Original Article

Prolonged air leak after video-assisted thoracic surgery lung cancer resection: risk factors and its effect on postoperative clinical recovery

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Background: Prolonged air leak (PAL) is one of the most common postoperative complications after pulmonary resection. The aim of this study was to reveal the incidence and risk factors of PAL in video-assisted thoracic surgery (VATS) lung cancer resection, and to evaluate the effect of PAL on postoperative complications, postoperative length of stay (PLOS), and medical costs.

Methods: Continuous patients who underwent VATS major pulmonary resection for lung cancer between January 2014 and December 2015 were studied. Clinical data of these patients were obtained from the Western China Lung Cancer Database. PAL was defined as air leak more than 5 days after surgery. The risk factors for PAL were analyzed, as well as the effect of PAL on postoperative clinical recovery.

Results: A total of 1,051 patients were enrolled in this study. The incidence of PAL was 10.6% (111/1,051). Pleural adhesion [odds ratio (OR), 2.38 for extensive *vs*. none, P=0.001] was identified as the only independent risk factors for PAL through multivariate analysis. The incidence of overall complications and pneumonia were significantly higher in patients with PAL (PAL group) than those without PAL (non-PAL group) (OR, 6.77, P=0.000; OR, 2.41, P=0.010, respectively). PAL was found to be associated with longer PLOS (11.7±6.6 *vs*. 6.5±3.6 days; P=0.000) and higher medical costs (¥62,042.5±18,072.0 *vs*. ¥52,291.3±13,845.5, P=0.000).

Conclusions: Pleural adhesion was associated with increased risk of PAL after VATS lung cancer resection. Those patients with PAL had more postoperative complications, stayed longer in the hospital after surgery, and paid higher medical costs.

Keywords: Prolonged air leak (PAL); thoracic surgery, video-assisted; risk factors; length of stay (LOS); medical costs

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Introduction

Prolonged air leak (PAL) is one of the major postoperative complications after lung surgery (1). According to previous studies, the incidence of PAL was approximately 10% (2,3). Several risk factors of PAL have been identified, including age, body mass index (BMI), surgeons and surgical site (4,5). Patients with PAL were also prone to have longer drainage time and higher incidence of postoperative complications (6-8). Therefore, those patients would have a prolonged length of stay (LOS) and increased medical costs than the

patients without any postoperative complications (3).

Most of the previous studies on PAL were based on the data of patients underwent open thoracotomy (2-4). It is widely accepted that video-assisted thoracoscopic surgery (VATS) has shown tremendous advantages in lung surgery. Mountain evidence revealed that VATS had equivalent long term outcomes, less trauma, faster postoperative recovery and lower incidence of postoperative complications when comparing with open thoracotomy (9,10). Nowadays, VATS is becoming the more preferred approach for surgical treatment of lung diseases, especially in lung cancer surgery. However, there are still few studies on PAL after VATS lung cancer resection. We aimed to reveal the incidence and risk factors of PAL in lung cancer patients who underwent VATS major pulmonary resection, and to assess its effect on postoperative clinical recovery, including postoperative complications, postoperative length of stay (PLOS), and medical costs.

Methods

Patients

This study is a review of the Western China Lung Cancer Database which was established in late 2011, and prospectively collecting clinical data of lung cancer patients who underwent surgery in the Department of Thoracic Surgery, West China Hospital, Sichuan University, Chengdu, China. Continuous patients who underwent VATS major pulmonary resection for lung cancer between January 2014 and December 2015 were studied. Patients who underwent wedge resection or pneumonectomy were excluded. Clinical data of those enrolled patients were obtained from the Western China Lung Cancer Database. The Institutional Review Board (IRB) of West China Hospital approved the use of these data (No. 2016-98). Patient's informed consent was waived for this study.

Surgical technique

VATS lobectomy in our center was carried out with the "single-direction" technique as we previously described (11), which is also known as a "fissure-last" technique. Systematic nodal dissection was accomplished using the "non-grasping" method for all the patients (12). Finally, a 28 Fr chest tube was placed through the thoracoscopic port. The tube was removed when chest drainage was less than 300 mL per 24 hrs without any air leak, and complete re-expansion of the residual lung.

