were found to become worse (14.3%, 3/21). These symptoms became worse due to the open thoracotomy and anesthesia. Also, 13 items were evaluated to be unchanged (61.9%, 13/21), that is, these symptoms appeared to be changes similar between the pre- and post-surgeries. For the residual 5 items, *i.e.*, "loss of motivation", "no feeling of happiness", "daily life is not enjoyable", "feeling of anxiety for no special reason", and "a vague feeling of fear", were found to change and become better (23.8%, 5/21). That is, these mental symptoms improved after the surgical treatment.

4. Discussion

Lung cancer is one of the most common malignant diseases and remains the leading cause of cancer-related deaths in Europe, the USA, and Japan [13] [14] [15]. The five-year survival rate after surgical treatment in the United States [16] was reported as follows: IA, 67%; IB, 27%; IIA, 55%; IIB, 39%; IIIA, 38%; IIIB, 3% - 7%; IV, 1%. In Japan, it was reported as follows: IA, 79.5%; IB, 60.1%; IIA, 59.9%; IIB, 42.2%; IIIA, 29.8%; IIIB, 19.3%; IV, 20.0% [17].

In the thoracic surgical field, the minimally invasive, video-assisted thoracic surgery (VATS) approach is world-wide becoming increasingly popular. In the past, based on a difference in surgical procedures, for example, the open lobectomy and VATS lobectomy, which involve complications, the outcomes, and QOL were studied and reported [18] [19] [20] [21]. The VATS procedure is well known to be associated with fewer complications and more-rapid recovery than is the standard open thoracotomy [22] [23].

Based on the result of a meta-analysis, I-staged NSCLC patients undergoing the VATS lobectomy had fewer complications than those who received the open thoracotomy [24]. The VATS lobectomy resulted in a lower total complication rate (OR 0.45, 95% CI 0.24- 0.84; p = 0.013) compared to the open lobectomy based on the data including a total of 23 studies [24]. Based on a systemic review and meta-analysis of the assessment of PROs after the lung cancer surgery [25], patients undergoing VATS have a better HR-QOL when compared to patients who receiving the thoracotomy. The consistent use of a lung cancer specific questionnaire for measuring the HR-QOL after surgery was reported to be encouraging [25].

On the other hand, the maximally invasive pneumonectomy has been reported as the most consistent and strongest predictor of a decline in the QOL after surgery. Schulte *et al.* (2006) [26] reported that a patient who underwent the pneumonectomy had significantly worse postoperative QOL values [statistical differences in physical function at 3 months, social function at 3 - 6 months, role function at 3 - 6 - 12 months, general health at 3 - 6 months and pain at 6 months] compared to those who underwent the lobectomy and bilobectomy.

There was a variety of management approaches including surgery, radiation, and systemic therapies, which may be used in lung cancer, depending on the histology, pathological disease-staging at diagnosis and patient's favorable selection. Both the status of the disease and contents of the treatment can influence the symptoms with profound effects on the patient's physical, social, and emotional functionings. Although survival outcomes are frequently collected, however, the outcomes of the patient's QOL related to the disease and its treatment are rarely routinely assessed.

In thoracic surgery, the use of the QOL assessment has certainly improved in recent years, but its use in real practice remains unclear and underestimated. Understanding the evolution of the QOL after surgical treatment for lung cancer by the surgeon may give the patient the possibility to proactively participate in the difficult decision making process [27]. We are all aware about raising interest

and expectations of the patients during counseling about the impairment in their daily lifestyle and their growing needs of a detailed comparison of the different approaches in terms of the QOL [28]. Some patients may regard in-hospital postoperative complications as an acceptable risk, but are not ready to accept a long-term disability in their lifestyle [28].

The effect of a disease and treatment on a patient's daily life is poor for clinicians to understand in detail [29]. In address this problem, more than hundreds of standardized measures have been performed to obtain patient reported outcomes including symptom status, physical function, mental health, social function, and well-being [30]. However, the movement of patient reported outcome measurements (PROMs) has largely been driven by the agenda of researchers or service payers, however, which has failed to effectively focus on improving the quality of care from the patient's perspective [30]. How to use PROMs in everyday practice has the potential to narrow the gap between the clinician's and patient's views of clinical reality [30], and help tailor treatment plans to meet the patient's preferences and needs [31].

PROM is sensitive to differences, which are related to the type of surgery and variations in the perioperative care. Although PROs have been widely accepted in clinical research [32] [33], the use of subjective outcomes in current perioperative practice is relatively novel, despite recent recognition of their potential benefits [34].

