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Original Article

Preoperative Smoking Cessation Period Is Not Related to Postoperative Respiratory Complications in Patients Undergoing Lung Cancer Surgery

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Purpose: Smoking is reported to be a risk factor for postoperative complications. However, there is no consensus regarding the length of time for which patients need to give up smoking. Therefore, we examined the relationship between preoperative smoking status and postoperative complications in patients who underwent lobectomy for treatment of lung cancer.

Methods: Between January 2009 and December 2014, 1380 patients underwent lobectomy for lung cancer at our institution. After excluding patients who had undergone induction therapy, 1248 patients were enrolled in this study. We examined the relationship between postoperative complications and preoperative smoking habitation.

Results: Among the enrolled patients, 1210 (97%) underwent video-assisted thoracoscopic lobectomy and 38 (3%) underwent lobectomy via open thoracotomy. The incidence of postoperative complications was higher in smokers than in nonsmokers, and the frequency of respiratory-related complications increased along with the number of pack-years. However, there was no relationship between the length of the preoperative smoking cessation period and the frequency of postoperative complications.

Conclusion: The risk of postoperative complications does not increase even if smoking is continued within 2 weeks before surgery. It seems unnecessary to delay the timing of surgery to allow patients to cease smoking, especially those scheduled for thoracoscopic surgery.

Keywords: smoking, cessation, postoperative complications

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Introduction

Smoking is well known to be a major cause of lung cancer and a risk factor for postoperative complications.[1–5] Continuation of smoking increases the likelihood of postoperative recurrence and reduces the postoperative survival rate.[6–8] Therefore, smoking cessation is necessary for patients who are being treated for lung cancer. Because smoking is reported to be associated with postoperative complications, giving up smoking before surgery has been advocated, and some authors and guidelines have recommended abstinence from

tobacco for at least 2–4 weeks prior to surgery.[2,3] However, there is no definite consensus about the period of preoperative smoking cessation and whether or not surgery needs to be postponed until the patient ceases smoking. As patients who may undergo resection need to do so as quickly as is feasible, the impact of smoking cessation in the preoperative period on postoperative complications is an important issue. To investigate the effect of preoperative smoking cessation on postoperative complications, we examined the relationship between preoperative smoking status and postoperative complications in patients who underwent lobectomy for treatment of lung cancer at our institution.

Patients and Methods

Between January 2009 and December 2014, 1380 patients underwent lobectomy for lung cancer at our institution. To eliminate differences in the frequency of postoperative complications due to the surgical procedure or induction therapy, we investigated only patients who had undergone lobectomy, and the patients who received induction chemotherapy or chemo-radiotherapy were excluded from this study. Therefore, 1248 patients were enrolled. We reviewed their medical charts and examined the relationship between postoperative complications and preoperative smoking habitation retrospectively.

Before the operation, physical examination, hematological and biochemical tests, electrocardiograms, chest radiographs, magnetic resonance imaging of brain, and computed tomography of the chest and abdomen were performed. Pulmonary function tests were routinely performed for all patients. However, measurement of carbon monoxide diffusion capacity (DL_{CO}) was not performed in all patients. Perioperative management was underwent using a critical path approach in all cases. Basically, the anesthetic, antibiotic, and analgesic agents were almost the same throughout the study period. Preoperative respiratory rehabilitation was not performed during this study period.

Among the 1248 patients, 819 were men and 429 were women, with an average age of 69.6 years; 1210 (97%) underwent video-assisted thoracoscopic lobectomy and only 38 (3%) underwent lobectomy via open thoracotomy. For video-assisted thoracoscopic surgery (VATS), all surgical procedures were performed through three ports while viewing the monitor via the thoracoscope. Mechanical wound retractor was not used. For open thoracotomy, postero-lateral thoracotomy was performed mainly.

