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Doctor of Medicine

Effect of inferior pulmonary ligament division on residual lung volume and function after right upper lobectomy

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of the University of Ulsan

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Effect of inferior pulmonary ligament division on residual lung volume and function after right upper lobectomy

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Abstract

Objective: Though the detailed procedures of lobectomy have been well structured, performance of inferior pulmonary ligament (IPL) division has not been determined definitely during upper lobectomy. Division of IPL could contribute on postoperative pulmonary conditions; we evaluated the influence of IPL division on alteration of anatomy, residual lung volume, and overall pulmonary function after lobectomy.

Methods: We evaluated 53 patients (mean age at operation 61±9 years) who underwent video assisted thoracoscopic surgery (VATS) lobectomy of right upper lobe (RUL) for early stage lung cancer in Asan medical center in Korea from January 2011 to April 2014. The patients who had pleural adhesion or experienced thoracotomy approach were excluded. They were categorized in two groups based on division of IPL; preservation group (group P, n=22), division group (group D, n=31). Bronchial angle measurement between bronchus intermedius and right middle lobe (RML) bronchus taken on pre-and postoperative chest computed tomography (CT) image, which was performed at 3 to 6 months after the operation. Right lower lobe (RLL) and RML volume was measured with the same CT images three-dimensionally. Existence of atelectasis, dead space and fluid collection was based on same CT. Postoperative pulmonary function within 1 year was compared with preoperative pulmonary function tests (PFT).

Results: Mean age was not statistically different between two groups (58.9±9.5 years in group P vs 62.4±8.5 years in group D, *p*=0.168). The prevalence of atelectasis (8/22, 36.4% in group P vs 11/31, 35.5% in group D, *p*=0.417), dead space which was filled with air (2/22, 9.1% in group P vs 7/31, 22.6% in group D, *p*=0.197), pleural effusion (9/22, 40.9% in group P vs 11/31, 35.5% in group D, *p*=0.688) was not statistically different between two groups. There were no significant differences in postoperative remaining lung volume (1757±400 ml in group P vs 1844±477 ml in group D, *p*=0.487). Also, there was no difference in postoperative bronchial angle between two groups (109.7°±13.7° vs 109.9°±13.5, *p*=0.954). There were no significant differences in postoperative FVC and FEV1 (3.25±0.63 in group P vs

3.05±0.63 in group D, p=0.289; 2.27±0.34 in group P vs 2.26±0.46 in group D, p=0.891). However, group D experienced more considerable loss of FVC after the operation than group P (-0.16±0.25 liters in group P vs -0.42±0.33 liters in group D, p<0.01). The amount of postoperative decrease of FEV1 is not significantly different (-0.31±0.2 liters in group P vs. -0.26±0.22 liters in group D, p=0.475).

Conclusions: Division of IPL did not show any benefit in postoperative lung volume, function, prevalence of complications during lobectomy of RUL. Moreover, preservation of IPL can contribute to conserve the pulmonary functional capacity better. Therefore, division of IPL should be performed in properly selected patients.

Key words: Lung volume, Lung function, Bronchial angle, Lobectomy of right upper lobe, inferior pulmonary ligament, Lung cancer

Contents

List of figures, tables & abbreviations

Introduction

After wide acceptance of anatomical resection for lung cancer treatment, lobectomy has been the treatment of choice for the lung cancer and it has been systematically done with safety [1,2]. However, division of inferior pulmonary ligament (IPL) still has been in discuss with few studies because it could reduce the dead space while causing the possibility of developing atelectasis after the operation [2]. Meanwhile, during the surveillance of the patients who underwent lobectomy, delayed atelectasis could be found often even several months over after surgery, in especially right middle lobe (RML) atelectasis after lobectomy of right upper lobe (RUL). Atelectasis can affect remaining lung volume anatomically and functionally. Therefore, we compared several parameters in computed tomography (CT) scanning, pulmonary function tests (PFT) and other clinical outcomes between two groups whether the performance of IPL division.

Methods

1. Patient population

We retrospectively reviewed the data from 181 patients who underwent video-assisted thoracoscopic surgery (VATS) lobectomy of RUL for lung cancer in our institution from January 2011 to April 2014. The patients who had interstitial lung disease or emphysematous destruction before the operation were excluded. And the patients who had partial or diffuse pleural adhesion or the patients whose surgical procedure was changed to thoracotomy approach from VATS were also excluded. The remaining 53 patients were divided into 2 groups based on procedures to the IPL: preservation (Group P, n=22) and division (Group D, n=31).

