



Postoperative pulmonary function changes according to the resected lobe: a 1-year follow-up study of lobectomized patients

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Background: Pulmonary function and patient complaints appear to improve up to 12 months after lobectomy but long-term prospective studies based on clinical data are scarce. Improvement in pulmonary function may depend on the area and extent of the resection and the time from the operation. This prospective study aimed to determine pulmonary function changes according to the resected lobe.

Methods: This prospective study included 59 patients requiring single lobectomy. Total volume and low-attenuation volume (LAV) for each lobe and the entire lungs were calculated based on helical computed tomography images. Vital capacity (VC), forced expiratory volume in one second (FEV₁), percent FEV₁ (%FEV₁), percent lung diffusion capacity for carbon monoxide (%DL_{co}), %DL_{co} divided by the alveolar volume (%DL_{co}/V_A), modified Medical Research Council (mMRC) grades, and COPD Assessment Test (CAT) scores were compared at 3, 6, and 12 months after surgery.

Results: VC was higher at 12 months than at 3 months after right upper lobectomy (RUL) or right lower lobectomy (RLL). FEV₁ and %FEV₁ were higher at 12 months than at 6 months after left lower lobectomy (LLL). %DL_{co} was higher at 12 months than at 3 months after RUL or left upper lobectomy (LUL). DL_{co}/V_A, mMRC grades, and CAT scores did not change significantly in the period from 3 to 12 months after any lobectomy procedure. Compared to the predicted postoperative values, the observed values of VC for RUL, RLL, and LUL; FEV₁ for RLL; %FEV₁ for RLL and LUL; %DL_{co} for LUL; and %DL_{co}/V_A for all lobectomy procedures were higher at 12 months.

Conclusions: Improvements in pulmonary function and symptoms varied according to the resected lobe. Some of the observed pulmonary function values were higher than the predicted postoperative values. Pulmonary function changes may be related to the location, volume, and extent of emphysematous changes.

Keywords: Lobectomy; low attenuation volume; postoperative pulmonary function

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Introduction

Surgical resection is the best treatment for patients with lung cancer. However, postoperative evaluation of the

pulmonary function is important for estimating the risk of complications and long-term disability after pulmonary resection. Predicted postoperative pulmonary function measures for forced expiratory volume in 1 second (FEV₁)

and lung diffusion capacity for carbon monoxide (DL_{CO}) are considered the mainstays for patient selection before major lung resection. In a patient undergoing lobectomy, the “anatomical method” is used to calculate the predicted postoperative (ppo) FEV_1 and DL_{CO} . The guidelines from the European Respiratory Society and the European Society of Thoracic Surgery (ERS/ESTS) recommend the use of these ppo values to estimate the risk of death and cardiopulmonary complications after resection surgery (1).

Lung lobectomy destroys part of the lung parenchyma and its pulmonary function, but it sometimes results in an unexpected improvement of the remaining pulmonary function in some patients with moderate-to-severe emphysema (2). The emphysematous changes are often shown in the background of the resected lobe in patients with lung cancer. Lung lobectomy for cancer sometimes results in volume reduction in patients with emphysema (3). The degree of lung expansion, which occurs in order for the lung to occupy the thoracic cavity, also affects the remaining pulmonary function. In addition, air flow and blood flow are different in the upper and lower lobes. Therefore, pulmonary function may improve depending on the area and extent of the resection and the time elapsed from the operation.

Several studies have shown that the pulmonary function can change up to 6 months after lobectomy (4-6). However, the prospective study focused on the change of pulmonary function up to 12 months after lobectomy has not been reported. The aim of this prospective study was also to determine pulmonary function changes according to the resected lobe. The vital capacity (VC), FEV_1 , % FEV_1 , % DL_{CO} , percent lung diffusion capacity for carbon monoxide divided by the alveolar volume (% DL_{CO}/V_A), modified Medical Research Council (mMRC) dyspnea grade, and COPD Assessment Test (CAT) score were compared at 3, 6 and 12 months after single lobectomy by video-assisted thoracoscopic surgery (VATS).

Methods

Patients

Between December 11, 2013 and March 28, 2016, 59 patients scheduled to undergo single lobectomy by VATS at Kitasato University Hospital were prospectively enrolled in this study after providing their informed consent. This study was approved by the Kitasato University Medical

Ethics Organization (approval KME0 B13-110). Using the “Algorithm for Thoracotomy and Major Anatomical Resection” (7), high risk patients (ppo FEV_1 or ppo% DL_{CO} <30%) were excluded as candidates for surgical treatment in our hospital. Patients underwent incentive spirometry before surgery according to the standard protocol for thoracic surgery in our hospital. However, they did not undergo focused perioperative or pulmonary rehabilitation before and after the surgery.

Pulmonary function tests

Pulmonary function tests were performed according to the guidelines of the Japanese Respiratory Society. Spirometric reference values of VC, forced vital capacity (FVC), FEV_1 , and FEV_1/FVC for Japanese adults were calculated with the LMS (lambda, mu, sigma) method (8).