For one patient, there was no description of smoking history on the medical chart. The preoperative smoking cessation period was not described in the medical record in five patients, and thus could not be confirmed. Smoking status was determined using questionnaires before surgery. Smoking intensity was defined in terms of pack-years. Past smokers were defined as patients who had quit smoking for more than 2 months before surgery, and patients who had smoked within 2 months before surgery were defined as current smokers.

We extracted postoperative complications that occurred during postoperative hospitalization or within 1 month after surgery. Postoperative complications are classified according to Common Terminology Criteria for Adverse Events (CTCAE) ver.4.

The Institutional Review Board approved this retrospective study. The need for subsequent individual consent from patients whose records were evaluated was waived because the individuals were not identified in this study.

Statistical analysis

Categorical data and continuous data were compared by Chi-squared test and Mann–Whitney U-test, respectively. Univariate and multivariate analyses were performed using the logistic regression analysis. Differences at $p < 0.05$ were considered to be significant. Statistical analysis was performed using the StatView 5.0 software package (SAS Institute Inc., Cary, NC, USA).

Results

Among the 1247 patients with a known smoking history (smoking history was unknown in one patients), 406 were never smokers and 841 were smokers. The pack-year data for smokers were as follows: 1–9: 39 patients, 10–29: 133 patients, and 30 and above: 669 patients. Among smokers, the preoperative smoking cessation period was 2 months or less in 331, 2 months to 2 years in 46, 2–10 years in 203, and more than 10 years in 256 (preoperative non-smoking period was unknown in five patients). Patients' characteristics in terms of pack-years (0, 1–9, 10–29, over 30) and preoperative smoking cessation periods (never, under 2 months, from 2 months to 10 years, over 10 years) are presented in **Table 1**.

Postoperative complications are described in **Table 2**. CTCAE Grade 2≤ complications during hospitalization or within 1 month after surgery occurred in 315 cases

Table 1 Patients' characteristics in terms of pack-year index and smoking cessation periods

	Pack-year index			
	0	1–9	10–29	30≤
Male/female	59/347	24/15	104/29	631/38
Age (year)	69.0 ± 10.1	68.1 ± 12.3	67.4 ± 11.5	70.5 ± 8.1
BMI (kg/m^2)	22.6 ± 3.4	22.3 ± 3.1	22.1 ± 3.0	22.7 ± 3.4
%FEV1 (%)	116.0 ± 21.6	111.6 ± 22.3	104.9 ± 20.4	96.4 ± 21.2
FEV1/FVC (%)	77.8 ± 7.3	77.8 ± 5.8	75.2 ± 9.7	69.4 ± 11.0

	Smoking history and smoking cessation periods			
	Never	<2 months	2 months–10 years	10 years≤
Male/female	59/347	287/42	226/24	241/16
age (year)	69.0 ± 10.1	67.2 ± 9.9	70.1 ± 8.1	73.2 ± 8.1
pack-years	0	54.2 ± 28.1	58.6 ± 33.3	39.4 ± 27.0
BMI (kg/m^2)	22.6 ± 3.4	21.8 ± 3.3	23.1 ± 3.6	22.9 ± 3.0
%FEV1 (%)	116.0 ± 21.6	94.8 ± 19.6	97.7 ± 23.3	103.9 ± 21.3
FEV1/FVC (%)	77.8 ± 7.3	70.2 ± 11.1	70.2 ± 11.3	72.0 ± 10.5

BMI: body mass index; %FEV1: percentage of predicted forced expiratory volume in one second; FEV1: forced expiratory volume in one second; FVC: forced vital capacity

Table 2 Postoperative respiratory and non-respiratory complications

Respiratory complications	G2	G3	G4	G5	Total
Air leak >7days	177	2			179
Pneumonia		21		1	22
Atelectasis	19				19
Hypoxia	14				14
Empyema/pleuritis	1	9		1	11
Interstitial pneumonitis		6		4	10
Respiratory failure/mechanical ventilation >24h	4	1			5
Pulmonary edema	4				4
Asthma attack	1				1
Bronchitis	1				1
Total					245 (19.6%)

