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ORIGINAL

Assessment of emphysematous change and pulmonary function after lobectomy for lung cancer - quantitative 3D-CT analysis

Junji NAKAZAWA[1, 2], Atsushi WATANABE[2], Keishi OGURA[3], Masahiro MIYAJIMA[2], Taijiro MISHINA[2], and Tetsuya HIGAMI[1]

[1] Department of Cardiovascular Surgery, Sapporo Medical University School of Medicine
[2] Department of Thoracic Surgery, Sapporo Medical University School of Medicine
[3] Division of Radiology and Nuclear Medicine, Sapporo Medical University Hospital

ABSTRACT

Background: Lung volume reduction surgery (LVRS) in patients with severe chronic pulmonary emphysema (CPE) results in postoperative improvement in pulmonary function. Lobectomy in patients with lung cancer also has the same effect.

Methods: One hundred fourteen patients underwent lobectomy for lung cancer from 2006 to 2011. Computed tomography (CT) and pulmonary function test (PFT) were performed preoperatively and six months to one half year after surgery. All CT examinations were performed using a 64-row multidetector CT scanner during a breath-hold at deep inspiration. Total lung volume (TLV), each lobe volume, and low attenuation area (LAA) were extracted from CT data of each patient.

Results: TLV after upper lobectomy was increased significantly compared with lower lobectomy (111.0 ± 18.9% vs 103.9 ± 16.1%; p=0.05). There was no relationship between lung volume change and preoperative LAA%. In contrast, LAA% change demonstrated a negative relationship with preoperative LAA% (r=0.4590). In the group defined as preoperative LAA% more than 20%, postoperative LAA% decreased significantly (34.9 ± 13.9% to 32.8 ± 18.4%; p<0.01) and FEV1% predicted improved (70. 3 ± 9.7% to 75.3 ± 12.7%; p=0.03).

Conclusions: The resected lobe region is more important than the resected lobe volume (RLV) and segment number in TLV change after lobectomy. Preoperative LAA% is a negative factor of LAA% change. Therefore patients with severe emphysematous lung are less likely to increase their postoperative LAA%. Lobectomy for patients with high LAA% provides improved FEV1 % predicted.

Key words: lung cancer, lobectomy, computed tomography, pulmonary function, low attenuation area, emphysema

1. Background

Lung volume reduction surgery (LVRS) has been associated with improved lung function in patients with severe pulmonary emphysema by resection of emphysematous lung[1-5]. After LVRS, computed tomography (CT) images show hyperinflation of preserved lung. Pulmonary function test (PFT), especially forced expiratory volumes in one second (FEV1) and FEV1 % of predicted (FEV1%) improves. Some researchers reported that lobectomy in patients with lung cancer provided the same volume reduction effect as LVRS[6-9]. In these studies, improvement in pulmonary function differed on the lung with resected lobe, and upper lobectomy was particularly better than lower lobectomy. Lobectomy in patients with severe emphysema and low FEV1 and FEV1% would also provide better effect in pulmonary function[6-9].

Chronic pulmonary emphysema (CPE) is classified chronic obstructive pulmonary disease (COPD) and is characterized by abnormal, permanent enlargement of air spaces distal to the terminal bronchioles accompanied by destruction of the bronchiolar walls. Previous reports suggested that low attenuation area (LAA) on CT images observed in patients with CPE correlated well with the results of tissue pathology and PFT[10-14]. Therefore, LAA is used for assessment of pulmonary function. After lobectomy for lung cancer, LAA increases because of hyperinflation of the preserved lung. However, we don't have a good explanation on a possible direct relationship between increased LAA and improved pulmonary function after lobectomy.

In this study, we evaluated the effects of lobectomy for lung cancer on postoperative total lung volume (TLV) and LAA% using 3-dimensional computed tomography (3D-CT) images and on postoperative PFT.