All patients underwent routine preoperative and cancer staging examination including chest CT and PFT. These examinations were performed before the operation within 1 month. Postoperative surveillance data including clinical records, chest roentgenogram

(X-ray), chest CT and PFT were collected. The presence of atelectasis, dead space or any results which were collected from CT images were based on the CT scanning which was done at 3 to 6 months after surgery during follow up periods. Postoperative results of PFT were collected from those performed about 1 year after the operation.

2. Operative method and postoperative management

All operations were done by two surgeons. The procedure was performed under general anesthesia followed by intubation with a double lumen endotracheal tube, allowing single-lung ventilation. The location of the tracheal tube was always checked with bronchoscopy. The patient was positioned in the left lateral decubitus position. The VATS lobectomy was performed using three incisions. Endoscopic staplers were used for individual ligation of the hilar structure, including the pulmonary vessels and bronchus. No patients underwent fixation of RML to prevent lobar torsion at the end of all procedures. Same oncological principles, such as complete anatomic resection with adequate margins and mediastinal lymph node dissection were implemented. Routinely, all patients extubated after the operation, and admitted to ward or intensive care unit according to the patient's baseline conditions. Chest X-ray was performed on daily basis and chest tube was removed if there is no air-leakage and an amount of drain had been decreased to 200~250 ml per day with the consideration of patient's body weight. At the day after removal of draining tube, most of the patients were discharged.

3. Volume measuring

Using in-house software, right lobe segmentation was semi-automatically performed. Lung, airway and pulmonary vessel were extracted using thresholding the simplest method of image segmentation, 3D region growing with semi-automatic interaction. Lobe segmentation was performed with 3D free-formed surface fitting on possible fissure voxels which were detected by hessian matrix analysis within lung except dilated airway and pulmonary vessel regions. And then, manual editing of the detected fissure and lobe split were performed. Using the result of lobe segmentation, each lobe volume was automatically calculated. All volume measurement procedures were done by one radiologic specialist.