VC, FEV_1 , % FEV_1 , % DL_{CO} , % DL_{CO}/V_A , mMRC grade, and CAT score were evaluated before the operation and at 3, 6, and 12 months postoperatively. A preoperative pulmonary function test was performed within one month prior to the surgery. For patients with chronic obstructive pulmonary disease (COPD), the preoperative pulmonary function test was performed more than 2 weeks after receiving treatment with a bronchodilator [inhaled long-acting muscarinic antagonist (LAMA) and/or long-acting beta-agonist (LABA)], which was maintained throughout the study. The percent predicted FEV_1 , VC, DL_{CO} , and DL_{CO}/V_A were expressed as the percentage of the predicted values for age, gender, and height. COPD and its severity were defined according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria.

Prediction of the postoperative pulmonary function

For VC, FEV_1 , % FEV_1 , % DL_{CO} , and % DL_{CO}/V_A , predicted postoperative (ppo) values were calculated based on the number of functioning/unobstructed segments to be removed during surgery (7): ppo value = preoperative value $\times (1-y/z)$, with [y] the number of functional or unobstructed lung segments to be removed and [z] the total number of functional segments.

Computed tomography (CT) scanning

Helical CT scans were obtained using 64-detector row CT scanners (Optima 660; GE Healthcare, Tokyo, Japan). With

the patient in the supine position, we obtained 1.25-mm high-resolution CT images of the entire lungs during a deep inspiratory breath hold. We used a 512×512 matrix, a 1.25-mm collimation, and a scan time of 0.5 s, at 120 kVp and 270 mA. This was a routine practice, and thus, patients were not exposed to any additional radiation for the purpose of measuring the radiological parameters in this study.

Image interpretation and data analysis

Three-dimensional volume rendering lung images were created using a commercially available, user-friendly imaging software program (Ziostation 2[®]; Ziosoft, Inc., Tokyo, Japan). Threshold limits of -600 to -1,024 HU were applied to segment the entire lungs and to exclude soft tissues surrounding the lungs and the large vessels, atelectasis, fibrosis, and tumors within the lung. The volume of a lung that was segmented by a certain threshold limit can be readily obtained with the imaging software program. We called the volume of the entire lungs (-600 to -1,024 HU), the total lung volume (TLV). The lungs were divided into two areas: low-attenuation areas, representing emphysematous lung tissue (<-950 HU); and normal-attenuation areas (-600 to -950 HU), representing normal lung fields. We calculated the entire volume and the low-attenuation volume (LAV) for each lobe and the entire lungs.

Statistical analysis

To evaluate the patients' characteristics, preoperative data were compared to between non-COPD, GOLD 1 COPD, and GOLD 2 COPD groups using the Kruskal-Wallis test. Mean values for VC, FEV₁, %FEV₁, %DL_{co}, and %DL_{co}/V_A were compared between (I) preoperative data and data obtained at 3, 6, and 12 months after lobectomy using the Friedman rank sum test; and (II) data obtained at 12 months and the ppo values using the Wilcoxon signed-rank test. mMRC grades and CAT scores were compared between pre-operation and 3, 6, and 12 months after lobectomy using the Friedman rank sum test. Holm corrections were used for post-hoc comparisons. A P value of less than 0.05 was considered statistically significant. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University), which is a graphical user interface for R (The R Foundation for Statistical Computing, version 3.0.2) (9). More precisely, it is a modified version

of R commander (version 2.0–3) that includes statistical functions that are frequently used in biostatistics.

Results

Preoperative data

Of the 75 patients eligible for VAT lobectomy, 16 were excluded because of chylothorax (n=1), pyothorax (n=2), lung cancer recurrence (n=3), cerebral vascular infarction (n=1), renal cell carcinoma (n=2), and withdrawal of consent (n=7). In addition, one of two pyothorax patient and a patient of cerebral vascular infarction were died within 12 months after surgery. Finally, 59 patients (mean age 69.0±8.2 years; range 43–84 years) with complete pulmonary function assessment were included in this study. The indications for lobectomy were adenocarcinoma (n=44), squamous cell carcinoma (n=10), adenosquamous carcinoma (n=1), small-cell carcinoma (n=1), large cell neuroendocrine carcinoma (n=1), pleomorphic carcinoma (n=1), and benign lymphoproliferable disorder (n=1). Preoperative patient characteristics are described in *Table 1*. Current and former smokers discontinued their smoking habits before surgery. The majority of the patients, including 16 of 20 non-COPD patients, 10 of 12 GOLD 1, and 7 of 8 GOLD 2 COPD patients, discontinued smoking more than 4 weeks prior to the pre-operational pulmonary function tests. The remaining 7 of 40 patients discontinued smoking just after the first set of pulmonary function tests. All patients discontinued smoking 24 hours prior to DL_{co} (and DL_{co}/V_A) measurements of the first set of pulmonary function tests to prevent smoking from affecting the results of the test. Thereafter, none of them resumed smoking.