2. Methods

This is a retrospective study on 114 patients who underwent lobectomy for lung cancer in our institution between April 2005 and October 2010. Thoracoscopic surgery was performed on all the patients using mini-thoracotomy with one or two ports. Chest CT scan was performed on all patients before surgery and 1year after lobectomy. The mean time interval between lobectomy and postoperative CT was 366.8 ± 115.7 days. Preoperative PFT was performed before surgery on all patients and postoperative PFT only on 55 patients at 6 months to 1 year after lobectomy[15,16]. Forced vital capacity % predicted (FVC%) and FEV1% were assessed. Patient characteristics are shown in Table 1.

Table1

	(%)
Age (year)	66.9 ± 9.6
Gender	
Male	73 (64.0)
Female	41 (36.0)
BMI	22.9 ± 3.4
Smokers	66 (57.9)
Brinkman Index	572.4 ± 708.7
Co-morbidities	
Interstitial pneumonia	10 (8.8)
Asthma	2 (1.8)
Respiratory parameters	
%FVC (%)	112.8 ± 19.3
FEV1% (%)	73.0 ± 9.8
Resected lobe	
Right upper lobe	40 (35.1)
Right middle lobe	8 (7.0)
Right lower lobe	17 (14.9)
Right middle & lower lol	3 (2.6)
Left upper lobe	23 (20.2)
Left lower lobe	23 (20.2)
Pathological stage	
I	70 (61.4)
II	21 (18.4)
III	23 (20.2)
Histology	
Adenocarcinoma	73 (64.0)
Suamous cell carcinoma	21 (18.5)
Other	20 (17.5)
Interval between surgery and postoperative CT (day)	367.8 ± 115.7

number = mean ± SD

All CT examinations were performed using a 64-row multidetector CT scanner (Aquilion 64; Toshiba Medical, Tokyo, Japan). Thin-section CT data were reconstructed at 1mm-thick slices with 5mm interval. CT was performed during a breath-hold at deep inspiration. All CT data for each patient were transferred to a computer workstation (SYNAPSE VINCENT; FUJIFILM, Tokyo, Japan) from which 3D models were reconstructed. The trachea, mainstem bronchus, and soft tissues surrounding the lungs were automatically excluded by the software. Minor and major fissures on 2D-CT images were manually traced to calculate the volume of each anatomic lobe. Then, TLV and each lobe volume were calculated (Figure 1). Postoperative TLV change was calculated by subtracting resected lobe volume (RLV) from preoperative TLV and then subtracting the difference from postoperative TLV. The volume of voxels with low attenuation values of less than -950HU was used as LAA14-17). LAA% was calculated by dividing the volume of LAA by TLV. Postoperative LAA% change was calculated by subtracting the preserved lung LAA% from postoperative LAA%. COPD was defined as patients with FEV1 / FVC less than 70% and without asthma.

The statistical analysis was performed using SPSS11.0 software (SPSS Inc, Chicago, IL, USA). All data are presented as mean ± standard deviation. Unpaired t-test was used for continuous variables. Fisher's exact test was used for nominal variables.

Single regression analysis was employed for correlation coefficients of continuous variables and considered the Pearson correlation coefficient of more than 0.4 as positive correlation. A p value of less than 0.05 was considered statistically significant.

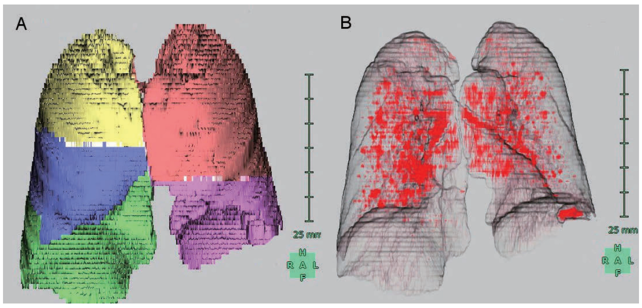

Figure 1 - An example of lobar segmentations and LAA on 3D-CT images.
A, The yellow, blue, green, red and purple areas represent, respectively, right upper lobe, right middle lobe, right lower lobe, left upper lobe and left lower lobe. B, The red area represent LAA.