Non-respiratory complications	G2	G3	G4	G5	Total
Atrial fibrillation	31				31
Delirium	26				26
Chylothorax	15	3			18
Bleeding (reoperation)		8			8
Bronchial fistula		4	1	1	6
Cerebral infarction		3			3
Urinary tract infection	1	2			3
Lung herniation		2			2
Gastric dyskinesia	3				3
Sepsis			2		2
Angina		2			2
Heart failure	1	1			2
Gastric ulcer	1	1			2
Middle lobe rotation		1			1
Transient ischemic attack	2				2
Others (*)	5	4			9

Others (*): liver abscess, liver dysfunction, diaphragm herniation, acute lower limb arterial occlusion, ventricular tachycardia, urinary bladder rupture, recurrent nerve palsy, wound infection, intravenous route infection.

Table 3 Univariate analysis: risk factors for postoperative respiratory-related complications

		Factors	OR	95% CI	p
Age	≤59 yr	60–69 yr	2.941	1.523–5.683	0.0013
		70–79 yr	3.839	2.002–7.358	<0.0001
		80 yr ≤	4.780	2.387–9.562	<0.0001
Sex	Female	Male	2.997	2.099–4.283	<0.0001
Surgical procedure	VATS	Thoracotomy	1.498	0.717–3.130	0.2822
%FEV1	80% ≤	<80%	2.191	1.538–3.126	<0.0001
FEV1/FVC	70% ≤	<70%	2.219	1.597–2.841	<0.0001
BMI	Normal	Low (<18.5 kg/m^2)	1.699	1.128–2.560	0.0112
		High (25 kg/m^2≤)	0.696	0.474–1.022	0.0639
Intraoperative bleeding volume	<110 g	110 g ≤	2.475	1.833–3.340	<0.0001
Operation time	<120 min	120 min ≤	2.039	1.535–2.711	<0.0001
Smoking status	Never	Current (<2 mo)	2.838	1.869–4.308	<0.0001
		Ex (2 mo ≤)	3.096	2.104–4.555	<0.0001
Smoking volume (pack-years)	0	1–9	1.711	0.674–4.341	0.2579
		10–29	2.178	1.261–3.765	0.0052
		30 ≤	3.257	2.245–4.728	<0.0001
Smoking cessation period	Current (<2 mo)	2 mo–10 yr	1.194	0.663–1.419	0.8790
		10 yr ≤	0.970	0.810–1.760	0.3609

BMI: body mass index; CI: confidence interval; %FEV1: percentage of predicted forced expiratory volume in one second; FEV1/FVC: forced expiratory volume in one second divided by forced vital capacity; mo: months; OR: odd ratio; VATS: video-assisted thoracoscopic surgery; yr: years

(25.2%), and respiratory-related complications occurred in 245 cases (19.6%).

Univariate analysis of risk factors for postoperative respiratory complications demonstrated that smoking history, number of pack-years, age, gender, percentage of predicted forced expiratory volume in one second (%FEV1), forced expiratory volume in one second divided by forced vital capacity (FEV1/FVC), body mass index (BMI), intraoperative blood loss, and operation time were significant risk factors (**Table 3**). The incidence of postoperative respiratory complications was significantly increased in smokers relative to non-smokers, and the incidence of respiratory-related complications increased along with the number of pack-years. However, there was no relationship between the length of the preoperative smoking cessation period and respiratory-related complications. Multivariate analysis demonstrated that higher age, insufficient pulmonary function (low FEV1/FVC), low BMI, excessive intraoperative blood loss, and longer operation time were independent and significant risk factors for postoperative respiratory-related complications (**Table 4**). Multivariate analysis showed that the pack-year index was not a significant risk factor for postoperative respiratory-related complications.

Because the present survey was based on statements from patients at their first visit or admission to hospital, there was a degree of ambiguity regarding the accuracy of the preoperative smoking cessation period. However, 114 patients clearly confirmed that they had smoked within 2 weeks before surgery because they continued smoking until outpatient visit or hospitalization. Even when these 114 patients were compared with the long-term smoking cessation group, no significant difference in the incidence of postoperative respiratory-related complications was found (**Table 5**).