The mean %LAV of the resected lobe [(LAV of the resected lobe/volume of the resected lobe) ×100] for the GOLD 2 group was higher than that for the non-COPD group. The mean %LAV of the entire lungs [(LAV of the entire lungs/volume of the entire lungs) ×100] for the GOLD 2 groups was also higher than that for the non-COPD group, yet not significantly so (P=0.055). There was no difference between groups for the LAV ratio between the resected lobe and the entire lungs (LAV of the resected lung/LAV of the entire lungs). The number of lobectomies and their mean LAV of the resected lobe are shown in *Table 2*. The mean %LAV of each lobe varied between 0.57% and 73.52%. The upper lobes, especially the left upper lobe (LUL), had higher %LAV values than the lower lobes.

Table 1 Preoperative patient characteristics

Characteristics	Non-COPD	COPD		P value
		GOLD 1	GOLD 2	
Number of patients	31	18	10	
Age (years)	69.5±9.8	70.7±7.3	69.0±8.2	0.880
Height (cm)	159.0±9.0	159.3±8.8	166.4±7.1	0.048
Body weight (kg)	56.8±9.9	61.7±10.9	62.0±7.8	0.193
BSA (m ²)	1.6±0.2	1.6±0.2	1.7±0.1	0.124
Smoking index (pack-years)	25.3±30.5	36.3±34.7	48.6±40.1	0.182
Never-smokers	11	6	2	
Current or former smokers	20	12	8	
mMRC grade (0/1/2/3/4)	23/8/0/0/0	11/4/1/2/0	6/4/0/0/0	
VC (mL)	3,287.14±716.76	3,357.78±704.04	3,622.00±588.01	0.289
FVC (mL)	3,104.19±816.44	3,287.22±693.79	3,526.00±577.26	0.237
%VC (%)	98.54±15.36	110.47±9.59*	107.79±10.63 [†]	0.025
FEV ₁ (mL)	2,474.82±515.03	2,186.11±433.10	1,979.00±251.73	0.109
FEV ₁ /FVC (%)	76.23±4.88	63.72±4.36*	57.01±8.64* [†]	<0.001
%FEV ₁ (%)	100.02±15.77	94.38±19.65	71.18±8.47* [†]	<0.001
%DL _{co} (%)	116.28±30.68	112.72±25.96	100.43±25.79	0.116
%DL _{co} /V _A (%)	99.37±24.50	92.14±21.46	82.13±20.95*	0.027
%LAV of the resected lobe (%)	2.67±6.11	2.56±3.54	4.81±3.63*	0.007
%LAV of the entire lung (%)	1.71±2.80	3.57±4.15	3.07±2.32	0.021
LAV of the resected lobe/LAV of the entire lung (%)	17.96±14.13	16.94±13.66	26.27±14.53	0.177

Values are represented mean ± SD. *, significantly different from the non-COPD group; [†], significantly different from the GOLD 1 group. P<0.05 was set as statistically significant. BSA, body surface area; COPD, chronic obstructive pulmonary disease; DL_{co}, lung diffusion capacity for carbon monoxide; DL_{co}/V_A, lung diffusion capacity for carbon monoxide divided by the alveolar volume; FEV₁, forced expiratory volume in one second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; LAV, low-attenuation volume; mMRC, modified Medical Research Council; VC, vital capacity.

Video-assisted thoracoscopic surgery for lobectomy and postoperative pain

PURE VATS using a 3-port technique was performed in 13 patients (9 non-COPD, 3 GOLD 1, and 1 GOLD 2 COPD) by four thoracic surgeons, and ASSIST VATS was performed in 46 patients by seven thoracic surgeons in our division. PURE VATS was used for 7 RUL lobectomies, 5 RLL lobectomies, and 1 LLL lobectomy. None of the patients underwent conversion from VATS to open

thoracotomy. Epidural analgesia was used during the surgeries. All patients received patient-controlled epidural analgesia (PCEA) until postoperative day (POD) 2 or 3. Thereafter, NSAIDs and/or opioid pain medications, such as tramadol hydrochloride, were administered during the hospitalization period, on an “as required” basis until 8 weeks after surgery. The pulmonary function tests obtained at 3, 6, and 12 months after surgery were performed under pain-free conditions and no patients complained of postoperative pain during the pulmonary function tests.

Table 2 Percentage of low-attenuation volume of the resected lobe compared to the entire lung

Variable	Right upper lobe	Right middle lobe	Right lower lobe	Left upper lobe	Left lower lobe
Number of patients (non-COPD/GOLD 1/2)	20 (14/4/2)	2 (1/1/0)	14 (10/4/0)	14 (3/3/8)	9 (3/6/0)
LAV of the resected lobe/LAV of the entire lung (%), mean \pm SD (range)	20.51 \pm 17.09 (6.04–73.52)	32.53 \pm 8.16 (26.76–38.30)	11.13 \pm 8.26 (0.57–27.36)	27.97 \pm 11.10 (15.33–55.65)	12.41 \pm 9.16 (2.59–28.52)

Values are represented as mean \pm SD. GOLD, Global Initiative for Chronic Obstructive Lung Disease; LAV, low-attenuation volume.