3. Results

3.1. Location of resected lobe and postoperative TLV and LAA% change

Preoperative and postoperative lung volume (LV), RLV, increased rate (IR), preoperative and postoperative LAA% and LAA% change in each lobe are shown in Table 1. Although postoperative LV increased in each lobe, the degree of increase was different from each other. There was no correlation between IR and number of lung segments in each group. Similarly, there is no correlation between IR and LAA% change. Tables 3and 4 show IR and LAA% changes of the upper and lower lobectomy groups and right and left lobectomy groups. Patients who underwent right middle lobectomy were included in the upper lobectomy group. In the upper lobectomy group IR (111.0 ± 18.9 vs 103.9 ± 16.1, p=0.05) and LAA% changes (8.0 ± 18.4 vs 0.5 ± 19.0, p=0.04) were significantly increased compared to the lower lobectomy group. In contrast, there was no significant difference between the right and left lobectomy groups.

3.2. Factor of postoperative TLV and LAA% change

The 55 patients who were able to undergo postoperative PFT were evaluated based on correlation coefficients between IR and LAA% change, lung subsegments and RLV, and preoperative and postoperative changes in PFT (FEV1 and FVC) and LAA% as shown in Table 5. Preoperative LAA% was correlated with LAA% change as shown in Figure 2 (r = 0.4590). However, the IR was not correlated with other factors.

3.3. Relationship between LAA% and PFT before and after surgery

All the patients were divided into two groups according to the mean preoperative LAA%; group 1 with preoperative LAA% < 20% and group 2 with preoperative LAA% ≥ 20%. In group 2, preoperative FEV1% was significantly lower (75.0 ± 9.1 vs 70.7 ± 10.2%, p=0.02) and postoperative LAA% was significantly decreased (20.0 ± 19.0 vs 32.8 ± 18.4%, p < 0.01) compared to group 1. However there was no significant difference in IR in each group (Table 5). Table 8 shows significant improvement in change of FEV1% in group 2 (0.4 ± 7.4 vs 5.0 ± 7.9%,

Table3

	Upper lobectomy (RUL+RML+LUL) N=71	Lower lobectomy (RLL+LLL) N=40	p value
Lung volume			
Increased volume after opration (n	347.1 ± 690	87.2 ± 536	0.04
Increased rate (%)	111.0 ± 18.9	103.9 ± 16.1	0.05
LAA% (%)			
Preoperative LAA%	18.9 ± 14.5	24.7 ± 19.5	0.07
Postoperative LAA%	26.9 ± 20.9	25.2 ± 17.6	0.66
Change of LAA%	8.0 ± 18.4	0.5 ± 19.0	0.04

RUL=Right upper lobectomy, RML=Right middle lobectomy, RLL= Right lower lobectomy, LUL= Left upper lobectomy, LLL=Left lower lobectomy
LAA=Low attenuation area, Number means mean ± SD

Table4

	Right side lobectomy (RUL+RML+RLL+RMLL) N=68	Left side lobectomy (LUL+LLL) N=46	p value
Lung volume			
Increased volume after opration (n	261.6 ± 706	256.8 ± 545	0.97
Increased rate (%)	109.0 ± 20.0	108.0 ± 15.0	0.79
LAA% (%)			
Preoperative LAA%	18.9 ± 15.2	23.6 ± 18.3	0.13
Postoperative LAA%	25.8 ± 20.0	25.9 ± 19.5	0.96
Change of LAA%	6.9 ± 19.0	2.3 ± 18.5	0.20

RUL=Right upper lobectomy, RML=Right middle lobectomy, RLL= Right lower lobectomy,
LUL= Left upper lobectomy, LLL=Left lower lobectomy, RMLL=right middel and lower bilobectomy
LAA=Low attenuation area, Number means mean ± SD

Table5

	Increesed rate R	Change of LAA% R
Lung subsegments	0.2427	0.0738
Resected lung volume	0.0236	0.0657
Preoperative FEV$_1$	0.1417	0.1417
Change of FEV$_1$	0.2071	0.1763
Preoperative FVC	0.1919	0.0518
Change of FVC	0.0426	0.0796
Preoperative LAA%	0.0847	0.4590
Change of LAA%	0.2801	-