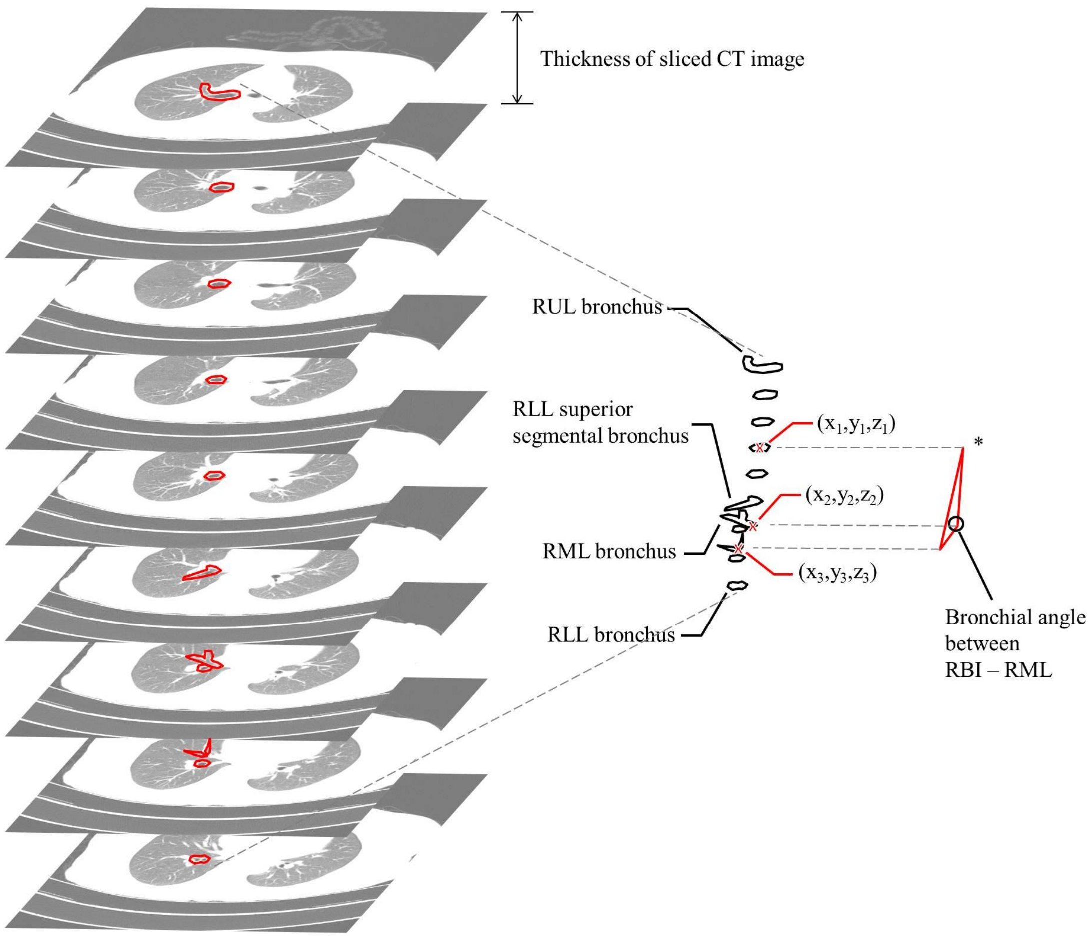
4. Bronchial angle measuring

Bronchial branching angle of right middle lobe was obtained by finding each midpoint of the bronchus. First of all, a triangle was made with these three points (midpoint of bronchus intermedius, RML bronchus before the branching of segmental bronchus, center of RML bronchus branching site), and two-dimensional coordinates was obtained in transverse section of CT imaging which has the thinnest slice depth. The coordinates of z-axis could be obtained from the thickness of sliced computed tomography image. Length of each side of the triangle was calculated by the

Pythagorean theorem with three dimensional coordinates in each point. The right middle lobar branching angle was calculated by the second law of cosines with the calculated length of each side. This method is illustrated in figure 1.

Figure 1. The methods for bronchial angle measuring. Three-dimensional coordinates of each point (center of right bronchus intermedius, right middle lobe bronchus and branching site) were collected. Branching angle was calculated by second law of cosines after calculating the distances from these three points by Pythagorean theorem.

* Note that the height of triangle is expressed longer than actual size to promote the understanding of method.



5. Statistical analysis

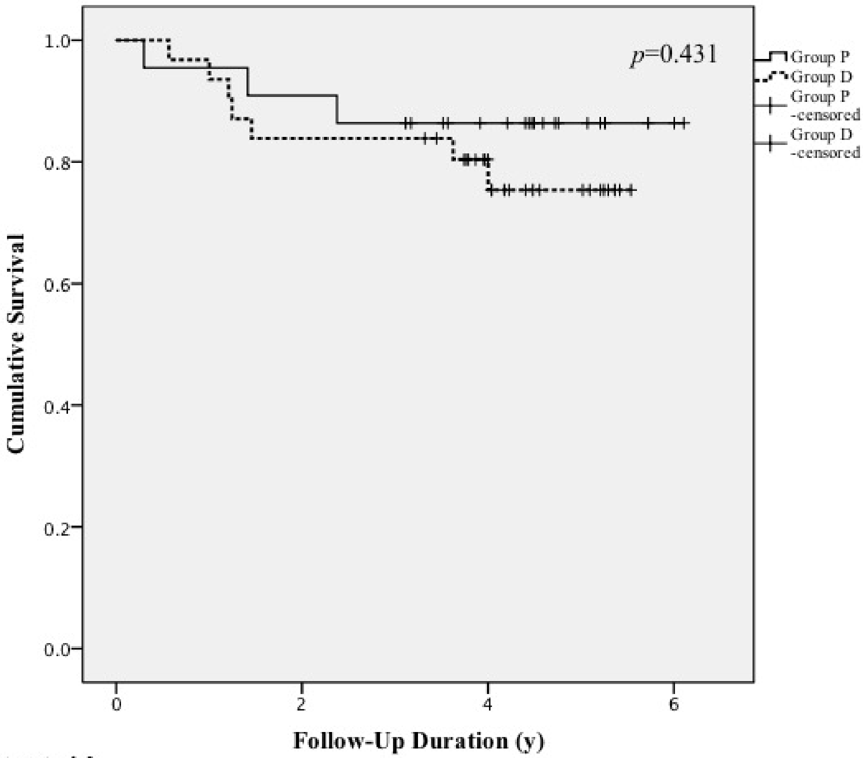
Statistical analysis was performed using IBM SPSS 22 Software (IBM Co., Chicago, IL, USA). Continuous values are expressed as mean ± standard deviation. χ^2 test or Fisher exact test were used for categorical variables between the groups. Unpaired Student's t-test and the Mann-Whitney test were used for discrete and continuous variables. A paired T-test was used to test between pre- and postoperative variables in the same patients. A value of p less than 0.05 was considered significant.

Results

1. Patients and outcomes

The mean age of the patients is 58.9 years in group P and 62.4 years in group D (p=0.168). Age, cancer stage, hospital stay was not different among the two groups. 1 patient in group D underwent neoadjuvant chemotherapy. No patients required re-admission or further treatment for surgical complications. There were no differences between two groups in incidence of atelectasis, dead space and prolonged pleural effusion. Overall survival rate was not different among two groups (Figure 2). Detailed characteristics are summarized in Table 1.

