

Original
Article

Prediction of Postoperative Respiratory Complications after Lobectomy in Lung Cancer Patients with COPD by Quantitative Image Analysis: A Historical Cohort Study

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Purpose: We examined whether preoperative assessment of percentage of low attenuation area (LAA %) on the non-resected side can predict postoperative respiratory complications (PRC) after lobectomy.

Materials and Methods: We conducted a historical cohort study of 217 smokers (175 males and 42 females) who underwent lobectomy for primary lung cancer at our hospital between January 2014 and March 2021. First, the relationship between LAA % and respiratory function parameters (RFPs) calculated for both the bilateral and non-resected sides was used to estimate the most effective patient group. Next, multivariate analyses of the relationship between LAA % of the non-resected side and PRC were performed using logistic regression analysis after adjusting for basic patient attributes and respiratory function.

Results: A correlation was found between LAA % and RFP in smoking males. Multivariate analysis showed a strong relationship between model 3, adjusted for basic patient attributes and lung function factors, and PRC (odds ratio, 2.43; 95% confidence interval, 1.05–5.63).

Conclusion: LAA % of the non-resected side suggested that it may be able to predict the occurrence of PRC after lung cancer lobectomy.

Keywords: lung cancer, thoracic surgery, respiratory complication, quantitative imaging

Introduction

In recent years, Japan's population has been aging, and the median age for undergoing surgery for lung

cancer has been increasing. According to a nationwide survey by the Japanese Association for Thoracic Surgery, patients aged 70–80 years accounted for about 50% of all primary lung cancer patients who underwent surgery in 2012 and 2017. Although there is concern about an increase in postoperative risk due to the aging of surgical patients, the data show that mortality rates within 30 days after surgery and in-hospital mortality rates have been decreasing over time.^{1,2)} This can be attributed to two facts: first, the rate of successful minimally invasive endoscopic surgery exceeded 70% in 2017. Second, the widespread adoption of lung cancer treatment guidelines has led to standardization of surgical indications and extent of resection among institutions.

However, the smoking rate among males and females in Japan remains higher than in other developed countries,³⁾ and a high proportion undergoing lung cancer surgery, with or without intervention, have concomitant

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chronic obstructive pulmonary disease (COPD).⁴⁾ Such patients are at an increased risk of perioperative respiratory complication such as atelectasis and pneumonia due to postoperative pain, restrictive disorders caused by lung volume reduction after lobectomy, and ventilation disorders caused by COPD. Therefore, it is urgent to accurately assess the preoperative respiratory function, estimate the postoperative risk, and establish perioperative management accordingly, which is important to reduce the postoperative risk.

Although spirometry is generally used to assess preoperative and postoperative respiratory function in lung cancer patients undergoing pulmonary resection,^{5,6)} the pandemic of coronavirus disease (COVID-19) infection from early 2020 changed the situation. In asymptomatic infected patients, spirometry with forced breathing was frequently avoided, even in pre- and postoperative patients, due to concerns about the possibility of spreading the infection around via contaminated droplets and aerosols. Therefore, devices such as handheld electronic spirometers and smartphone-based mobile health tools have been developed to replace spirometry as a method of assessing respiratory function with low risk of infection.⁷⁾

However, early clinical use of these devices has been difficult due to economic, technical, and pharmaceutical legal issues. Therefore, we focused on quantitative computed tomography (CT) imaging, in which conventional CT images are analyzed by 3D image processing software. This method has been widely used in the fields of respiratory medicine and radiology because it enables morphological and functional evaluation of respiratory diseases.^{8,9)} In addition, unlike spirometry, there is no viral exposure from the patient; moreover, it may be possible to prognosis by understanding the morphological and functional changes in the lung over time before and after surgery. Notably, partial lung function can be assessed. This is very useful for assessing lung function in patients who are scheduled for lobectomy performed under one-lung ventilation. The reason for this is that during anesthesia under one-lung ventilation and in the early postoperative period, it is not an exaggeration to say that the unilateral lung of the non-resected side alone is doing the work of bilateral lungs. All conventional methods for estimating postoperative partial lung function and residual lung volume have been based on various lung ventilation values obtained from spirometry.^{10–12)}