Pulmonary function and symptoms after lobectomy

Only one GOLD 1 COPD patient developed pneumonia on the sixth postoperative day. He was treated by antibiotics for 7 days and had an uneventful recovery. He required low flow oxygen therapy, but did not require high flow oxygen therapy or mechanical ventilation (invasive or non-invasive ventilation). Other patients did not suffer from postoperative complications such as pneumonia, and did not require invasive or non-invasive mechanical ventilation postoperatively. Three patients who had LUL involvement required domiciliary oxygen therapy at the time of hospital discharge which was withdrawn within 3 months after surgery. One of them was GOLD 1 and the others were GOLD 2 COPD patients who had quit smoking several years ago. Among these patients, %LAV of the resected lobe measured 7.66%, 6.27%, and 10.68% and the ratio of LAV of resected lobe/LAV of entire lung was 20.18%, 15.33%, and 24.03%.

Table 3 and Figure 1 shows the preoperative values, postoperative values at 3, 6, and 12 months after lobectomy, and ppo values for VC, FEV₁, %FEV₁, %DL_{co}, and %DL_{co}/V_A. The patients with right middle lobectomy (RML) were excluded from this analysis because of the small number of subjects. Table 4 shows the preoperative and postoperative values at 3, 6, and 12 months after lobectomy for mMRC grade and CAT score.

Preoperative and postoperative values

Postoperative VC values from 3 to 12 months were lower than the preoperative values for each lobectomy location. FEV₁ and %FEV₁ values from 3 to 12 months were also lower than the preoperative values, with the exception of the values at 6 months for the right lower lobectomy (RLL) and at 12 months for the left lower lobectomy (LLL). DL_{co} values from 3 to 12 months were lower than the preoperative values, while DL_{co}/V_A values were not, with the exception of the values at 3 months for the right upper lobectomy (RUL). Both mMRC grade and CAT score were

higher after lobectomy. mMRC grades at 3 months for RUL and at 6 and 12 months for LUL were significantly higher than the preoperative values.

Changes in postoperative values from 3 to 12 months after lobectomy

VC values at 6 and 12 months were higher than at 3 months for RUL, and values at 12 months were higher than at 3 and 6 months for RLL. In contrast, there were no differences between 3, 6, and 12 months for left lung lobectomy (LUL and LLL). For FEV₁, only LUL at 12 months was higher than at 6 months. %FEV₁ for LUL at 12 months was also higher than at 6 months. %FEV₁ at 6 months was higher than at 3 months, but it did not differ from that at 12 months for right lung lobectomy (RUL and RLL). %DL_{co} at 6 and 12 months was higher than at 3 months for RUL, and that at 12 months was also higher than at 3 months for LUL. In addition, there were no differences between 3, 6, and 12 months for both RLL and LLL. In contrast, DL_{co}/V_A showed no significant changes from 3 to 12 months for any of the lobectomies. Neither mMRC grade nor CAT score showed significant changes from 3 to 12 months for any of the lobectomies.

Predicted postoperative values and values obtained at 12 months after lobectomy

The obtained values at 12 months of (I) VC for RUL, RLL, and LUL; (II) FEV₁ for RLL; (III) %FEV₁ for RLL and LUL; (IV) %DL_{co} for LUL; and (V) %DL_{co}/V_A for all lobectomies were higher than the ppo values. Table 5 shows the numbers and percentages of patients who had lower pulmonary function values at 12 months after lobectomy than the calculated ppo values. With respect to the VC, FEV₁ and %FEV₁ values, more non-COPD and GOLD 1 COPD patients showed smaller actual values at 12 months after surgery than the ppo values, than GOLD 2 COPD patients. With respect to the %DL_{co}, more GOLD 1 and GOLD 2 COPD patients showed smaller actual 12-month values compared to the ppo values, than non-COPD