Figure 2. Overall survival curve of patients stratified by division of inferior pulmonary ligament



Patients at risk

Group P	22	20	14	2
Group D	31	26	16	0

Table 1. Baseline characteristics (n=53)

	Preservation group (n=22)	**Division group (n=31)**	***p* value**
Age (years)	58.9±9.5	62.4±8.5	0.168
Sex			0.799
Male	12 (54.5%)	18 (58.1%)	
Femele	10 (45.5%)	13 (41.9%)	
Hospital stay (days)	5 (IQR; 5-7)	5 (IQR; 5-7)	0.251
Histology			0.112
Adenocarcinoma	20	22	
Squamous cell carcinoma	1	5	
Others	1	4	
Pathological cancer stage			0.304
I	16	27	
II	1	2	
III	4	1	
IV	1	1	
Follow up duration (y)	4.45 (IQR; 3.52-5.07)	4.00 (IQR; 3.68-4.79)	0.417
Atelectasis	8 (36.4%)	11 (35.5%)	0.948
Dead space	2 (9.1%)	7 (22.6%)	0.197
Delayed pleural effusion	9 (40.9%)	11 (35.5%)	0.688
5 year survival rate (%)	86.4	75.4	0.431

IQR, interquartile range

2. Volume

The preoperative volume of RML, RLL, and sum of these in group P were revealed as 385±149 ml, 1018±296 ml and 1403±358 ml, respectively. These values of group D were 396±144 ml, 1143±292 ml and 1538±358 ml, respectively. The difference was not significant between two groups in these values (p=0.787, 0.133 and 0.180), respectively. The preoperative whole lung volumes were not significantly different between those groups (2237±511 ml in group P and 2444±445 ml in group D, p=0.124), respectively.

Postoperatively, volume of RML in group P was 363±168 ml and that in group D was 367±188 ml (p=0.947). Postoperative volume of RLL in group P was 1393±364 ml and in group D was 1477±402 ml (p=0.440). Sum of RML, RLL volume was 1757±400 ml in group P and was 1844±478 ml in group D (p=0.487). There were no differences in these values between two groups. The whole lung volume after right upper lobectomy (sum of RML, RLL volumes) represented 81% of preoperative whole lung volume in group P and 75% in group D. Lower proportion was found in group D, however, this finding was not statistically significant (*p*=0.225).

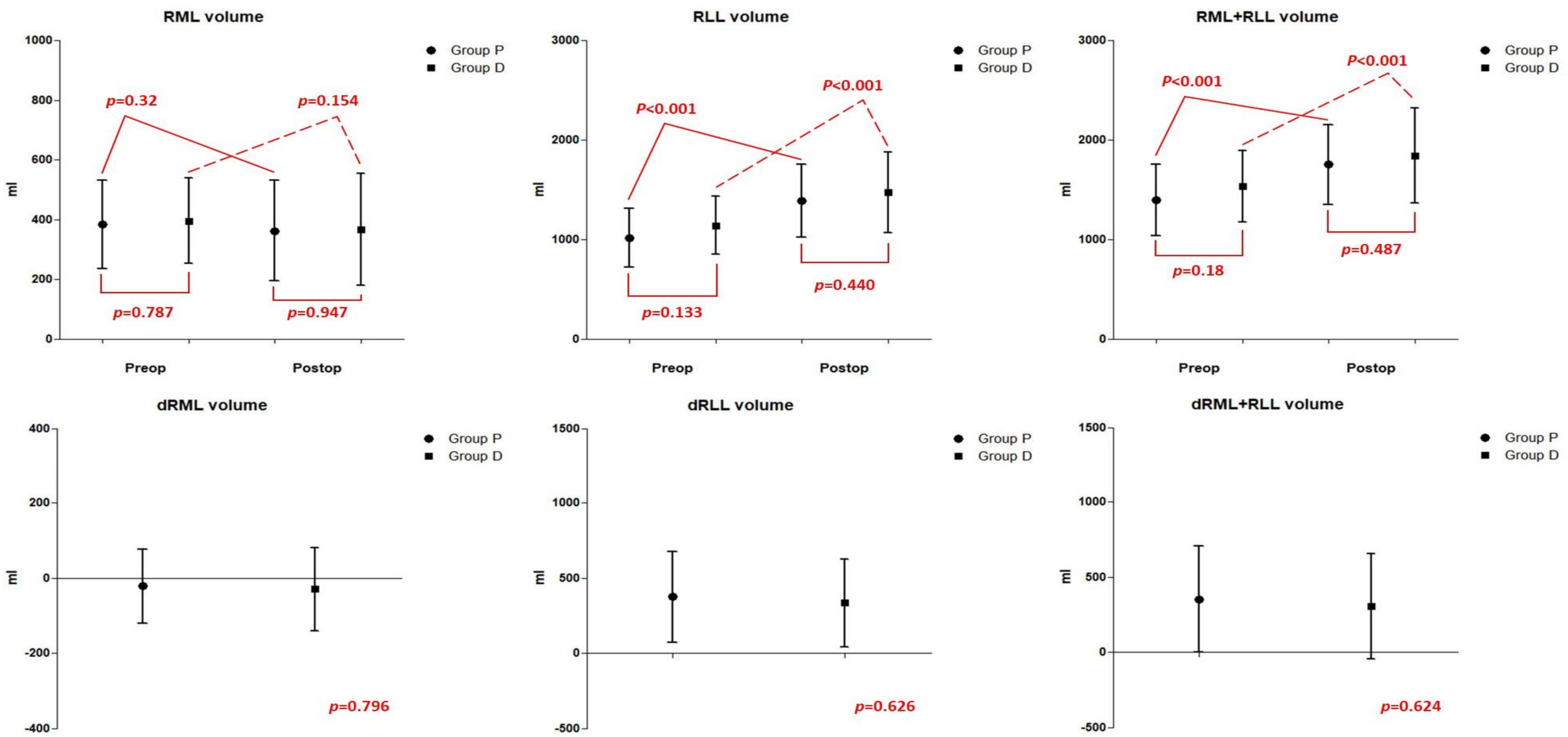
Postoperatively, RLL volume was increased significantly in each groups ($p<0.001$ in both groups). However, RML volume was slightly decreased in both group, however, there were no statistical significance (*p*=0.32 in group P, *p*=0.154 in group D). The amount of volume loss before and after the operation was calculated, however, there were no differences between two groups. Differences of RML volume was revealed as -21±99 ml in group P and -29±111 ml in group D (*p*=0.796), and differences of expanded RLL volume was found as 375±303 ml in group P and 335±294 ml in group D (*p*=0.626). Differences of sum of RML and RLL volume was 354±354 ml in group P and 306±350 ml in group D (*p*=0.624). These findings are summarized in table 2 and figure 3.