The purpose of this study was to evaluate preoperative partial lung function in patients scheduled for lobectomy

for lung cancer using quantitative CT imaging analysis. As an evaluation index, we used the ratio of the low attenuation area (LAA) of the non-resected lung side to the non-resected field of view (the non-resected side percentage of the low attenuation area [LAA%]), which was calculated based on quantitative CT image analysis. We analyzed the relationship between LAA% of the non-resected side and various values obtained from preoperative respiratory function tests, and also examined whether LAA% of the non-resected side was associated with the occurrence of PRC in a previous cohort.

Materials and Methods

In this historical cohort study, we used a database of surgical records recorded at a single institution from January 2014 to March 2021. Male and female smokers with primary lung cancer who underwent lobectomy within the observation period were included in the study.

For the patient background, the following items were extracted from the database: basic patient attributes (age, Brinkman index [BI], body mass index [BMI], history of preoperative inhalant use), side of surgery, respiratory function parameters (RFPs) (partial pressure of arterial oxygen [PaO_2], partial pressure of arterial carbon dioxide [PaCO_2], percentage predicted vital capacity [%VC], forced expiratory volume in 1 second [FEV_1], percentage predicted FEV_1 [% FEV_1], and FEV_1 /forced vital capacity [FVC], expiratory rate at 25% of total lung capacity [V_{25}], expiratory rate at 50% of total lung capacity [V_{50}], and peak flow rates [PFRs]), LAA% of the bilateral side and the non-resected side lung, and perioperative items (postoperative oxygen inhalation period, drainage period, postoperative oxygen inhalation period, drain placement period postoperative hospitalization period, and PRC). At our facilities, diffusing capacity of the lungs for carbon monoxide (D_{LCO}) was evaluated only in subjects exhibiting interstitial changes in preoperative CT images. Therefore, patients with interstitial changes on preoperative CT were excluded in this study. There were no surgery-related deaths during the observation period.

The relationship between LAA% and respiratory function assessed in the bilateral side and the non-resected side lung was analyzed for sex.

PRC was defined as pleurisy, pneumonia, drainage more than 7 days after surgery, and oxygen inhalation more than 7 days after surgery occurring within 1 month after surgery.

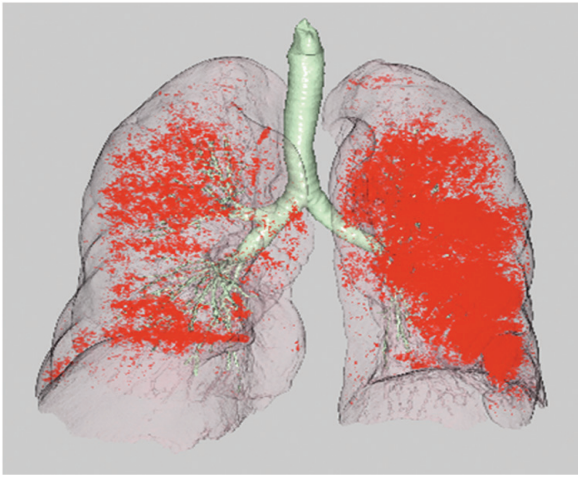


Fig. 1 LAA is shown in the red area. The LAA% of the non-resected side lung (non-resected side LAA%) is calculated as follows: non-resected side LAA% = LAA (voxel) of the non-resected side/total lung voxel of the non-resected side \times 100. LAA: low attenuation area

This study was approved by the ethics committee of Tohoku Medical and Pharmaceutical University Hospital. Informed consent to study subjects was provided on an opt-out basis.

