

## Surgical Treatment for Lung Cancer Patients with Poor Pulmonary Function

Kiyoshi Koizumi, MD, Shuji Haraguchi, MD, Tomomi Hirata, MD, Kyoji Hirai, MD, Iwao Mikami, MD, Daisuke Okada, MD, Shigeki Yamagishi, MD, Tetsuo Kawashima, MD, Hiroyasu Kinoshita, MD, Yutaka Enomoto, MD, Yuki Nakajima, MD, and Kazuo Shimizu, MD

**This retrospective study was aimed to review the risk factors of postoperative hospital death in lung cancer patients with poor pulmonary reserves. We performed surgery on 30 lung cancer patients (average age: 71 years) with less than 1.0L of preoperative forced expiratory volume in one second (FEV<sub>1.0</sub><1.0L) between 1982 and 2003. The preoperative FEV<sub>1.0</sub> of these 30 patients was 0.81±0.1L on average. Six of 20 patients who underwent surgery between 1982 and 1997 died during their postoperative hospital stay (hospital death group). Between 1998 and 2003, 10 patients underwent surgery with uneventful postoperative courses. The clinical background was evaluated between the hospital death group (n=6) and the survivor group (n=24). The single-variable analysis of the preoperative conditions of the postoperative hospital death revealed the presence of two or more preoperative concomitant diseases (p<0.001) and a performance status of grade 2 or higher (p=0.005). Peripheral obstructive pneumonia with abscess and chronic pleurisy with adhesion influenced surgery and related to their postoperative hospital death. Whereas, patients with chronic obstructive pulmonary diseases (COPD) tended to show that pulmonary resection resulted in an improvement of pulmonary functions.**

**Conclusion: To achieve better results of surgical treatment for patients with preoperative FEV<sub>1.0</sub><1.0L, patient selection should be required based on precise evaluation of physical conditions and management of infectious diseases. Moreover, we thought that a preoperative performance status of grade 1 or lower, at most one preoperative concomitant disease, and a COPD are desirable for deciding the surgical indication. (Ann Thorac Cardiovasc Surg 2005; 11: 87-92)**

**Key words:** lung cancer surgery, poor pulmonary function, postoperative hospital death, risk factors

### Introduction

The limitation of pulmonary resection regarding pulmonary functions has been advised by many researchers.<sup>1-4)</sup> In particular, the surgical treatment of lung cancer patients with FEV<sub>1.0</sub><1.0L is still a controversial issue, so that the refinement of various surgical approaches and

perioperative care have been investigated.<sup>5-8)</sup> Between 1982 and 2003, we encountered 30 lung cancer patients with preoperative FEV<sub>1.0</sub><1.0L, who were recommended to undergo surgical treatment by a chemotherapist and/or a radiologist because of various physical conditions. However 6 of 20 patients who underwent surgery between 1982 and 1997 died during their postoperative hospital stay. Previous studies indicated that the management of concomitant diseases focusing on infectious diseases, cardiopulmonary care and evaluation of types of ventilatory disturbance are important factors for deciding surgical indication.<sup>8-11)</sup> Between 1998 and 2003, 10 patients underwent surgery under careful management and showed uneventful postoperative courses. Therefore, we recon-

*From Division of Thoracic Surgery, Department of Surgery, Nippon Medical School, Tokyo, Japan*

Received June 10, 2004; accepted for publication October 17, 2004.

Address reprint requests to Kiyoshi Koizumi, MD: Department of Surgery II, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan.

**Table 1. Demographics of patients studied**

n=30 (1982-2003)		
Age	Years	71 (55-84)
Gender	Male/female	(15/15)
Performance status	(0/1/2/3/4)	(3/18/7/2/0)
Hugh-Jones dyspnea score	(I/II/III/IV/V)	(8/15/5/2/0)
Brinkman index	Tobaccos/day x years	1038 (0-3000)
Pathological stage	IA/IB/IIA/IIB/IIIA/IIIB	(5/7/1/10/5/2/0)
Histological type	Sq/Ad/La/Sm	(12/16/1/1)
Preoperative pulmonary function		
FEV <sub>1.0</sub>	L	0.81 (0.49-0.98)
FEV <sub>1.0</sub> /m <sup>2</sup>	L	0.56 (0.37-0.76)
%FEV <sub>1.0</sub>	%	44 (23-68)
%VC	%	71 (40-88)
FEV <sub>1.0</sub> (%)	%	45 (26-73)

%VC, percent vital capacity; FEV<sub>1.0</sub>, forced expiratory volume in one second; Sq, squamous cell carcinoma; Ad, adenocarcinoma; La, large-cell carcinoma; Sm, small-cell carcinoma.