For patients with pleural adhesions, especially for those with complete pleural symphysis, adhesiolysis was carried out by constructing tunnels (13). Pleural adhesions were divided into three groups during surgery: (I) none pleural adhesion: without any adhesion; (II) minimal pleural adhesion: adhesiolysis within 30 minutes; and (III) extensive pleural adhesion: adhesiolysis for 30 minutes or longer.

Variables analyzed

PAL was defined as persistent air leak for more than 5 days after surgery. Baseline clinical parameters, including age, gender, smoking history, preoperative respiratory comorbidities, histological type, TNM stage, fissure development, pleural adhesion, surgical procedure, surgical site, and surgeon's background, were analyzed for the risk factors of PAL. Surgeons were divided into two groups according to their background: (I) mainly focusing on lung and mediastinum diseases; (II) mainly focusing on esophageal diseases. Incidence of postoperative complications, PLOS and medical costs were analyzed to reveal the effect of PAL on patients' clinical recovery. We mainly focused on postoperative respiratory and circulatory complications in this study, including pulmonary atelectasis, pneumonia, empyema, bronchopleural fistula, respiratory failure, pulmonary embolism, deep venous thrombosis, myocardial infarction, arrhythmia and heart failure. We also paid attention to urinary tract infection, unplanned reoperation after surgery and perioperative death (within 30 days after surgery).

Statistical analysis

Categorical variables were analyzed using χ^2-test. The quantitative continuous variables were compared using the Student's *t*-test or Mann-Whitney U test. All were two-tailed tests with the level of significance set at 0.05. Logistic regression was further performed to identify the risk factors of PAL out of the variables that were significant in univariate analyses. Odds ratio (OR) and 95% confidence interval (CI) were estimated using logistic regression. Unstandardized coefficients were estimated using linear regression analysis model. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) Version 22.0 for windows (Armonk, NY, USA: IBM Corp.).

Results

Patient characteristics

From January 2014 to December 2015, 1,175 continuous patients who underwent VATS pulmonary resection for lung cancer were identified from the Western China Lung Cancer Database. Among these patients, 190 of them were excluded, including 118 cases of wedge resection, 6 cases of pneumonectomy. Ultimately, a total of 1,051 patients were enrolled in this study. The patients were divided into two groups based on the absence or presence of PAL. Characteristics of these patients were listed in *Table 1*. The incidence of PAL was 10.6% (111/1,051). Ninety-four patients had preoperative respiratory comorbidities, of whom 16 (17.0%) had PAL. Among the 841 patients who had lung adenocarcinoma, 92 (10.9%) had PAL. The most common surgical procedure was lobectomy (n=886, 81.4%). And 99 of the patients (11.2%) who underwent VATS lobectomy had PAL after surgery.

Risk factors for PAL

Gender (P=0.002), smoking history (P=0.016), preoperative respiratory comorbidities (P=0.033) and pleural adhesion (P=0.001) were identified as potential risk factors for PAL through univariate analysis (*Table 1*). Further multivariate analysis confirmed that pleural adhesion (P=0.004) was the only independent risk factor for PAL (*Table 2*). The incidence of PAL was significantly higher in patients with extensive pleural adhesion than the patients without pleural adhesion (17.3% *vs.* 7.6%; OR, 2.38; 95% CI: 1.43 to 3.95; P=0.001).

The effect of PAL on postoperative complications

Two hundred and ten (20.0%) patients presented with postoperative complications other than PAL. One died during the perioperative period. Fifty-seven (5.4%) patients had postoperative pneumonia (*Table 3*). The incidence of postoperative complications and postoperative pneumonia were 55.9% and 10.8% in PAL group, while 15.7% and 4.8% in non-PAL group, respectively. PAL was associated with higher risk of postoperative complications (OR, 6.77, 95% CI: 4.48 to 10.24; P=0.000) and postoperative pneumonia (OR, 2.41, 95% CI: 1.23 to 4.71; P=0.010). The incidence of other postoperative complications between PAL group and non-PAL group were insignificant.

The effect of PAL on PLOS and medical costs

The PLOS was significantly extended in PAL group than the non-PAL group (11.7±6.6 *vs.* 6.5±3.6 days; P=0.000). Total medical cost was 15.7% higher in the PAL group than non-PAL group (¥62,042.5±18,072.0 *vs.* ¥52,291.3±13,845.5, P=0.000) (*Table 4*).