Discussion

Because smoking is reported to be a risk factor for postoperative complications, smoking cessation before surgery is recommended.[2,3] Many reports have indicated that smokers are at high risk of postoperative complications, and several reports have demonstrated that preoperative smoking cessation is effective for reducing

Table 4 Multivariate analysis: risk factors for postoperative respiratory-related complications

		Factors	OR	95% CI	p
Age	≤59 yr	60–69 yr	2.834	1.403–5.730	0.0037
		70–79 yr	3.541	1.767–7.105	0.0004
		80 yr ≤	4.307	2.049–9.050	0.0001
Sex	Female	Male	1.545	0.892–2.675	0.1195
Smoking volume (pack-years)	0	1–9	1.359	0.498–3.708	0.5486
		10–29	1.397	0.713–2.735	0.3297
		30 <	1.661	0.931–2.960	0.0850
FEV1/FVC	70% ≤	<70%	1.499	1.091–2.060	0.0124
BMI	Normal	Low (<18.5 kg/m^2)	2.026	1.298–3.161	0.0018
		High (25 kg/m^2 ≤)	0.655	0.439–0.977	0.0382
Intraoperative bleeding volume	<110 g	110 g ≤	1.682	1.184–2.389	0.0037
Operation time	<120 min	120 min ≤	1.474	1.054–2.061	0.0230

BMI: body mass index; CI: confidence interval; FEV1/FVC: forced expiratory volume in one second divided by forced vital capacity; OR: odds ratio; yr: years

Table 5 Postoperative complications according to preoperative smoking cessation period (comparison of smoking cessation period within 2 weeks group versus long-term smoking cessation group)

	Smoking cessation periods	OR	95% CI	p
G2 ≤ complications	≤2 wk	1		
	2 mo–10 yr	1.455	0.881–2.403	0.1436
	10 yr ≤	1.136	0.684–1.888	0.6217
G3 ≤ complications	≤2 wk	1		
	2 mo–10 yr	1.635	0.642–4.166	0.3030
	10 yr ≤	1.343	0.518–3.482	0.5435
Respiratory-related complications	≤2 wk	1		
	2 mo–10 yr	1.668	0.955–2.917	0.0728
	10 yr ≤	1.355	0.771–2.383	0.2914

CI: confidential interval; G2: grade 2; G3: grade 3; mo: months; OR: odds ratio; wk: weeks; yr: years

the incidence of such complications.[1–3,9–12] However, there has been no consensus regarding the period of preoperative smoking cessation that is effective for reducing the incidence of postoperative complications. Celli et al.[9] reported that quitting smoking immediately before surgery was beneficial, and Kallar et al.[10] suggested that individuals should quit at least several days prior to surgery. However, Lawrence et al.[13] suggested that smoking cessation immediately before surgery did not appear to significantly reduce the risk of postoperative pulmonary complications. Nakagawa et al.[1] demonstrated that preoperative smoking cessation for 4 weeks decreased the frequency of postoperative respiratory complications and recommended smoking cessation for 4 weeks before operation. Nakagawa et al.[1] also demonstrated that preoperative smoking cessation for over 10 weeks decreased the frequency of postoperative respiratory complications into non-smokers' level. Moores et al.[11] maintained that smoking cessation 6–8 weeks prior to surgery was optimal. Mason et al.[2] reported that the longer a patient stopped smoking, the lower the risk of postoperative pulmonary complications became, but they were unable to suggest an optimal duration of smoking cessation. The reduction of postoperative respiratory complications following smoking cessation is thought to be related to physiologic improvement of ciliary function, macrophage activity, and the reduction of sputum production. Because it may take weeks or months for these changes to appear, a considerable amount of time is needed for smoking cessation effects to become apparent.