**Table 2. Detail of patients who died during postoperative hospital stay (1982-1997)**

Case	Age	Gender	Concomitant disease	Approach	Surgery	BL	DOS	P/O days	Cause of death
Case 1	72	Female	OMI, lung abscess	PLT	RM&LL	1730	390	53	Bronchial fistula, pneumonia
Case 2	82	Female	Pulmonary emphysema	PLT	RLL	2570	320	35	Pneumonia
Case 3	65	Female	DM, P/O breast ca, lung abscess, scoliosis	PLT	RU Sleeve L	1780	420	30	Intrabronchial bleeding
Case 4	75	Female	MR, bronchitis	VATS	RS6 Seg	250	160	60	Acute myocardial infarction
Case 5	83	Male	PF, lung abscess, brain infarct	VATS	RLL	1685	325	13	Brain infarct, pneumonia
Case 6	76	Male	Giant bullae	VATS	RS6 & RS2 Seg	350	170	36	Left tension pneumothorax

BL, blood loss; DOS, duration of surgery; P/O days, postoperative days; OMI, old myocardial infarction; DM, diabetes mellitus; P/O Breast ca, postoperation of breast cancer; MR, mitral valve regurgitation; PF, pulmonary fibrosis; PLT, posterolateral thoracotomy; VATS, video-assisted thoracic surgery; RM&LL, right middle and lower lobectomy; RLL, right lower lobectomy; RU sleeve L, right upper sleeve lobectomy; RS6 Seg., right superior-inferior segmentectomy; RS2 Seg., right posterior segmentectomy.

sidered the cause of death, and determined the risk factors in pre-, intra-, and post-operative outcomes.<sup>9,12-14</sup> As for the difference in ventilatory disturbance, several researchers reported that lung cancer surgery itself is as advantageous as lung volume reduction in treating patients with severe pulmonary emphysema.<sup>15-20</sup> Regarding surgical indications for the patients with preoperative FEV<sub>1.0</sub><1.0L, we would like to review the background of the patients and the risk factors that influenced their post-operative hospital death.

## Subjects and Methods

From June 1982 to June 2003, 1070 patients underwent pulmonary resection for primary lung cancer at the Nippon Medical School Hospital. Among them, 30 (15 males and 15 females with a mean age of 71 (range, 55 to 84) underwent pulmonary resection (Table 1). These patients

were classified into two groups: the hospital death group (n=6, Table 2) and the survivor group (n=24). The risk factors for the hospital death group were analyzed in terms of preoperative conditions, surgically related factors and postoperative complications (Table 3). Stage demographics were described according to the TNM classification revised in 1997.

## Surgical technique

A posterolateral thoracotomy (PLT) was performed with a 25-cm-long posterolateral skin incision with the separation of the muscle layer and the partial resection of the fifth rib. A muscle-sparing thoracotomy (MST) was performed with a 15-cm-long lateral skin incision with the partial resection of the fifth rib without the separation of the muscle layer. A video-assisted thoracic surgery (VATS) was performed under a 7-cm-long skin incision on average (range, 4 to 10 cm) with three trocar ports. A median

**Table 3. Preoperative conditions of patients in hospital death and survivor group**

Groups Number	(n)	Deaths (1982-1997) 6	Survivor (1982-2003) 24	Statistics	P value
Age	Years old	75±6	69±7	ns	0.09
Gender	Male / female	(4/2)	(13/11)	ns	0.36
Performance status	(0/ 1/ 2/ 3/ 4)	(1/1/2/2/0)	(2/17/5/0/0)	Significant	0.005
Hugh-Jones score	(I/ II/ III/ IV)	(0/4/1/1/0)	(8/11/4/1/0)	ns	0.31
Brinkman index	Tobaccos / day x years	674±943	1130±822	ns	0.24
Pulmonary function test					
FEV <sub>1.0</sub>	L	0.82±0.18	0.80±0.12	ns	0.82
FEV <sub>1.0</sub> /m <sup>2</sup>	L	0.60±0.15	0.55±0.08	ns	0.31
%FEV <sub>1.0</sub>	%	52±15	42±13	ns	0.1
%VC	%	64±15	73±9	ns	0.06
FEV <sub>1.0</sub> (%)	%	55±15	42±9	Significant	0.01
Concomitant diseases					
Incidence rate	Events / patient	2.5	1.5	Significant	0.038
Respiratory disease		7	17	Significant	0.001
	COPD	3	9		
	Chronic inflammation	2	5		
	Interstitial pneumonia	1	3		
Cardiac disease		2	2	ns	0.114
	Old myocardial infarction	1	1		
	Valvar disease	1	0		
	Arrhythmia	0	1		
Others		6	16	ns	0.578
	P/O for other diseases (cancer)	1 (1)	9 (6)		
	Hepatitis	2	3		
	Renal insufficiency	1	2		
	Diabetes mellitus	1	1		
	Brain infarction	1	1		

The 6 hospital deaths showed a marked deterioration in preoperative performance status. A high incidence of preoperative respiratory diseases was shown in the 6 hospital deaths. %VC, percent vital capacity; FEV<sub>1.0</sub>, forced expiratory volume in one second; %MVV, percent maximal ventilatory volume; COPD, chronic obstructive pulmonary disease; P/O, postoperation.

sternotomy (MS) was employed when necessary to dissect the pulmonary arteries in the pericardium. The bronchus was transected using an endoscopic stapler (Ethicon Endo-Surgery Inc., Cincinnati, OH, USA and U.S. Surgical Corp. Philadelphia, PA, USA).