Table 3 Changes in pulmonary function at 3, 6, and 12 months after lobectomy

Variable	Pre-operation	3 months	6 months	12 months	P value	ppo value	P value
VC							
RUL	3,317.00±762.76	2,794.50±799.24 [¶]	2,954.00±833.02 ^{¶†}	3,001.00±806.06 ^{¶†*}	<0.001	2,793.26± 642.32	0.033
RLL	3,139.29±910.95	2,410.00±785.27 [¶]	2,487.86±752.10 [¶]	2,587.86±808.52 ^{¶†*}	<0.001	2,313.16±671.22	0.004
LUL	3,561.43±614.19	2,949.29±652.09 [¶]	3,001.43±643.24 [¶]	3,062.86±708.35 ^{¶*}	<0.001	2,811.65±484.89	0.029
LLL	3,082.22±634.88	2,470.00±645.60 [¶]	2,551.11±640.20 [¶]	2,671.11±747.74 [¶]	<0.001	2,433.33±501.22	0.074
FEV₁							
RUL	2,264.50±518.75	1,890.50±480.53 [¶]	2,005.50±604.37 [¶]	1,900.50±460.54 [¶]	<0.001	1,906.95± 436.84	0.985
RLL	2,199.29±521.62	1,790.00±441.59 [¶]	1,975.00±545.65	1,881.43±479.84 ^{¶*}	<0.001	1,620.53±384.35	0.001
LUL	2,142.14±393.84	1,785.00±360.29 [¶]	1,790.00±359.19 [¶]	1,857.14±363.83 ^{¶†}	<0.001	1,691.17±310.93	0.058
LLL	2,263.33±462.68	1,743.33±411.70 [¶]	1,748.89±376.31 [¶]	1,803.33±445.20	0.002	1,786.84±365.28	0.820
%FEV₁							
RUL	91.66±11.77	76.18±11.09 [¶]	80.77±16.29 ^{¶†}	77.45±15.02 [¶]	<0.001	77.19±9.92	0.956
RLL	100.46±22.72	81.21±14.74 [¶]	89.62±19.06 [†]	85.59±16.43 ^{¶*}	<0.001	74.03±16.74	0.001
LUL	80.81±14.17	67.32±13.54 [¶]	67.85±14.88 [¶]	70.36±15.12 ^{¶†*}	<0.001	63.79±11.19	0.049
LLL	101.68±25.61	76.34±7.08 [¶]	76.88±7.00 [¶]	79.07±8.81	0.002	80.27±20.22	1.000
%DL_{co}							
RUL	118.83±30.02	98.71±21.21 [¶]	108.62±27.47 ^{¶†}	106.83±26.84 ^{¶†}	<0.001	100.03±25.33	0.058
RLL	118.91±29.92	96.86±26.28 [¶]	101.22±30.58 [¶]	103.27±29.97 [¶]	0.003	87.62±22.05	0.067
LUL	104.34±23.35	84.84±22.43 [¶]	89.23±23.93 [¶]	94.49±24.63 ^{¶†}	<0.001	82.30±18.50*	0.003
LLL	115.58±23.06	88.59±22.85 [¶]	90.67±25.11 [¶]	93.73±19.15 [¶]	0.001	91.25±18.21	0.734
%DL_{co}/V_A							
RUL	102.62±23.88	94.95±20.51 [¶]	98.56±22.42	98.87±22.54*	0.003	86.42±20.11	<0.001
RLL	95.63±23.98	94.94±26.42	91.73±22.66	92.86±23.82*	0.733	70.46±17.67	<0.001
LUL	84.70±21.60	79.50±20.24	81.47±19.99	81.15±19.66*	0.433	66.87±17.06	<0.001
LLL	100.91±14.69	89.94±20.74	91.31±22.77	92.22±15.10*	0.081	79.67±11.60	<0.004

Values are represented as mean ± SD. [¶], significantly different compared to pre-operation; [†], significantly different compared to 3 months; [‡], significantly different compared to 6 months values; *, significantly different compared to the ppo value. P<0.05 was set as statistically significant. DL_{co}, lung diffusion capacity for carbon monoxide; DL_{co}/V_A, lung diffusion capacity for carbon monoxide divided by the alveolar volume; FEV₁, forced expiratory volume in one second; LLL, left lower lobectomy; LUL, left upper lobectomy; ppo, predicted postoperative; RLL, right lower lobectomy; RUL, right upper lobectomy; VC, vital capacity.

patients. For %DL_{co}/V_A, the actual number of patients who showed small actual value at 12 months after surgery compared to the ppo value were less than those for %DL_{co}.

Discussion

Several studies have established a correlation between

predicted and observed postoperative pulmonary function values (10-12). However, only few have considered the surgical methods and postoperative evaluation times (5,6).

Many of our patients complained of postoperative pain at 1–2 months after surgery, but the pulmonary function could not be evaluated correctly at that time point. Therefore, we decided to perform the pulmonary function tests at