Discussion

PAL is one of the most common postoperative complications in patients who underwent pulmonary resection, and it may affect the patient's postoperative clinical recovery. The definition of PAL is divergent in different studies. The two most popular definitions of PAL are air leak >5 or ≥7 days after surgery (2,5,14,15). Current opinion prefers to consider an air leak as prolonged if it increased the length of an otherwise uncomplicated postoperative hospitalization (14). With the development of fast track surgery, the average PLOS of the patients who underwent lobectomy has been reduced to about 5 days (16). Therefore, we defined PAL as air leak more than 5 days after surgery. And the incidence of PAL with this definition is approximately 10% (2,3), which is consistent with our observation (10.6%).

A number of studies have assessed the risk factors of PAL. Male patients (5,17), patients with preoperative pulmonary dysfunction (such as emphysema and COPD) (8,18,19), pleural adhesion and less developed fissure (14,20) were prone to have PAL. The operation performed by different surgeons would also affect the incidence of PAL (4). In addition to the studies for the risk factors of PAL, a considerable number of studies have reported the postoperative effects of PAL. Patients with PAL were more likely to concurrent with pneumonia, empyema and other postoperative complications (3,4,7,17). However, most of the previous studies were based on the data of open thoracotomy, and the studied population included the patients with various pulmonary diseases. Lung cancer is the most common cancer-related deaths worldwide, and VATS is becoming the most popular surgical approach for lung cancer treatment. In this study, we focused on the risk factors of PAL and its effect on postoperative clinical recovery for lung cancer patients who underwent VATS major pulmonary resection.

Incomplete fissure was considered to increase the risk of PAL. However, our data showed that this is not an

Table 1 Characteristics of patients based on absence or presence of prolonged air leak (N=1,051)

Characteristics	n	PAL		Non-PAL		P
		No.	%	No.	%	
Age						0.410
≤60	569	56	50.5	513	54.6	
>60	482	55	49.5	427	45.4	
Median [range]	59 [17–84]	60 [24–79]		59 [17–84]		
Gender						0.002
Male	519	70	63.1	449	47.8	
Female	532	41	36.9	491	52.2	
Smoking history						0.016
Nonsmoker	641	56	50.5	585	62.2	
Smoker/former smoker	410	55	49.5	355	37.8	
Preoperative respiratory complications						0.033
N	957	95	85.6	862	91.7	
Y	94	16	14.4	78	8.3	
Histological type						0.122
Adenocarcinoma	841	90	81.1	749	79.7	
Squamous carcinoma	124	16	14.4	107	11.4	
Others	86	5	4.5	84	8.9	
TNM stage						0.481
0	26	1	0.9	25	2.7	
I	726	76	68.5	650	69.1	
II	128	13	11.7	115	12.2	
III	138	19	17.1	119	12.7	
IV	33	2	1.8	31	3.3	
Fissure development						0.725
Undeveloped	34	5	4.5	29	3.1	
Not fully developed	684	71	64.0	613	65.2	
Well developed	333	35	31.5	298	31.7	
Pleural adhesions						0.001
None	540	41	36.9	499	53.1	
Minimal	326	38	34.2	288	30.6	
Extensive	185	32	28.8	153	16.3	
Sub-professional group						0.318
Lung and mediastinum	743	83	74.8	660	70.2	
Esophagus	308	28	25.2	280	29.8	

Table 1 (*continued*)

Table 1 (*continued*)

Characteristics	n	PAL		Non-PAL		P
		No.	%	No.	%	
Surgical approach						0.059
Lobectomy	886	99	89.2	787	83.7	
Segmentectomy	135	7	6.3	128	13.6	
Sleeve lobectomy	30	5	4.5	25	2.7	
Surgical site						0.729
Right upper lobe	329	36	32.4	293	31.2	
Right middle lobe	121	10	9.0	111	11.8	
Right lower lobe	201	24	21.6	177	18.8	
Left upper lobe	236	27	24.3	209	22.2	
Left lower lobe	164	14	12.6	150	16.0	

PAL, prolonged air leak; VATS, video-assisted thoracoscopic surgery.