FEV$_1$ = Forced expiratory volume in 1 second, FVC= Forced vital capacity,
LAA=Low attenuation area, LAA%=LAA/lung volume ×100

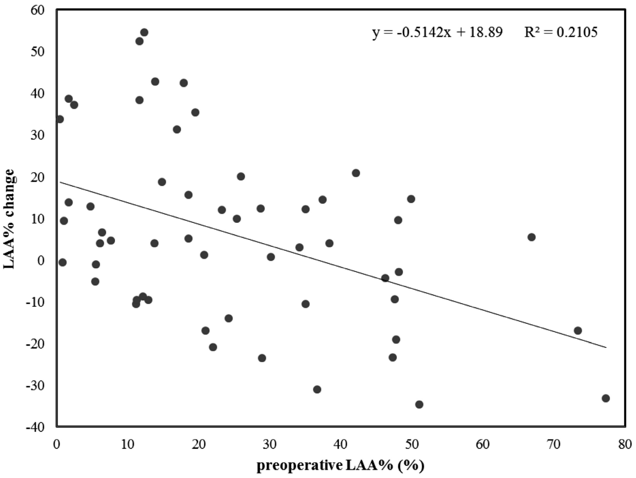

Figure 2 - Correlation between preoperative LAA% and LAA% change.

p=0.03). There was no significant difference in FVC% in both groups.

3.4. Relationship between COPD and TLV, LAA%, and PFT

Tables 7 and 9 show the comparison between COPD and non-COPD cases. Although there was a significantly higher preoperative LAA% and FEV1% in the COPD group, there was no significant change in LAA% in both groups. Similarly, there was no significant difference in change of FEV1% in both groups (Table 9).

4. Discussion

Assessments of emphysematous lung with the use of CT scans have been reported, such as the Goddard method, in which three points in the CT images are used[10,18]. There are reports on easy ways to calculate the lung volume and LAA in each lobe with 3D-CT images[14,19,20]. We can access several commercial workstations used to measure objective and precise TLV and LAA% changes before and after surgery in 3D-CT images without complex programs[1,11-14]. Numerous studies have shown that LAA, which consists of pixels with attenuation values of -910 to -970 HU on thin-section CT scans, is correlated well with results on pathologic distributions of emphysema. Therefore, LAA has been recognized as an objective test value. In this study, we evaluated the effects of lobectomy for lung cancer with the use of 3D-CT images and PFT on what we considered an opposite phenomena, in which the LAA% increased in the postoperative lung in correlation with an improved postoperative FEV1%[6-9].

Table 2 shows that the mean postoperative TLV and LAA% increased in all patients. We estimated that hyperinflation of the preserved lung occurred after lobectomy in order to fill the space of the resected lung, which resulted in increased LAA% after lobectomy. Table 3 shows the significantly less IR and LAA% changes in the lower lobectomy group. We also believed that the space where the resected lung previously existed was decreased because the diaphragm became elevated. This condition controlled hyperinflation of the preserved lung. Table 5 shows that the IR is not correlated with the subsegments, RLV, preoperative and postoperative changes in PFT (FEV1 and FVC) and LAA%. This findings entail that the resected region is important than the RLV and preoperative LAA% in terms of postoperative TLV change.

The absence of correlation between LAA% and IR change and negative correlation between LAA% change and preoperative LAA% suggest the existence of a different mechanism. Negative correlation between LAA% change and preoperative LAA% means that a lung with more emphysematous lesion is less likely to develop further emphysematous change after lobectomy. We estimate the mechanism of emphysematous change after lobectomy is not as the histological tissue change like emphysema as the change of intake pressure action. In other words, the