Image analysis

Chest CT was performed before surgery using a high-resolution CT (Aquilion 64, ONE, Prime SP; Toshiba, Tochigi, Japan). The images were taken in the helical mode from the apex to the base of the lung in the supine position with full inspiration. The CT scan parameters were tube current 236.9 ± 88.2 mA, tube potential 119.3 ± 3.6 kVp, matrix size 512×512 , and slice thickness 1 mm. The digital images were transferred to a 3D image analysis software (SYNAPSE VINCENT; Fujifilm, Tokyo, Japan) and reconstructed into a 3D model. The lung was segmented using the CT attenuation minus 400 HU as the threshold, excluding the surrounding soft tissues, pulmonary vessels, trachea, and bronchi.

The threshold of LAA was calculated as the average of the CT values of the air in the trachea at the height of the supra-aortic margin and of the whole lung field based on previous studies¹³⁾ (**Fig. 1**).

Statistical analysis

First, the relationship between LAA% and spirometrically obtained RFP (%VC, FEV₁, %FEV₁, FEV₁/FVC, V₂₅, V₅₀, and PFR) was analyzed using Spearman rank correlation coefficient by sex. At this time, LAA% and RFP were evaluated in two patterns: bilateral side and

non-resected side. We found that LAA% correlated better with RFP in males than in females. Since the difference in BI was assumed to be related to the difference in the patient background by sex, we added a comparison by BI.

Basic patient attributes (age, BI, BMI, history of preoperative inhalant use, and surgical side), preoperative factors (PaO₂, PaCO₂, %VC, FEV₁, %FEV₁, FEV₁/FVC, V₂₅, V₅₀, PFR, and LAA% of the non-resected side), and postoperative factors (duration of postoperative oxygenation, duration of drainage, duration of postoperative hospitalization, PRC) were presented as mean \pm standard deviation or median and interquartile range (IQR), as appropriate. Comparisons between the two groups were performed using the Mann–Whitney U test, Student's t test, or Fisher's exact test. In order to estimate the association between LAA% of the non-resected side and PRC, the following three models were constructed by logistic regression analysis using the direct imputation method. Model 1 was corrected for only LAA% of the non-resected side, Model 2 was corrected for basic patient attributes, and Model 3 was corrected for basic patient attributes and preoperative factors. The standard value of LAA% was obtained by the equal bisection method was uses. All analyses were performed using R version 4.0.3 (Saitama Medical Center, Jichi Medical School, Saitama, Japan), and a value of $p < 0.05$ was considered significant. Since this was an exploratory study to estimate the association between non-resected lung LAA% and PRC, rather than a hypothesis-testing analysis, no prior sample size calculation was performed. The number of samples was therefore set to the maximum number of data we could obtain during the period analyzed.

Results

Comparison of patient background by sex

The background characteristics of the 217 cases (175 males and 42 females) are shown in **Table 1**.

The background characteristics by sex are shown in **Table 1**. The median age, BI, and BMI by sex (males vs females) were 71.0 vs 69.5, 940.0 vs 512.5, and 24.0 vs 23.0, respectively. All of the patients who used preoperative inhalers were males. Median values of PaO₂, PaCO₂, and RFP of the bilateral side by sex (FEV₁, %FEV₁, FEV₁/FVC, VC, %VC, V₂₅, V₅₀, and PFR) were 87.0 vs 86.80 mmHg, 38.15 vs 39.70 mmHg, 2.39 vs 1.75 L, 84.10% vs 92.5%, 68.42% vs 74.23%, 3.45 vs 2.53 L, 98.7% vs 101.6%, 0.49 vs 0.40 L/sec, 2.06 vs 2.15 L/sec,