Table 2 Multivariate logistic-regression analysis of risk factors of prolonged air leak

Variables	Categories	OR (95% CI)	P
Gender	Female	Ref	0.083
	Male	1.69 (0.93 to 3.05)	
Smoking history	Nonsmoker	Ref	0.885
	Smoker/former smoker	1.05 (0.58 to 1.89)	
Preoperative respiratory complications	N	Ref	0.181
	Y	1.50 (0.83 to 2.73)	
Pleural adhesions	None	Ref	0.004
	Mild	1.54 (0.96 to 2.47)	0.072
	Extensive	2.38 (1.43 to 3.95)	0.001

OR, odds ratio; CI, confidence interval.

Table 3 Morbidity of postoperative complications according to absence or presence of prolonged air leak (N=1,051)

Postoperative complications	n	PAL		Non-PAL		P
		No.	%	No.	%	
Postoperative complications overall						0.000
Y	210	62	55.9	148	15.7	
N	841	49	44.1	792	84.3	
Postoperative pneumonia						0.010
Y	57	12	10.8	45	4.8	
N	994	99	89.2	895	95.2	

PAL, prolonged air leak.

Table 4 Postoperative length of stay and hospital cost according to absence or presence of prolonged air leak

Events	PAL		Non-PAL		B	P
	Mean	SD	Mean	SD		
PLOS	11.7	6.6	6.5	3.6	5.14	0.000
Medical cost	62,042.5	18,072.0	52,291.3	13,845.5	9,751.19	0.000

PAL, prolonged air leak; PLOS, postoperative length of stay; B, unstandardized coefficient; CI, confidence interval; SD, standard deviation.

independent risk factor for PAL in this group of patients. This may be due to the "single-direction/fissure last" surgical technique, which divided the lung parenchyma lastly during surgery and avoided to mobilize the pulmonary artery through the lung fissures (11). Stamenovic and his colleagues have reported that the fissure last VATS lobectomy appears to be a superior technique to conventional VATS lobectomy in terms of preventing PAL (21). Based on our data, we also believe that the "single-direction" procedure may reduce the risk of air leak after surgery.

Okereke and his colleagues have demonstrated that different surgeons would also affect the incidence of PAL (4). We further analyzed whether the difference was associated with surgeons' background. The surgeons were divided into two groups according to their background, one is mainly focusing on lung and mediastinum diseases, the others are mainly focusing on esophageal diseases. However, the occurrence of PAL between the two groups of surgeons was the same. With standardized training, surgeon's background is not a risk factor of PAL.

Gender, smoking history and preoperative respiratory comorbidities were statistically significant in the univariate analysis, but these factors were not identified as independent risk factors in further multivariate analysis. The only risk factor of PAL in this group of patients was pleural adhesion. For the patients with pleural adhesion, especially for those with extensive adhesion, it is difficult to avoid lung parenchyma damage during adhesiolysis. And this would directly lead to the occurrence of air leak.

When studying the effect of PAL on postoperative clinical recovery, we found that the incidence of pneumonia and total complications was significantly higher in patients with PAL than those without. PAL has been found to increase various cardio-pulmonary complications in previous studies (3,4). We further compared the PAL group with non-PAL group on PLOS and medical costs. PAL prolonged PLOS and increased medical costs; this is because PAL patients require longer time of drainage, which may cause other insidious costs. On the other hand, PAL increased other complications, which may also prolong PLOS and increase medical costs. Varela and his colleagues have shown that PAL can lead to an increase of PLOS and medical costs, and giving the first detailed number of increased medical costs (3). We confirmed their findings and given the increased medical costs in China.

In this study, we firstly showed the risk factors and the postoperative effect of PAL in lung cancer patients who underwent VATS resection. In addition, the database we used has a rather larger sample size until now. Nonetheless, several limitations exist in this study. First, this is a review of a prospective database which allows the possibility of unobserved and therefore uncontrolled confounding factors. Thus, prospective multicenter observational studies are encouraged to acquire more detailed data. Second, the data of pulmonary function test and BMI was unavailable in some patients, and this limited our further study on analyzing some potential risk factors.

Conclusions

Intraoperative pleural adhesion could increase the risk of PAL. Lung cancer patients who had PAL after VATS had more postoperative complications, longer PLOS and higher medical cost.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by the Institutional Review Board of West China Hospital (No.

2016-98). Informed consent was waived for this study.

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