Table 2. Measured perioperative lung volumes in each lobes

	Preservation group (n=22)	Division group (n=31)	*p* value
Preoperative (ml)			
RUL	835±241	906±186	0.233
RML	385±149	396±144	0.787
RLL	1018±296	1143±292	0.133
RML+RLL	1403±358	1538±358	0.18
Whole lung	2237±511	2444±445	0.124
Postoperative (ml)			
RML	363±168	367±188	0.947
RLL	1393±364	1477±402	0.44
RML+RLL	1757±400	1844±478	0.487
Difference (ml)			
RML	-21±99	-29±111	0.796
RLL	375±303	335±294	0.626
RML+RLL	354±354	306±350	0.624
Postoperative whole lung / preoperative whole lung	0.81±0.19	0.75±0.13	0.225

RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe

Figure 3. Measured perioperative lung volumes in each lobes



RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; dRML, difference between pre- and postoperative right middle lobe; dRLL, difference between pre- and postoperative right lower lobe; dRML+RLL, difference between sum of pre- and postoperative right middle lobe and right lower lobe

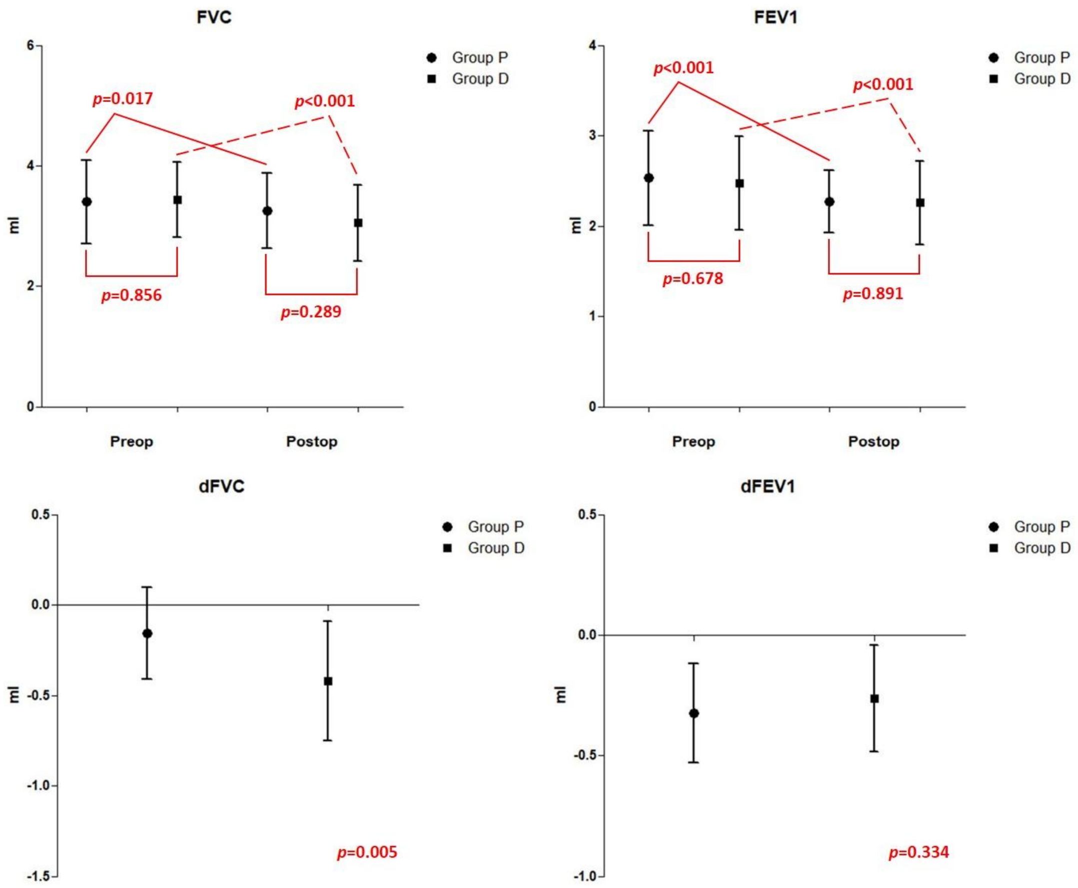
3. Bronchial angle

The measured preoperative angle between RML bronchus and bronchus intermedius is found as 135.8°±7.5° in group P and 136.6°±6.6° in group D (*p*=0.668). These angles significantly decreased after the operation (-26.0°±13.4° in group P (*p*<0.001)and -26.7°±13.6° in group D (*p*<0.001)). The amount of angle change was not different between two groups (*p* = 0.869). Also, there was no difference in postoperative bronchial angle between two groups (109.7°±13.7°vs 109.9°±13.5, *p*=0.954).

4. Pulmonary function tests

Postoperative PFT surveillance was performed except 5 patients. The reasons for missing of PFT were follow-up loss, mortality or morbidity. The preoperative mean values of forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1) in group P were 3.40±0.69 liters and 2.54±0.52 liters, respectively. These values in group D were 3.44±0.62 liters and 2.47±0.52 liters, respectively. There was no significant difference between two groups (p=0.856, 0.678). The postoperative FVC, FEV1 in group P were 3.25±0.63 liters and 2.27±0.34 liters, respectively. And these values in group D were 3.05±0.63 liters and 2.26±0.46 liters, respectively. There were no significant differences between groups in these values (p=0.289, 0.891). However, the amount of postoperative loss of FVC is significantly different between two groups (-0.15±0.26 liters in group P vs. -0.42±0.33 liters in group D, p=0.005). The amount of postoperative decrease of FEV1 is not significantly different (-0.32±0.21 liters in group P vs. -0.26±0.22 liters in group D, p=0.334). These findings are illustrated in figure 4.