Table 1 Comparison of patient background by sex

Variables	Males (n = 175)	Females (n = 42)	p-value
Age	71.0 (76.0–65.0)	69.5 (74.75–64.25)	0.3
BMI	24.0 (26.0–21.5)	23.0 (26.75–19.0)	0.33
BI	940.0 (1220–680)	512.5 (686.25–246.25)	<0.0001
Inhalant (%)	21 (1.4)	0 (0)	0.016
Surgical side			0.48
Right	109 (62.3)	29 (69.0)	
Left	66 (37.7)	13 (31.0)	
PaO ₂	87.0 (94.0–80.0)	86.80 (93.75–78.93)	0.79
PaCO ₂	38.15 (50.7–35.68)	39.70 (42.63–37.0)	0.14
RFP and LAA% of bilateral side (median)			
FEV ₁	2.39 (2.72–2.03)	1.75 (1.99–1.465)	<0.0001
%FEV ₁	84.10 (98.1–73.1)	92.5 (109.83–85.25)	0.0015
FEV ₁ /FVC	68.42 (75.6–62.7)	74.23 (77.91–68.58)	0.055
VC	3.45 (3.85–3.15)	2.53 (2.77–2.08)	<0.0001
%VC	98.7 (107.8–90.1)	101.6 (114.88–88.13)	0.498
V ₂₅	0.49 (0.70–0.33)	0.4 (0.60–0.24)	0.047
V ₅₀	2.06 (2.96–1.31)	2.15 (2.63–1.18)	0.28
PFR	7.09 (8.38–5.71)	4.47 (5.51–4.02)	<0.0001
LAA%	6.40 (15.35–2.7)	2.30 (7.25–0.80)	0.0012
RFP and LAA% of non-resected side (median)			
FEV ₁	1.18 (1.36–0.99)	0.86 (0.98–0.71)	<0.0001
%FEV ₁	42.14 (48.30–37.28)	46.43 (55.0–41.36)	0.18
FEV ₁ /FVC	35 (38.0–30)	3638.8–33.0)	0.182
VC	1.74 (1.95–1.54)	1.255 (1.38–1.02)	<0.0001
%VC	48.74 (53.92–44.62)	49.57 (54.65–44.82)	0.58
V ₂₅	0.25 (0.35–0.17)	0.205 (0.32–0.12)	0.05
V ₅₀	1.05 (1.49–0.68)	1.02 (1.26–0.57)	0.23
PFR	3.46 (4.19–2.76)	2.16 (2.74–1.99)	<0.0001
LAA%	6.60 (15.0–2.35)	2.65 (6.60–0.70)	0.002
Postoperative O ₂ period (days)	5.33 ± 8.20	4.32 ± 2.05	0.45
Duration of drain (days)	3.25 ± 2.55	2.63 ± 1.93	0.15
Postoperative period of stay (days)	12.57 ± 8.54	12.98 ± 10.87	0.8
Respiratory complications (%)	51 (29.1)	9 (21.4)	0.35
Oxygen inhalation more than 7 days after surgery	37	5	
Drainage more than 7 days after surgery	11	3	
Pneumonia	2	1	
Pleurisy	1	0	

BMI: body mass index; BI: Brinkman index; PaO₂: partial pressure of arterial oxygen; PaCO₂: partial pressure of arterial carbon dioxide; RFP: respiratory function parameter; LAA%: percentage of low attenuation area; FEV₁: forced expiratory volume in 1 second; %FEV₁: percentage predicted FEV₁; FVC: forced vital capacity; VC: vital capacity; %VC: percentage predicted vital capacity; V₂₅: expiratory rate at 25% of total lung capacity; V₅₀: expiratory rate at 50% of total lung capacity; PFR: peak flow rate

Table 2 Relationships between RFP and LAA% in the bilateral side and non-resected side in all patients

RFP	LAA% of bilateral side		LAA% of non-resected side	
		<i>p</i> -value	γ	<i>p</i> -value
FEV ₁	-0.019	0.78	-0.0356	0.602
%FEV ₁	-0.134	0.049	-0.135	0.0483
FEV ₁ /FVC	-0.472	<0.0001	-0.419	<0.0001
VC	0.28	<0.0001	0.257	0.000133
%VC	0.287	<0.0001	0.285	<0.0001
V ₂₅	-0.214	0.0016	-0.223	0.001
V ₅₀	-0.353	<0.0001	-0.359	<0.0001
PFR	-0.045	0.509	-0.0578	0.399