Table7

	non-COPD N=63	COPD N=51	p value
Respiratory parameters			
Preoperative FEV1% (%)	79.8 ± 5.8	64.5 ± 6.4	< 0.01
Preoperative %FVC (%)	114.1 ± 19.8	111.1 ± 18.6	0.41
Lung volume			
Increased volume after opration (n	369.6 ± 516	123.7 ± 755	0.04
Increased rate (%)	112.0 ± 16.5	104.3 ± 19.1	0.02
LAA% (%)			
Preoperative LAA%	17.6 ± 16.6	24.8 ± 15.9	0.02
Postoperative LAA%	21.5 ± 18.5	31.2 ± 20.0	< 0.01
Change of LAA%	3.9 ± 17.9	6.4 ± 20.1	0.47

COPD=Chronic obstructive pulmonar disease
FEV1＝Forced expiratory volume in 1 second, FVC= Forced vital capacity,
FEV1%=FEV1/FVC, %FVC=Percent-predicted forced vital capacity,
LAA=Low attenuation area, LAA%=LAA/lung volume ×100

Table8

	Group 1 preLAA% < 20% N=26	Group 2 preLAA% ≧ 20% N=29	p value
Respiratory parameters (%)			
Preoperative FEV1%	74.9 ± 9.2	70.3 ± 9.7	0.08
Postoperative FEV1%	75.3 ± 12.3	75.3 ± 12.7	0.99
Change of FEV1%	0.4 ± 7.4	5.0 ± 7.9	0.03
Preoperative %FVC	109.7 ± 21.4	120.0 ± 16.5	0.05
Postoperative %FVC	96.4 ± 24.6	99.9 ± 19.8	0.56
Change of %FVC	Δ 13.3 ± 13.3	Δ 20.1 ± 15.5	0.09
LAA% (%)			
Preoperative LAA%	9.6 ± 6.0	38.8 ± 15.6	< 0.01
Postoperative LAA%	25.9 ± 22.0	35.7 ± 19.5	0.09
Change of LAA%	16.3 ± 20.6	Δ 3.1 ± 18.1	< 0.01

FEV1＝Forced expiratory volume in 1 second, FVC= Forced vital capacity,
FEV1%=FEV1/FVC, %FVC=Percent-predicted forced vital capacity,
LAA=Low attenuation area, LAA%=LAA/lung volume ×100, Number means mean ± SD

Table9

	non-COPD N=30	COPD N=25	p value
Respiratory parameters (%)			
Preoperative FEV1%	79.6 ± 5.1	64.0 ± 6.2	< 0.01
Postoperative FEV1%	81.5 ± 7.9	67.8 ± 12.8	< 0.01
Change of FEV1%	1.93 ± 7.2	3.86 ± 8.8	0.37
Preoperative %FVC	116.4 ± 17.8	113.6 ± 21.6	0.61
Postoperative %FVC	101.6 ± 22.6	94.2 ± 21.2	0.22
Change of %FVC	Δ 14.8 ± 14.4	Δ 19.5 ± 15.2	0.25
LAA% (%)			
Preoperative LAA%	21.4 ± 20.1	29.2 ± 16.8	0.13
Postoperative LAA%	25.9 ± 20.8	37.2 ± 20.2	0.05
Change of LAA%	4.4 ± 22.5	8.0 ± 20.4	0.54

COPD=Chronic obstructive pulmonar disease
FEV1＝Forced expiratory volume in 1 second, FVC= Forced vital capacity,
FEV1%=FEV1/FVC, %FVC=Percent-predicted forced vital capacity,
LAA=Low attenuation area, LAA%=LAA/lung volume ×100, Number means mean ± SD