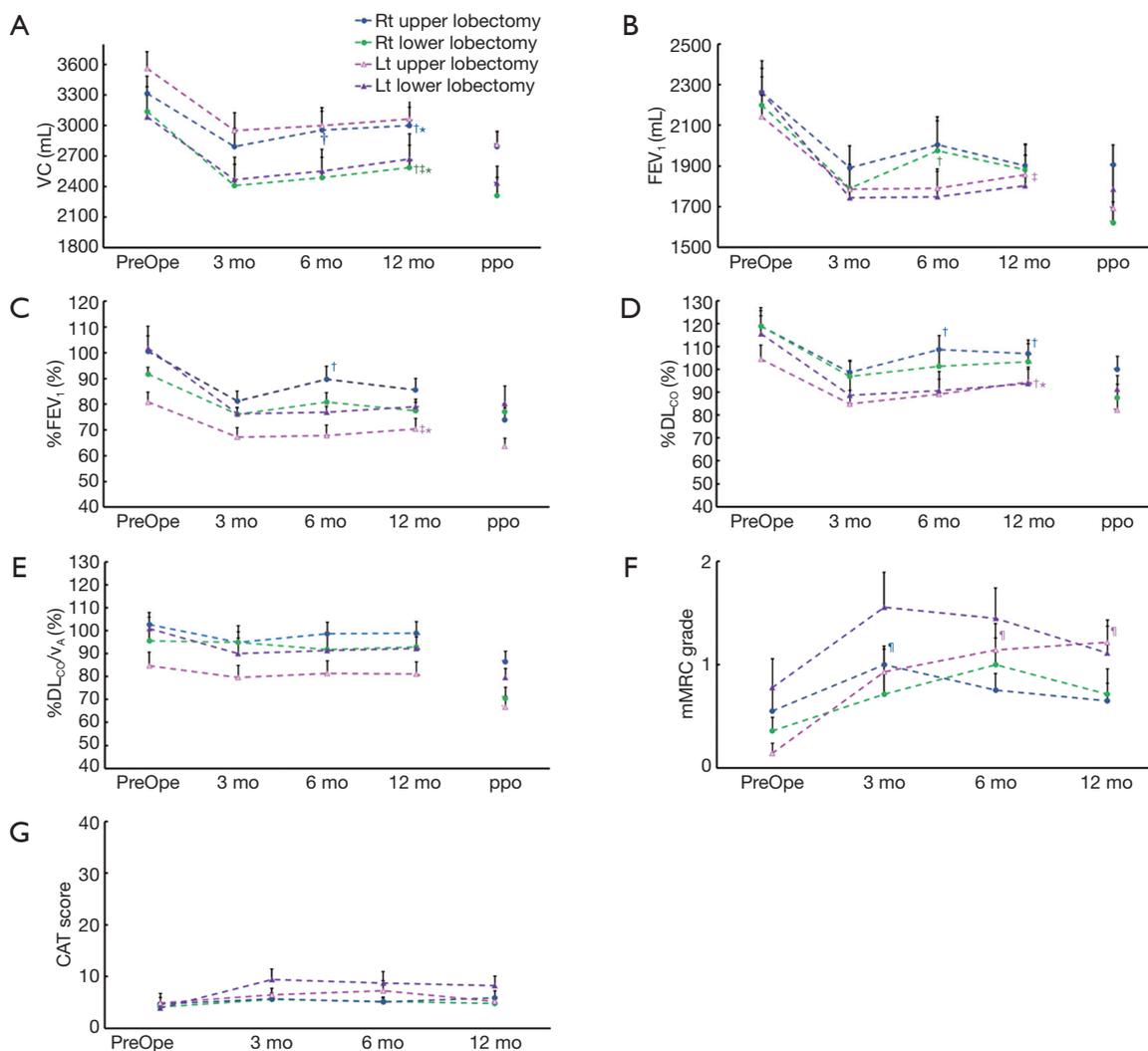


Figure 1 Changes in pulmonary function tests and symptoms according to follow-up duration and resected lobe: (A) vital capacity (VC); (B) forced expiratory volume in one second (FEV_1); (C) percent FEV_1 ($\%FEV_1$); (D) percent lung diffusion capacity for carbon monoxide ($\%DL_{co}$); (E) $\%DL_{co}$ divided by the alveolar volume ($\%DL_{co}/V_A$); (F) modified Medical Research Council (mMRC) grades; (G) COPD Assessment Test (CAT) scores. Values are mean \pm SEM, \dagger , $P < 0.05$ compared to 3 months; \ddagger , $P < 0.05$ compared to 6 months; $*$, $P < 0.05$ compared to ppo; $\dagger\dagger$, $P < 0.05$ compared to the pre-operation.

3 months postoperatively for short-term follow-up. In some of the patients, the symptoms and pulmonary function kept improving until 12 months postoperatively. So far, few studies have reported changes in pulmonary function at 12 months after surgery (13). Thus, we decided to perform the pulmonary function tests at 6 and 12 months for middle- and long-term follow-up. The International Association for the Study of Pain (14) defines chronic postsurgical pain as pain persisting at least 3 months after surgery. It was reported that after VATS lobectomies, 7.5–25% of patients

will have chronic pain (15,16). In contrast, our patients did not complain of postoperative pain and did not require pain relief medications beyond 3 months after thoracic surgery. We believe the pulmonary function tests obtained at 3, 6 and 12 months after surgery were performed under pain-free conditions.

The postoperative lung volume and its function may change depending on the resected lobe (17). In patients with emphysema, lung lobectomy may result in volume reduction (3,12). Then, LAV values were calculated with

Table 4 Changes in mMRC grades and CAT scores at 3, 6, and 12 months after lobectomy

Variable	Pre-operation	3 months	6 months	12 months	P value
mMRC grade					
RUL	0.55±0.94	1.00±0.79 [†]	0.75±0.72	0.65±0.75	0.025
RLL	0.36±0.50	0.71±0.73	1.00±0.96	0.71±0.91	0.135
LUL	0.14±0.36	0.93±0.82	1.14±0.95 [†]	1.21±0.80 [†]	<0.001
LLL	0.78±0.83	1.56±1.01	1.44±0.88	1.11±0.78	0.210
CAT score					
RUL	3.25±3.02	5.60±3.93	5.15±3.99	4.80±4.27	0.884
RLL	4.71±4.56	5.64±4.50	5.14±2.71	5.93±4.94	0.884
LUL	4.86±6.93	6.50±4.69	7.29±6.92	5.21±3.45	0.124
LLL	3.89±3.14	9.44±5.88	8.78±6.63	8.22±5.47	0.061

Values are represented as mean ± SD. [†], significantly different compared to pre-operation. P<0.05 was set as statistically significant. CAT, COPD assessment test; LLL, left lower lobectomy; LUL, left upper lobectomy; mMRC, modified Medical Research Council; RLL, right lower lobectomy; RUL, right upper lobectomy.