RFP: respiratory function parameter; LAA%: percentage of low attenuation area; FEV₁: forced expiratory volume in 1 second; %FEV₁: percentage predicted FEV₁; FVC: forced vital capacity; VC: vital capacity; %VC: percentage predicted vital capacity; V₂₅: expiratory rate at 25% of total lung capacity; V₅₀: expiratory rate at 50% of total lung capacity; PFR: peak flow rate

and 7.09 vs 4.47 L/sec, respectively. The median LAA% evaluated on the bilateral side and non-resected side in males was 6.40% and 6.60%, respectively. On the other hand, the median LAA% evaluated on the bilateral side and non-resected side in females was 2.30% and 2.65%, respectively. There was a significant difference in LAA% between males and females when evaluated in the bilateral side or non-resected side ($p = 0.0012$ and $p = 0.00199$, respectively). PRC was observed in 60 patients (27.6%). PRC was observed in 51 males (29.1) and 9 females (21.4). In males, 37 had oxygen inhalation more than 7 days after surgery, 11 had drainage more than 7 days after surgery, 2 had pneumonia, and 1 had pleurisy. In females, 5 had oxygen inhalation more than 7 days after surgery, 3 had drainage more than 7 days after surgery, and 1 had pneumonia.

Relationship between LAA% and RFP of the bilateral side in all patients

Spearman's rank correlation coefficient was used to show the relationship between LAA% and the RFP of the bilateral side (**Table 2**). There was no correlation between LAA% and FEV₁, and %FEV₁ and PFR of the bilateral side (FEV₁: $\gamma = -0.019$, $p = 0.78$; %FEV₁: $\gamma = -0.134$, $p = 0.049$; PFR: $\gamma = -0.045$, $p = 0.509$). On the other hand, there was a significant correlation between LAA% and FEV₁/FVC, VC, %VC, V₂₅, and V₅₀ of the bilateral side (FEV₁/FVC: $\gamma = -0.472$, $p < 0.0001$; VC: $\gamma = 0.28$, $p < 0.0001$; %VC: $\gamma = 0.287$, $p < 0.0001$; V₂₅: $\gamma = -0.214$, $p = 0.0016$; V₅₀: $\gamma = -0.353$, $p < 0.0001$).

Relationship between LAA% and estimated RFP of the non-resected side in all patients

The respiratory function of one lung was calculated by multiplying each value of RFP obtained by preoperative spirometry by the number of lung segments on the non-resected side (10 segments for the right side or 9 segments for the left side) and dividing by the total number of lung segments (19 segments) of both lungs. Spearman rank correlation coefficient was used to show the relationship between LAA% and the estimated RFP of the non-resected side (**Table 2**). There was no correlation between LAA% and FEV₁, and %FEV₁ and PFR of the non-resected side (FEV₁: $\gamma = -0.0356$, $p = 0.602$; %FEV₁: $\gamma = -0.135$, $p = 0.0483$; PFR: $\gamma = -0.0578$, $p = 0.399$). On the other hand, there was a significant correlation between LAA% and FEV₁/FVC, VC, %VC, V₂₅, and V₅₀ of the non-resected side (FEV₁/FVC: $\gamma = -0.419$, $p < 0.0001$; VC: $\gamma = 0.257$, $p = 0.000133$; %VC: $\gamma = 0.285$, $p < 0.0001$; V₂₅: $\gamma = -0.223$, $p = 0.001$; V₅₀: $\gamma = -0.359$, $p < 0.0001$).