Table2

	RUL	RML	RLL	RMLL	LUL	LLL	Total
Number of patients	40	8	17	3	23	23	114
Lung segments	3	2	5	7	4	4	3.6
Lung subsegments	6	4	12	16	10	10	8.4
Lung volume							
(a) Preoperative lung volume	4723.7 ± 1177	4557.9 ± 1035	4218.1 ± 1423	4859.8 ± 130	4259.7 ± 985	4820.8 ± 1033	4652.2 ± 1126
(b) Resected lobe volume	986.1 ± 296	408.1 ± 97	898.7 ± 288	1392.4 ± 74	1118.2 ± 324	933.3 ± 344	953.9 ± 345
(c) Postoperative lung volume	4032.4 ± 1169	4387.4 ± 227	3474.2 ± 1290	3955.4 ± 262	4044.1 ± 963	3924.7 ± 696	3952.7 ± 1030
(d) Increased volume after opration (d) = (c) - { (a) - (b) }	294.8 ± 806	237.5 ± 532	154.8 ± 574	487.9 ± 421	476.3 ± 493	37.2 ± 513	259.6 ± 644
Increased rate (%)	110.0	108.5	105.9	114.5	113.6	102.5	108.7
LAA% (%)							
(a) Preoperative LAA%	19.2 ± 14.9	15.1 ± 10.7	20.8 ± 18.0	13.6 ± 15.9	19.7 ± 15.3	27.6 ± 20.5	20.8 ± 16.6
(b) Postoperative LAA%	26.0 ± 21.0	34.9 ± 17.8	24.1 ± 18.8	8.1 ± 1.2	25.9 ± 22.1	26.0 ± 17.0	25.8 ± 19.7
Percentage change between (a) & (b)	6.8 ± 18.2	19.8 ± 16.8	3.3 ± 20.6	Δ 5.5 ± 15.3	6.1 ± 18.6	Δ 1.6 ± 18.1	5.0 ± 18.9

RUL=Right upper lobectomy, RML=Right middle lobectomy, RLL= Right lower lobectomy, LUL= Left upper lobectomy, LLL=Left lower lobectomy
RMLL=right middel and lower bilobectomy, LAA=Low attenuation area, LAA%=LAA/lung volume ×100

Table6

	Group 1 preLAA% < 20% N=62	Group 2 preLAA% ≧ 20% N=52	p value
Respiratory parameters			
Preoperative FEV_1% (%)	75.0 ± 9.1	70.7 ± 10.2	0.02
Preoperative %FVC (%)	109.9 ± 21.0	116.2 ± 16.3	0.08
Lung volume			
Increased volume after opration (n	220.5 ± 696	306.2 ± 578	0.48
Increased rate (%)	108.5 ± 20.3	108.7 ± 15.1	0.94
LAA% (%)			
Preoperative LAA%	9.1 ± 6.4	34.9 ± 13.9	< 0.01
Postoperative LAA%	20.0 ± 19.0	32.8 ± 18.4	< 0.01
Change of LAA%	10.9 ± 17.1	Δ 2.0 ± 18.7	< 0.01

FEV_1=Forced expiratory volume in 1 second, FVC= Forced vital capacity,
FEV1%=FEV1/FVC, %FVC=Percent-predicted forced vital capacity,
LAA=Low attenuation area, LAA%=LAA/lung volume ×100

lung with higher compliance like a healthy lung or one with less emphysematous lesion is more likely to inflate after lobectomy. This hypothesis seems to explain the opposite phenomenon, which is the increased LAA% in the postoperative preserved lung but also the same effect of LVRS after lobectomy. However, LAA is defined as the difference in CT values; wherein, we cannot distinguish enlargement of the alveolus by hyperinflation from histological tissue change, like emphysema, if we assess only CT images. Therefore, further studies with lung tissues in patients with re-lobectomy are needed to verify this hypothesis.

As postoperative LAA% was significantly decreased in the group with preoperative LAA% ≥ 20%, lobectomy in patients with more emphysematous lesion resulted in decreased postoperative LAA%. The same effect does not occur in comparing between COPD and non-COPD groups, so that imaging tests might estimate more accurately than PFT the postoperative emphysematous change. Table 8 includes postoperative PFT, which shows significant improvement in postoperative FEV1% in the group with preoperative LAA% ≥ 20%. Table 9, however, shows no significant difference in postoperative FEV1% between COPD and non-COPD groups. Therefore, a high preoperative LAA% might be a factor for predicting improvement of postoperative FEV1% after lobectomy.