Table 5 Numbers and percentage of patients having smaller pulmonary function values at 12 months after lobectomy than the calculated ppo values

Variable	Non-COPD (%) (N=31)	GOLD 1 COPD (%) (N=18)	GOLD 2 COPD (%) (N=10)
VC	10 (32.3)	4 (22.2)	2 (20.0)
FEV ₁	10 (32.3)	7 (38.9)	2 (20.0)
%FEV ₁	10 (32.3)	7 (38.9)	2 (20.0)
%DL _{CO}	8 (25.8)	7 (38.9)	3 (30.0)
%DL _{CO} /V _A	3 (9.68)	1 (5.56)	1 (10.0)

Values are represented as number and percentage.

three-dimensional CT to evaluate the emphysematous changes, which were considered to influence a patient's recovery.

Postoperative complications such as pneumonia, and/or the postoperative requirement for mechanical ventilation sometimes play a role in lung function impairment following surgery. In this study, one patient had pneumonia, but recovered uneventfully. In his case, we believe that the pulmonary function tests obtained after surgery were not affected by such issues.

Several investigators had reported that postoperative incentive spirometry did not improve overall recovery of lung function or frequency of postoperative pulmonary complications (18,19). In this study, our patients did not agree to undergo postoperative rehabilitation as they wanted to return to work and get back into society earlier; therefore, we could not estimate the relationship

between postoperative complications and postoperative rehabilitation, including physiotherapy and incentive spirometry.

Improvement of the pulmonary function according to the resected lobe

VC is a lung volume measurement that can be measured as slow VC or FVC. There is little or no difference between VC and FVC in normal subjects (20). However, FVC sometimes becomes smaller than VC in patients with COPD because of airflow limitations (20-22). Thus, slow VC, and not FVC, was assessed to avoid an underestimate of the pulmonary function in both non-COPD and COPD patients in this study.

To estimate the risk of complications, including atelectasis and pneumonia, thoracic surgery-related

mortality (23-25), VC or FVC, and FEV₁ have been studied in the last quarter of the 1900s (10,25,26) Current guidelines from the American College of Chest Physicians (ACCP) and the ERS recommend the use of not only FEV₁, but also DL_{co} and maximal oxygen consumption (VO₂) to assess the risk of complications associated with lung resection (1,7). In clinical practice, stair climbing or the shuttle walk test is used because VO₂ testing is not practical.

Sengul *et al.* (17) reported that FVC decreased more 3 months after lower lobectomy than after upper lobectomy in 30 patients who underwent lung resection. In their study, CT images taken in supine position showed higher postoperative contralateral lung expansion and minor volume loss of the remaining ipsilateral lung in lower lobectomy, especially right lower lobectomy.

In our study, we did not analyze the volume changes for each remaining lobe by CT images. However, we found that VC observed in the supine position kept increasing until 12 months after right upper or lower lobectomy more than after left lobectomy. Anatomically, the heart might prohibit the expansion of the remaining left lobe after left-side lobectomy compared to the expansion of the right lobe after right-side lobectomy. Another explanation is that after right-side lobectomy, there remain two ipsilateral lobes, whereas after left-side lobectomy, only one ipsilateral lobe remains.

One previous investigation reported that FEV₁ did not improve further after 3 months until 6 months after lobectomy (6). In our study, patients with LUL showed increased FEV₁ and %FEV₁ at 12 months compared to 3 months without significantly increasing VC. This discrepancy may be related with the methods of analysis, which focused on the resected lobe or not. The improvements of FEV₁ and %FEV₁ in patients with LUL may be explained by the fact that LUL will lose more emphysematous lung parenchyma than other lobectomized patients.

When pulmonary emphysema progresses, the alveolus gas exchange area decreases because the alveolus wall is destroyed, and blood flow decreases because the pulmonary capillary bed is destroyed, thus reducing DL_{co}. If the V_A reflects the gas exchange area, DL_{co}/V_A indicates DL_{co} per unit of gas exchange area. In the actual measurements, total lung capacity (TLC) is used instead of the V_A. Patients with COPD who have larger TLC have a %DL_{co}/V_A that is smaller than %DL_{co}. In our study, TLC was measured at each time point and DL_{co}/V_A was calculated.

Lobectomy affects the lung parenchyma including

the alveolar and pulmonary capillary bed, but the total amount of blood remains unchanged. The remaining lung tissue is subjected to an increased pulmonary artery flow (27). That results in pulmonary capillary recruitment and distension for the remaining capillary bed and keeps %DL_{co}/V_A after surgery comparable to the preoperative values. RLL consisting of 5 segments leads to a reduction in the gas exchange area by 66% more than RUL composed of 3 segments $\{[(5/3)-1] \times 100 = 66\%$, while LUL and LLL lead an equal loss of gas exchange area (50% each). Both ventilation and blood flow per unit volume decrease from the bottom to the top of the upright lung. In addition, the percentage of LAV was larger in the upper lobes than in the lower lobes in our subjects. Lower lobe lobectomy loses 50% of one lung with larger ventilation and blood flow, leaving one lower lobe with smaller LAV and two upper lobes with larger LAV. The pulmonary capillary recruitment and distension on those remaining “worse” lobes can keep the overall %DL_{co}, but do not improve from 3 to 12 months after surgery. On the other hand, upper lobe lobectomy loses 30–50% of one lung with smaller ventilation and blood flow, leaving two lower lobes with smaller LAV and one upper lobe with larger LAV. The pulmonary capillary recruitment and distension on those remaining “better” lobes showed improved %DL_{co} after surgery.