Correlation between RFP and LAA% by sex and BI

The relationship between LAA% and RFP was compared by sex and BI using Spearman's rank correlation coefficient (**Table 3**). In males when evaluated in the bilateral side, FEV₁/FVC ($\gamma = -0.483$, $p < 0.0001$), %VC ($\gamma = 0.323$, $p < 0.0001$), V₂₅ ($\gamma = -0.274$, $p < 0.000258$), V₅₀ ($\gamma = -0.380$, $p < 0.0001$), and PFR ($\gamma = -0.207$, $p = 0.00633$) showed a correlation. On the other hand, in females, only FEV₁/FVC ($\gamma = -0.359$, $p = 0.0196$) and V₅₀ ($\gamma = -0.401$, $p = 0.00849$) showed a correlation. When evaluated on the non-resected side, correlations were found for FEV₁/FVC, %VC, V₂₅, V₅₀, and PFR in males. However, only V₅₀ was found among females. Based on the overall patient background, we considered that this difference between male and female was largely due to differences in BI, and the differences were evaluated by BI. Based on a median BI of 880, the high BI group (BI ≥ 880) was correlated with RFP (FEV₁/FVC, %VC, V₂₅, V₅₀), reflecting more obstructive ventilatory impairment and peripheral airflow limitation than the low BI group (BI < 880).

Prediction of PRC by LAA%

Table 4 shows whether LAA% can significantly predict the occurrence of PRC after accounting for various confounding factors by multiple logistic regression analysis. **Tables 4-1** and **4-2** show the results of the bilateral side and the non-resected side, respectively. The cutoff values of LAA% were obtained by the equal

Table 3 Correlation between RFP and LAA % by sex and BI: upper panel for bilateral side and lower panel for non-resected side

	Males		Females		High BI (≥ 880)		Low BI (< 880)	
	γ	<i>p</i> -value	γ	<i>p</i> -value	γ	<i>p</i> -value	γ	<i>p</i> -value
Bilateral side: RFP vs LAA %								
FEV ₁	-0.136	0.074	-0.195	0.215	-0.182	0.054	0.172	0.08
%FEV ₁	-0.083	0.274	-0.163	0.303	-0.184	0.054	-0.000218	0.998
FEV ₁ /FVC	-0.483	<0.0001	-0.359	0.02	-0.539	<0.0001	-0.272	0.005
VC	0.191	0.011	0.076	0.63	0.11	0.246	0.359	0.000167
%VC	0.323	<0.0001	0.231	0.14	0.221	0.019	0.342	0.000356
V ₂₅	-0.274	0.000258	-0.185	0.24	-0.315	0.008	-0.0267	0.787
V ₅₀	-0.38	<0.0001	-0.401	0.008	-0.437	<0.0001	-0.166	0.091
PFR	-0.207	0.006	-0.179	0.257	-0.131	0.173	0.022	0.823
Non-resected side: RFP vs LAA %								
FEV ₁	-0.155	0.041	-0.108	0.496	-0.185	0.05	0.145	0.14
%FEV ₁	-0.109	0.15	-0.092	0.563	-0.178	0.062	-0.002	0.98
FEV ₁ /FVC	-0.451	<0.0001	-0.258	0.099	-0.509	<0.0001	-0.221	0.024
VC	0.159	0.036	0.166	0.293	0.089	0.349	0.336	0.000457
%VC	0.307	<0.0001	0.282	0.071	0.218	0.021	0.342	0.000363
V ₂₅	-0.288	0.000124	-0.149	0.346	-0.322	0.000613	-0.039	0.695
V ₅₀	-0.393	<0.0001	-0.37	0.002	-0.436	<0.0001	-0.182	0.0634
PFR	-0.216	0.004	-0.103	0.518	-0.127	0.184	-0.02	0.843

RFP: respiratory function parameter; LAA%: percentage of low attenuation area; BI: Brinkman index; FEV₁: forced expiratory volume in 1 second; %FEV₁: percentage predicted FEV₁; FVC: forced vital capacity; VC: vital capacity; %VC: percentage predicted vital capacity; V₂₅: expiratory rate at 25% of total lung capacity; V₅₀: expiratory rate at 50% of total lung capacity; PFR: peak flow rate

dividing method, and the cutoff values for the bilateral side and the non-resected side were 6.4 and 6.5, respectively. In LAA% of the bilateral side, the odds ratio (OR) for model 1 was 2.23 (95% confidence interval [CI] 1.13–4.37), which was still significant after adjusting for basic patient attributes such as age, BMI, and BI. However, in model 3, which corrected for preoperative RFP, the association between LAA% of the bilateral side and the incidence of PRC was not significant (OR 1.61; 95% CI 0.73–3.57). On the other hand, the incidence of PRC was significantly associated not only with Models 1 and 2 but also with Model 3 corrected for each RFP in LAA% on the non-resected side (OR 2.43; 95% CI 1.05–5.63).