On the other hand, some studies have suggested that quitting smoking only a few weeks before surgery may lead to an unexpected or paradoxical increase in the rate of postoperative respiratory complications.[3,14] Such an increased risk among those patients who

reduced their consumption of cigarettes close to surgery could be related to nicotine withdrawal. Bluman et al.[3] suggested that short-term withdrawal of cigarette consumption before surgery may be contraindication in patients who already have a high risk of postoperative respiratory complications. Another potential explanation is ineffective sputum removal. Because cigarette smoking is associated with a decrease in mucociliary clearance combined with the production of more viscous mucus, smokers become more reliant on coughing to remove lung secretions. However, several days after patients have stopped smoking, the volume of sputum may increase temporarily and cough is reduced due to a decrease in smoke-induced irritation. This phenomenon may explain an association between recent smoking cessation and an increase in postoperative pulmonary complications.

In this study, there was no correlation between the preoperative smoking cessation period and the incidence of postoperative respiratory complications. The incidence of such complications did not decrease even in patients who had quit smoking for a long period, and did not increase even in patients with a very short smoking cessation period. Recently, similar to our result, several reports demonstrated that preoperative smoking cessation period does not affect postoperative complications.[5,7,15,16] Groth et al.[17] suggested that improvements in perioperative care including early ambulation and improvements in respiratory therapy could lead to a reduction of postoperative complications. They suggested that increases in the quality of preoperative and postoperative management and surgical procedures had decreased the impact of smoking on the development of postoperative pulmonary complications. The difference between the frequency of postoperative complications due to preoperative smoking cessation in previous reports may have been influenced by developments in perioperative management and differences in the proportion of patients undergoing thoracoscopic surgery. Thoracoscopic surgery is minimally invasive and associated with fewer postoperative respiratory complications than thoracotomy.[18,19] Even in patients with low pulmonary function, both mortality and morbidity have been reported to be reduced in those undergoing VATS compared with those undergoing thoracotomy.[20] Therefore, for thoracoscopic surgery, it may be difficult to demonstrate any reduction effect of preoperative smoking cessation on the incidence of postoperative complications. In the present study, because most patients underwent thoracoscopic surgery, any correlation between the preoperative smoking cessation period and postoperative pulmonary complications may have been obscured. In thoracoscopic surgery, the preventive effect of smoking cessation on postoperative respiratory complications may be reduced. In this study, although univariate analysis showed that the pack-year index was a significant risk factor for postoperative respiratory complications, no significant difference was detected by multivariate analysis. Seok et al.[15] also reported that the pack-year index was not a significant risk factor for postoperative pulmonary complications. With the increase in thoracoscopic surgery and progress in perioperative management, the influence of preoperative smoking on the postoperative complications may decrease.

Although the present study demonstrated no association between preoperative smoking cessation and the incidence of postoperative complications, smoking cessation is important in the treatment of lung cancer because smoking is a prognostic factor for patients with lung cancer.

This study had some limitations. First, smoking volume and the date of quitting smoking were based on declarations from patients, and no objective verification of smoking status was performed by nicotine metabolite testing. Because most smokers tended to report a better smoking status than was actually the case, a possible bias effect due to self-underreporting might have underestimated the true effect. However, in view of the single-institution nature of the database examined, we suspect that the smoking misclassification rate would have been low. Second, in this study, the majority of patients were received thoracoscopic surgery, so it was not possible to compare the duration of smoking cessation periods and postoperative complications between thoracoscopic surgery and thoracotomy. Third, because we analyzed the patients at a single institution retrospectively, a further large-scale prospective study will be necessary to investigate the role of the preoperative smoking cessation period in the surgical treatment of lung cancer.

Conclusions

Although smoking cessation is important in the treatment of lung cancer, we found no increase in the risk of postoperative complications even in patients who had continued to smoke within 2 weeks before surgery. From the results of this study, it seems unnecessary to delay

surgical treatment to allow smoking cessation, especially when thoracoscopic surgery is planned.

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Disclosure Statement

Conflict of interest: none declared.

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