Assessing %DL_{co}/V_A is as important as %DL_{co} for understanding the patients’ status pathophysiologically. However, only few studies have focused on the changes of DL_{co}/V_A for pre- and post-lung resection. Our current study supports the previous investigation that the DL_{co} falls after pulmonary resection, but DL_{co}/V_A does not decrease (28). In addition, indication for lung resection may be considered with stable %DL_{co}/V_A, which did not change from pre-operation to 12 months after surgery compared to %DL_{co}.

Preoperative predicted lung function and postoperative values at 12 months after lobectomy

The evaluation of postoperative pulmonary function is important for patient selection before lung surgery. Postoperative pain can cause a number of peri- and postoperative complications both immediately and long after the surgery (29). Most pulmonary function tests require the patient’s effort and that effort sometimes causes pain, possibly resulting in pulmonary function underestimation. Therefore, we compared the ppo values and the actual values obtained at 12 months after surgery.

VC, FEV₁, and DL_{co} decreased over time. However,

VC at 12 months was higher than the ppo value, except for LLL. %FEV₁ and %DL_{co} are usually used for patient's selection before major lung resection (1). However, FEV₁, %FEV₁, and %DL_{co} at 12 months after lobectomy were sometimes higher than the ppo values. That is not related with lobular volume or LAV of the resected lobe. Interestingly, the actual values and ppo values of not only %FEV₁ and %DL_{co}, but also FEV₁ and VC were similar for LLL. Patient selection based on the ppo might be stricter for lower lobectomy planned patients than for other lobectomy patients. When the focus is shifted from the resected lobe to the presence or severity of COPD, non-COPD and GOLD 1 COPD patients appear to have a tendency of lower recovery with respect to VC, FEV₁ and %FEV₁ values than GOLD 2 patients. The number of patients who showed a small recovery of DL_{co} was larger than that for %DL_{co}/V_A, regardless of the presence or absence of COPD.

Changes in symptoms between pre-operation and post-operation

The mMRC grade and CAT score became higher than the preoperative values, but only LUL and RUL showed significant changes after lobectomy, because of their wide variations. The patients who underwent upper lobe lobectomy had higher mMRC grade after surgery, while the LLL group tended to have higher CAT score compared to the other groups. mMRC and CAT questionnaires focus on different aspects: mMRC focuses on the degree of breathlessness related to activity (30) and CAT assesses all aspects of the impact of COPD (cough, sputum, breathlessness, chest tightness, confidence, activity, sleep, and energy levels) on a 1- to 5-point scale that measures health-related quality of life (31). In this study, the number of non-COPD, GOLD 1 COPD, and GOLD 2 COPD patients who had a CAT score ≥ 10 was 1/4/1 preoperatively and 4/3/1 at 12 months after lobectomy. By contrast, the number of patients with an mMRC grade ≥ 2 was 1/3/0 preoperatively and 1/3/0 at 12 months after lobectomy. The changes in those scores were not related with the changes in pulmonary function, percent volume of the resected lobe, or the emphysematous LAV of the resected lobe. Patients with lung cancer diagnosed as GOLD 3 or 4 or having higher LAV on the resected lobe might show volume reduction effects after lobectomy (2,12). However, the National Emphysema Treatment Trial suggested that patients with a homogeneous emphysema distribution and very low FEV₁

(predicted <20%) are high-risk patients for surgical lung volume reduction (32).

The GOLD 1 and GOLD 2 patients who required temporary domiciliary oxygen therapy had higher level of %LAV of resected left upper lobe than the other LUL patients, and the ratio of the LAV of resected lobe/LAV of the entire lung was low. In case of LUL involvement, if the left upper lobe had a higher %LAV than the LUL itself, and a lower LAV ratio compared to the LAV of entire lung, domiciliary oxygen therapy might be needed for a while.

Study limitations

First, the number of patients per lobectomy location was small. The total number of lobectomies by VATS lobectomy has been increasing, but it is not easy to match the number of resected lobes and the number of patients who are diagnosed as non-COPD or COPD with GOLD classification. Second, there were no high-risk patients in this study. We found the FEV₁ and %DL_{co} at 12 months after surgery were sometimes larger than the ppo values for the low and moderate-risk patients. Further research is needed to elucidate the postoperative pulmonary function changes of severely affected patients.

Conclusions

Improvements in pulmonary function and symptoms varied according to the resected lobe. Pulmonary function changes may relate with the location, volume, and extent of emphysematous changes of the resected lobe, and estimated time elapsed from surgery. When selecting patients for lobectomy based on FEV₁ and DL_{co} ppo values, physicians should take into account that the actual values obtained at 12 months after lobectomy become lower than the calculated ppo values in some cases. The use of DL_{co} or DL_{co}/V_A ppo values for the patients' selection related to the lung resection needs further study focused on the incidence rate of complications and mortality.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest

to declare.

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