Discussion

The standard treatment for clinical stage I–II non-small cell lung cancer is surgical resection. Based on the results of a clinical trial reported in 1995, lobectomy and lymph node dissection of the hilar and mediastinal regions of the lung are considered standard.¹⁴ Preoperative respiratory

function tests and cardiovascular function assessment are essential to ensure the safety of surgical resection, and it is also important to predict residual postoperative respiratory function, which is likely to affect the prognosis after pneumonectomy. In particular, lung cancer patients with COPD are at an increased risk of postoperative cardiorespiratory complications due to further loss of lung volume after pneumonectomy, because the reserve volume of the pulmonary vascular bed is reduced due to lung disease.

As a method of predicting residual postoperative respiratory function, it has been reported that preoperative spirometry and postoperative predictive respiratory function using pulmonary blood flow scintigraphy showed a good correlation with actual postoperative measured respiratory function and the predicted postoperative FEV₁.^{5,6} However, pulmonary blood flow scintigraphy requires a special imaging system, and there is a burden of radioisotope exposure to the patient, so the method of predicting only from the number of residual pulmonary segments and spirometry is common.

Spirometry has several problems: it relies on effort breathing, which is not reproducible, and it carries the

Table 4 Multiple logistic regression analysis of predictive factors for postoperative respiratory complications (Table 4-1: bilateral side and Table 4-2: non-resected side)

Table 4-1	Model 1			Model 2			Model 3		
Factors	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
LAA% \geq 6.4	2.23	1.13–4.37	0.020	2.16	1.07–4.36	0.030	1.61	0.73–3.57	0.240
Age				1.03	0.99–1.08	0.170	1.02	0.97–1.08	0.466
BMI				1.01	0.92–1.10	0.828	1.02	0.93–1.12	0.716
BI				1.00	0.99–1.10	0.939	1.00	0.99–1.00	0.335
PaO ₂							0.98	0.95–1.02	0.330
%FEV ₁							0.99	0.92–1.08	0.47
%VC							1.01	0.98–1.04	0.65
V ₂₅							0.46	0.04–4.99	0.52
V ₅₀							1.16	0.60–2.22	0.66
PFR							0.76	0.57–1.00	0.05

Table 4-2	Model 1			Model 2			Model 3		
Factors	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
LAA% \geq 6.5	2.64	1.33–5.23	0.005	2.46	1.21–4.98	0.013	2.43	1.05–5.63	0.038
Age				1.03	0.986–1.08	0.183	1.02	0.97–1.01	0.407
BMI				0.98	0.877–1.09	0.686	1.00	0.88–1.13	0.978
BI				1.00	0.999–1.00	0.984	1.00	0.999–1.000	0.343
PaO ₂							0.98	0.95–1.02	0.320
%FEV ₁							1.00	0.93–1.09	0.92
%VC							1.03	0.97–1.03	0.85
V ₂₅							3.27	0.02–3.27	0.3
V ₅₀							2.58	0.68–2.58	0.4
PFR							1.00	0.559–0.999	0.05

OR: odds ratio; CI: confidence interval; LAA%: percentage of low attenuation area; BMI: body mass index; BI: Brinkman index; PaO₂: partial pressure of arterial oxygen; %FEV₁: percentage predicted FEV₁; %VC: percentage predicted vital capacity; V₂₅: expiratory rate at 25% of total lung capacity; V₅₀: expiratory rate at 50% of total lung capacity; PFR: peak flow rate

risk of droplet dispersion. The latter is more serious with the spread of COVID-19, which has been expanding since 2020. From the viewpoint of infection prevention, spirometry is becoming more difficult to perform, and there is an urgent need to establish a non-infectious and highly reproducible alternative test.