5. Conclusions

In the present study, we demonstrated that the resected lobe region is more important than the RLV and segment number in postoperative TLV change after lobectomy, especially upper lobectomy which is the most effective. Preoperative LAA% is a negative factor of LAA% change. Therefore, patients with severe emphysematous lung are less likely to increase their postoperative LAA%. Preoperative LAA% could be a predictive factor for improvement in FEV1% after lobectomy for lung cancer.

6. Abbreviations

LVRS, Lung volume reduction surgery; CT, computed tomography; PFT, pulmonary function test; FEV1, forced expiratory volumes in one second; FEV1%, FEV1 % of predicted; CPE, chronic pulmonary emphysema; COPD, chronic obstructive pulmonary disease; LAA, low attenuation area; 3D-CT, 3-dimensional computed tomography; FVC, forced vital capacity; TLV, total lung volume; RLV, resected lobe volume; IR, increased rate

7. Competing interests

The authors declare that they have no competing interests.

8. Authors' contributions

JN participated in study conception and design, data acquisition and analysis and drafted the manuscript. AW participated in study conception and design and critically revised drafts of the manuscript. KO, MM, TH participated in study conception and design. All authors read and approved the final manuscript.

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CT画像を用いた肺癌に対する肺葉切除後の気腫性変化と呼吸機能変化の検討

仲 澤 順 二[1, 2)], 渡 辺 敦[2)], 小 倉 圭 司[3)],
宮 島 正 博[2)], 三 品 泰 二 朗[2)], 樋 上 哲 哉[1)]

1) 札幌医科大学医学部心臓血管外科学講座
2) 札幌医科大学医学部呼吸器外科学
3) 札幌医科大学附属病院放射線部

背景：現在までに重症のCOPDに対する肺減量手術後に, 呼吸機能が改善することが報告されている．また，同様の効果が肺癌に対する肺葉切除後にも生じるという報告もある．しかし，肺の膨張による気腫性変化と呼吸機能改善の関係には不明な点が多い．本研究では，1）切除肺葉部位，切除肺区域数，術前肺の気腫の程度などが，術後残存肺体積，術後の気腫性変化などに影響を及ぼすか，2）術後残存肺体積変化と術後気腫性変化とが，術後呼吸機能に影響を及ぼすかを明らかにすることを目的とした．

対象と方法：対象は2006～2011年に当院にて肺癌に対して肺葉切除を行われ, 術前後（術後約1年）で胸部CT検査を行われた114例である．本研究では，肺葉切除前後のCT画像を3次元構築し，術前後の肺体積と気腫性変化部位（LAA：CT値 -950HU以下を示す部位）の体積を測定した後，LAA%（LAA体積／肺体積）とLAA%変化（術後LAA%−術前LAA%）を算出した．切除肺葉部位との関連においては，肺葉を上下，左右に分類し検討した．LAA%と残存肺体積変化に関しては，術前LAA%＝20%をカットオフ値として2群に分けて検討した．COPDはFEV1 /FVC < 70%かつ非喘息症例として，COPDの有無で分類し検討した．術後に呼吸機能を計測しえたのは55例で，LAA%変化と術前後のFVC％変化量，FEV1.0%変化量を検討した．

結果：上葉切除と下葉切除の比較では，術後肺体積が上葉切除後に有意に増加していたが(p=0.05)，LAA％変化には有意差を認めなかった（p=0.17）．肺体積変化と術前後肺諸量との間には相関係数を認めなかったが，LAA％変化と術前LAA％との間には弱い負の相関関係を認めた（r = 0.4588）．術前LAA％が20％を超える群では，術後LAA％は有意に改善していた（p<0.01）．さらに術前LAA％が20%を超える群では，術後FEV1％が有意に改善していた(p=0.02)．

結論：1）残存肺の体積増加には，切除肺体積や切除区域数よりも切除部位が重要で，特に上葉切除後に術後肺体積の増大を認めた．2）術前LAA％は術後残存肺が気腫性変化することの負の規定因子であり，術前気腫肺が術後さらに気腫性変化をきたすわけではない．3）術前LAA％は術後FEV1％の改善を予測する指標の一つとなる可能性がある．