To evaluate perioperative care, PROs have yet to be integrated with traditional clinical outcomes (such as the length of the hospital stay). The longitudinal PRO assessments were used to define the postoperative symptom recovery trajectory in patients undergoing thoracic surgery for lung cancer [35]. By using the MD Anderson Symptom Inventory [35], the most-severe postoperative symptoms were fatigue, pain, shortness of breath, disturbed sleep, and drowsiness. The median time to return to mild symptom severity for these 5 symptoms was shorter than the time to return to the baseline severity with fatigue taking longer. It is an effective strategy for evaluating the perioperative care in order to assess symptoms from the patient's perspective throughout the postoperative recovery period [35]. It is a sensitive tool for detecting symptomatic recovery to use the symptom inventory with an expected relationship among the surgical procedure type, preoperative performance status, and comorbid conditions [35].

However, to the best of our knowledge, no empirical time course and developmental trajectory of postoperative symptoms were characterized by the PRO data, especially during the time frame spanning from the hospital discharge to the return of normal functions [36]. Regarding the definition and measurement of symptomatic and functional recovery after major cancer surgery from the patients' perspective, there is no research and there is also an important gap in comprehensive postoperative care.

Studying the outcomes of a treatment from the patient's viewpoint is also of crucial importance for quality purposes and for the improvement of patient-centered care. Lung resection for NSCLC should aim at improving the sur-

vival outcome and cancer-related symptoms without compromising the dignity of an acceptable QOL. The short and long-term effects of the resection on the QOL should be mandatory information provided to the patient during the preoperative counseling and the patient has the right to be informed about it [28].

In this study, based on the concept of the PROs, we used the famous EORTC QLQ-C30 questionnaire survey [8] [9], which has been widely used around the world as a cancer-specific scale and we used a "common questionnaire survey of anti-aging QOL assessment (aa-QOL)" [10]. Based on the results of the outcomes of the EORTC QLQ-C30 questionnaire, two scales (physical, social functioning scales) became significantly worse and the global QOL became significantly better compared to those at pre-surgery. On the symptom scales at post-surgery, three scales ("nausea and vomiting", "pain", and "appetite loss") became significantly worse compared to those at pre-surgery. Regarding the results of the outcomes of the AA-QOL, 6 items of physical symptoms (muscular pain/stiffness, palpitations, dyspnea, no feeling of good health, anorexia, and coughing and sputum) became significantly worse compared to those at pre-surgery. Regarding the mental symptoms, there were no significant differences. In advance, for the second evaluation of the physical symptoms, 12 items showed worse changes (40%, 12/30), and 18 items were unchanged (60%, 18/30). For the second evaluation of mental symptoms, 3 items showed worse changes (14.3%, 3/21), 13 items were unchanged (61.9%, 13/21), and 5 items showed better changes (23.8%, 5/21). Based on the outcomes of the symptomatic changes in the QOL after the surgery, the physical symptoms had become worse, however, the mental ones did not become worse.

Due to the limitation of this study, we did not decide on the appropriate sample size, and that was too low a number and the data used was slightly old. The newest data from recent patients undergoing the open thoracotomy were not used. At the present time of minimally invasive surgery, we have not evaluated the PRO of video-assisted thoracic surgery for the NSCLC. As a questionnaire of the EORTC-C30 QLQ for recent chemotherapeutic clinical trials, it has been actively used as the PRO of chemotherapy. However, in the surgical field, it has not been routinely used and generally known. Also, regarding the questionnaire of the AA-QOL, which was only slightly used world-wide, it might be the first to be used for aging surgical patients. The evaluation of PRO of an open thoracotomy by AA-QOL and EORTC-C30 QLQ might possibly be unsuitable because of the many dynamic symptomatic changes in a short perioperative term.

No specific validated questionnaire has yet been developed for the lung cancer surgical patient population. However, the development of more specific surgical-related questionnaires may help the thoracic surgeon community to implement future research about the QOL outcomes. To clarify the perioperative healthy changes of the QOL reported by a patient with lung cancer is very important for doctors and nurses, which should play a role in giving appropriate care and treatment in order to realize satisfaction by the patients and their support.

For a patient undergoing surgery (open thoracotomy) for lung cancer, and for a doctor with a multidisciplinary approach, the PROs should become very helpful information and significantly contribute to future surgical patients to obtain informed consent in making-decision for undergoing surgery, which will encourage future preoperative surgical patients to use as a reference in considering the postoperative physical and mental symptomatic changes and healthy changes.

5. Conclusion

The results of PROs in surgery (open thoracotomy) should provide helpful and novel information for future preoperative patients undergoing a lobectomy for lung cancer. Because perioperative symptomatic changes before and after surgery should be exactly explained in order to obtain informed consent, this process should become important in the making-decision for selecting the appropriate procedure. The PRO would encourage patients to use it as a reference when considering the postoperative symptomatic changes.

Abbreviations

EORTC-C30 QLQ: the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire;

QOL: quality of life;

PRO: patient-reported outcome;

AA-QOL: anti-aging quality of life assessment.

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