Therefore, we focused our attention on a method called quantitative CT imaging analysis. Quantitative CT imaging analysis is a system that converts CT images into images that can be analyzed quantitatively by importing them into 3D image analysis software, which is already widely used in many medical institutions for 3D morphological evaluation of blood vessels in organs. In addition, several reports showing the correlation between quantitative image analysis and respiratory function indicate that this examination method is capable of not only morphological but also functional evaluation of organs. Although conventional imaging diagnosis had a strong subjective

component, quantification of emphysematous changes in the lung calculated by quantitative CT imaging analysis has increased its objectivity and reproducibility, and its representative index, LAA%, is now used in the Goddard classification of COPD.^{15,16)}

This quantitative CT imaging is excellent for both understanding the pathophysiology and assessing the functional tolerance of the lung, and therefore has the potential to be used to evaluate only one lung as well as both lungs. Although there are scattered reports on the relationship between preoperative respiratory function of bilateral lungs and PRC, no report has examined the relationship between unilateral anatomical lung function and PRC. Since lung cancer surgery is performed under isolated lung ventilation anesthesia and is strongly affected by positive pressure ventilation, an accurate understanding of the anatomical and physiological lung function of the non-resected side is very important for

perioperative management. Furthermore, it may be underestimated in patients with advanced emphysema. In this study, we attempted quantitative CT imaging analysis of the non-resected lung to evaluate the true perioperative lung function tolerance of patients undergoing pneumonectomy.

First, the optimal patient group for quantitative image analysis was investigated. The characteristics of quantitative image analysis are best utilized in cases with emphysematous background lungs. Males in particular tend to present with emphysematous changes more frequently than females. The present study found differences in the relationship between LAA% and RFP between males and females. Although respiratory dysfunction due to emphysematous changes is mainly caused by airflow limitation in the peripheral airways, the LAA% correlated more strongly with RFPs such as FEV₁/FVC, V₂₅, V₅₀, and PFR, which reflects these parameters, in the male group than in the female group. This may be due to the difference in BI, but quantitative imaging may be more useful for smokers.

Previous studies have shown that LAA% of the total lung field correlates with RFP in bilateral lungs.^{17,18)} It was an important first step to determine if a similar relationship could be found in the non-resected lung. In the present study, we also found a correlation between LAA% and RFP in bilateral lungs, which was also true when evaluated on the non-resected side. To determine whether LAA% on the non-resected side can predict the occurrence of PRC, a model was constructed by multiple logistic regression analysis adjusting for basic patient attributes and RFP for the bilateral side and the non-resected side. Only LAA% evaluated on the non-resected side showed a strong association with PRC, even in Model 3 adjusted for basic patient attributes and RFP.

On the other hand, several problems emerged with the quantitative CT imaging analysis method.

The first is that the threshold of the LAA differs among studies.^{17,18)} Since the same CT system and imaging conditions are essential for calculating the LAA%, it is not meaningful to compare the LAA% values among institutions, and it is difficult to set a certain cutoff criterion. Therefore, it is necessary for each institution to set its own cutoff value. In addition, the radiographic transparency of the thoracic cavity is affected by the thickness of the chest wall, which hampers the standardization of LAA%. Fortunately, the SYNAPSE VINCENT software used in this study is equipped with a system to correct for

this, and the correction is based on the CT value of intratracheal air at the level of the supra-aortic border.¹³⁾ How to treat smokers with interstitial shadows, who were excluded from the present study, is a future issue.

Conclusion

We demonstrated the possibility of the LAA% of the non-resected side using the method of quantitative CT imaging analysis. Furthermore, based on the accuracy of its reproducibility, the LAA% of the non-resected side showed a strong correlation with the occurrence of PRC. Therefore, this value could be used to stratify patients according to the risk of such complications. In the future, we hope to extend this study and establish the LAA% of the non-resected side as a new parameter to assess surgical tolerance of lung cancer lobectomy.

Disclosure Statement

The authors declare no competing interests.

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