Figure 4. Measured pulmonary function test values



FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; dFVC, difference between pre- and postoperative forced vital capacity values; dFEV1, difference between pre- and postoperative forced expiratory volume in 1 second values

Discussion

The preservation of IPL can affect on alteration of the volume, anatomy and function, and we want to analyze these outcomes. However, because of possible theoretical interferences from thoracotomy approach on postoperative changes, we selected the patients who underwent VATS lobectomy only. VATS approach has several advantages over thoracotomy approach such as preservation of pulmonary function, reduced pain and better prognosis [3-5]. Moreover, greater incision and rib fracture or resection usually required during thoracotomy approach. Therefore, chest wall deformity can be more profound, and the movement of chest wall can be more interrupted also when thoracotomy approach is compared to VATS approach. Hence, chest wall compliance and pulmonary function could be more deteriorated during thoracotomy approach [6]. Moreover, pleural adhesion with chest wall can be more intense because thoracotomy requires greater size of incision and has more direct manipulation to pleural surface and visceral organs with the surgeon’s hand and instruments during the procedures. Therefore, pleural irritation and direct contact with greater wound can make the adhesion extensive. In addition, postoperative inflammatory change within lung parenchyme can result in greater incidence of atelectasis or associated loss of pulmonary function and anatomical alteration.

Meanwhile, IPL makes a lower lobe to adhere with the mediastinal structures from diaphragmatic folding inferiorly, to hilar level superiorly, especially inferior pulmonary veins. During the performance of lower lobectomy, division of IPL must be done, however, it is not a routine procedure during upper lobectomy [7,8]. The choice of performing IPL division is mainly based on surgeon's preference. There has been a concern about whether this procedure will provide favorable outcomes with fewer complications.

During the division of IPL, some benefits could be resulted by releasing residual lower lobes. After removal of lung, the cavity, which had been occupied with lung to be removed, is created and has to be filled with remnant structures. Reposition of mediastinal structures toward the side of operation and elevation of diaphragm may count on filling cavity [9]. However, major sources of filling cavity are overexpansion and redistribution of remnant lung in the cavity. Therefore, it has been thought that release of lower lobe from mediastinal adherence can facilitate filling the dead space, theoretically [2].

However, too much relocation of remnant lung may compromise lung function by kinking and obstruction of rearranged bronchus [10,11]. Especially, after RUL lobectomy, superior and posterior reposition of RML can be observed frequently. In some patients, postoperative directional change of middle lobe bronchus might be slightly heavy, therefore, bronchial kinking and atelectasis could be observed. Moreover, these changes could impair the residual pulmonary function [12,13].

Meanwhile, division of IPL and upward movement of residual lobes has benefits, either.

This procedure can reduce dead space after the operation. Enough expansion and reposition can reduce the dead space, however, remaining IPL can interfere the expansion. Dead space is also associated with prolonged need for draining effusion, moreover, there are some risks of infection. Therefore, dead space can make patients to require more times to recover or needs for further intervention.

There have been theoretical debates as mentioned above, however, we could not demonstrate the differences of outcomes about complications such as delayed effusion that requires prolonged hospitalization or frequency of obvious atelectasis between two groups. And any incidence of complications and long term survival was not different also.

Previous report performed by Seok et al in 2015 declared that dissecting IPL during right upper lobectomy can significantly change bronchial angle transversely with minimal benefits [14]. As mentioned above, we compared the angle between RML bronchus and bronchus intermedius three-dimensionally. Because the angle does not located within coronal or horizontal plane strictly, the measurement of angle can’t be taken easily. Moreover, because RML tends to move posterior and superior direction in the same time after RUL lobectomy, just comparing the angle change in two-dimensional plane cannot explain actual complex rearrangement. So, we compared the narrowest angle between these bronchus, and the angle was decreased after lobectomy significantly in all groups. However, there were no differences between two groups divided by performance of IPL division. It is thought that the division of IPL could count on the degrees of angle change and the amount of relocation of RML, however, there might be something that influences more than division of IPL on RML movement. For example, completeness of major fissure, the amount of hilar dissection and mobilization can influence the RML movement also.

However, if the higher resolution and delicate slice of CT had been obtained, more precise angle can be measured. Therefore, more meticulous studies are warranted to explain the different results with previous studies and to get a more information about bronchial angle change.

Bu et al reported about PFT analysis and volume measuring by CT scan previously. There are no differences between two groups divided by division of IPL most of findings. However, the pulmonary capacity and FEV1 were significantly different between two groups after right or left upper lobectomy in that study [15]. Our study was confined in the patients who underwent RUL lobectomy because we thought that volume compromise and atelectasis were mainly found in RML after RUL lobectomy. As seen in result, there were no significant differences between two groups in their volume change of RML, RLL or total lung volume. Meanwhile, RLL volume was significantly increased after the operation in both groups as we thought that it would be overexpanded, however, RML volume did not changed significantly. These finding can be thought as overexpansion of RLL can compress RML not to be overexpanded. Moreover, relative RML bronchial narrowing after rearrangement of RML can impair RML capacity.

We also compared PFT findings, however, we could not find differences except amount of FVC loss. More profound loss of FVC was found in the patients who underwent IPL division and relative lower result of FVC was found also. We thought that loss of FVC can be matched with postoperative proportional volume loss in CT findings. Even though there were no significant differences between two groups, group D has relative greater proportional loss of lung volume. Paradoxically, division of IPL can compromise the expansion capacity of remaining lung after the operation. Meanwhile, this finding could be resulted by atelectasis or dead space. However, because there was no significant difference in number of patients suffering definite atelectasis or dead space on CT scan, it is hard to conclude that the FVC loss is caused by atelectasis or dead space. Nevertheless, we only concluded that the prevalence of dead space, pleural effusion and atelectasis is not different between two groups rather than comparing the amount or severity of complications in this study. Therefore, further studies which investigate about these volumetric information could be helpful. Moreover, analysis about pulmonary capacity in greater patient population could be worthwhile to provide the effect of IPL division on patient's status.

There are other concerns about possibility of proper dissection of mediastinal lymph nodes without IPL division. Though proper dissection of inferior mediastinal node can be achieved without IPL division, some nodes that lies on IPL or paraesophageal nodes can be done only after IPL division. However, lung cancer in RUL rarely metastasize to inferior mediastinal nodes as discussed in earlier studies [16,17].

Moreover, survival detriment was not found in the patients who underwent selective mediastinal lymph node dissection [18]. We also cannot found inferior lymph node metastasis or survival difference in IPL-dissected patients, therefore, we thought that the complete dissection of lower mediastinal lymph node during RUL lobectomy does not effect on cancer related survival.

Conclusions

We conclude that division of IPL does not cause any significant benefits in lung volume or bronchial angle of right middle lobe which is measured in CT. However, division of IPL can compromise functional capacity more. Dissection of IPL is recommended in selected patients. If other useful parameters in PFT (i.e. diffusion capacity of carbon monoxide, residual volume) could be applied in analysis, the obliteration of pulmonary function or the effects of right middle lobe atelectasis after IPL division could be elucidated better. Moreover, review of the symptoms such as long-lasting cough several months after the operation could be valuable information with correlation of the results. However, because this study is conducted as retrospective manner, the clinical symptoms could not be fully obtained accurately. This study also has other limitations because of designed retrospectively, small size of samples within single center, therefore, further investigation is required to analyze detailed information.

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Korean abstracts (국문 요약)

서론: 비록 폐엽 절제술의 상세한 방법이 잘 정립되었으나, 상엽절제술에 있어서 폐간막 절제 여부는 아직 명확하게 정해지지 않았다. 폐간막 절제는 수술 후 폐 상태에 영향을 미칠 수 있기 때문에, 본 논문에서는 폐간막 절제가 해부학적, 잔존 폐 용량 및 기능에 미치는 영향을 분석하고자 하였다.

연구 재료와 연구 방법: 서울아산병원에서 2011년 1월부터 2014년 4월까지, 조기 폐암으로 흉강경하 우상엽 절제술을 시행한 53명 (수술 시 평균 나이 61±9세)를 대상으로 하였다. 환자들 중 흉막 유착이 심하였거나 수술 시 개흉술로 전환이 된 경우는 제외하였다. 환자들은 폐간막의 절제 여부에 따라 두 군으로 나누어졌다; 보존 군 (22명), 절제 군 (31명). 수술 전 및 수술 3에서 6개월 후에 시행한 폐 전산화 단층 촬영 영상(CT)에서 중간 기관지와 우중엽 기관지 사이의 기관지 각도를 측정하였다. 우하엽 및 우중엽의 3차원적인 용량 또한 같은 영상에서 측정되었다. 무기폐, 사강 및 흉수 저류의 유무도 같은 영상에서 조사하였다. 수술 후 약 1년경에 시행한 폐기능 검사도 수술 전과 비교하였다.

결과: 양 군에서 평균 나이는 의미있는 차이를 보이지 않았다. (보존 군, 58.9±9.5세; 절제 군, 62.4±8.5세; p=0.168). 무기폐 (보존 군, 8/22, 36.4%; 절제 군, 11/31, 35.5%; p=0.417), 사강 (보존 군, 2/22, 9.1%; 절제 군, 7/31, 22.6%; p=0.197), 흉수 저류 (보존 군, 9/22, 40.9%; 절제 군, 11/31, 35.5%; p=0.688) 의 빈도는 양 군에서 차이가 없었다. 수술 후 폐 용량도 양 군에서 차이가 없었다 (보존 군, 1757±400 ml; 절제 군, 1844±477 ml; p=0.487). 또한, 기관지의 각도 또한 양 군에서 차이가 없었다 (보존 군, 109.7°±13.7°; 절제 군, 109.9°±13.5; p = 0.954). 수술 후 강제폐활량(FVC), (보존 군, 3.25±0.63 liters; 절제 군, 3.05±0.63 liters ; p=0.289) 및 1초간 강제호기량(FEV1), (보존 군, 2.27±0.34 liters; 절제 군, 2.26±0.46 liters; p=0.891) 에서도 양 군에서 차이를 보이지 않았다. 그러나, 절제 군에서 강제폐활량의 감소가 더욱 뚜렷하였다 (보존 군, -0.16±0.25 liters; 절제 군, -0.42±0.33 liters; p<0.01). 1초간 강제호기량의 감소량은 양 군에서 의미있는 차이가 나타나지 않았다 (보존 군, -0.31±0.2 liters; 절제 군, -0.26±0.22 liters; p=0.475).

고찰 및 결론: 폐간막의 절제는 우상엽 절제술에서 폐 용적 및 기능, 합병증의

빈도에서 의미있는 차이를 보이지 못하였다. 또한 폐간막의 보존은 수술 후 강제 폐활량의 감소량을 줄이는 데 기여할 수 있었다. 따라서 우상엽 절제술에 있어서 폐간막의 절제는 적절히 선택된 환자에서만 시행하여야 할 것으로 보인다.