### Statistical analyses

Analyses were performed using the software package of Stat View 5.0 (SAS Inc., Chicago, IL, USA). The chi-square test was used to analyze nominal data. The mean values were compared using Student's t-test. Performance status was analyzed by the Mann-Whitney rank sum test. Single-variable analyses were conducted to test the risk factors for postoperative hospital death. Survival rate was analyzed using Kaplan-Meier estimated survival curves, and the significance of difference was analyzed by the log-rank test. A *p*-value of less than 0.05 was considered

significant.

### Results

The average age was 75 years (range, 65 to 83) for the hospital death group and 69 years (range, 55 to 84) for the survivor group. Of the 30 patients, nine had a performance status of grade 2 or higher and 22 had Hugh-Jones exertion dyspnea of grade II or higher.<sup>21)</sup> The preoperative FEV<sub>1.0</sub> of 30 patients was 0.81L on average (range, 0.49 to 0.98) (Table 1). Six of the 20 patients who underwent surgery during 1982 and 1997 died during their postoperative hospital stay (Table 2). The remaining 24 patients showed uneventful postoperative courses including 10 patients who underwent surgery during 1998 and 2003.

Preoperative performance status deteriorated in the

**Table 4. Surgically related factors and postoperative complications of patients in the hospital death and survivor group**

Groups Number	(n)	Death (1982-1997) 6	Survivor (1982-2003) 24	Statistics	P value
Surgically related factors					
Side	(Right/Left)	(5/1)	(13/11)	ns	0.19
Approach	(PLT/MST/VATS/MS)	(3/0/3/0)	(12/4/7/1)	ns	0.26
Procedures	(Pn/Lo/PR)	(0/4/2)	(1/18/5)	ns	0.7
Combined resection	Partial resection of ribs	1	6	ns	0.06
Lymphadenectomy	ND1/ND2a	(2/3)	(8/16)	ns	0.71
Duration of surgery	min	297±109	275±90	ns	0.61
Blood loss	ml	919±421	618±455	ns	0.29
Max. serum CPK	IU/L/M <sup>2</sup>	528±275	684±393	ns	0.43
Postoperative complications					
Incidence	Events / patient	2.5	0.6	Significant	<0.001
Respiratory disease		9	13	Significant	0.008
Air leak	7 days or more	0	5		
Atelectasis	Care necessary	1	3		
Pneumonia		3	3		
Pyothorax	Drainage and lavage	1	0		
Tension pneumothorax	Opposite lung	1	0		
Bronchofistula		2	0		
Lung edema		1	1		
Asthma		0	1		
Cardiac disease		4	2	Significant	<0.001
Arrhythmia		2	3		
Myocardial infarction		1	0		
Cardiac insufficiency		1	0		
Others		2	0	Significant	0.003
Renal insufficiency		1	0		
Brain infarction		1	0		

PLT, posterolateral thoracotomy; MST, muscle-sparing thoracotomy; VATS, video-assisted thoracic surgery; MS, median sternotomy; Pn, pneumonectomy; Lo, lobectomy; PR, partial resection; ND, lymphadenectomy; Max. serum CPK, maximal serum creatinine phosphokinase; IU/L/M<sup>2</sup>, international unit/liter/body surface.

hospital death group ( $p < 0.005$ ) (Table 3). Even though no significant differences in the percent vital capacity (% VC), FEV<sub>1.0</sub> and % FEV<sub>1.0</sub> were observed, the FEV<sub>1.0</sub>/VC (FEV<sub>1.0</sub> (%)) ( $P = 0.01$ ) was significantly low in the survivor group compared with the hospital death group (Table 3). Twenty-two (92%) of the 24 survivors showed preoperative FEV<sub>1.0</sub> (%) values 55% or lower of these survivors, 9 had pulmonary emphysema and 5 had bronchial asthma.

Preoperative concomitant diseases were observed at an incidence rate of 2.5 events per patient on average in the hospital death group and 1.5 events per patient in the survivor group (Table 3). The preoperative concomitant diseases frequently observed were respiratory diseases (peripheral obstructive pneumonia with abscess, interstitial pneumonia, bronchial asthma, and bullous pulmonary emphysema) and cardiovascular diseases. The incidence of preoperative respiratory diseases was higher in the

hospital death than in the survivor group. Brain infarction and diabetes mellitus were also concomitant diseases. Ten of the 30 patients underwent other surgeries including seven surgeries treating malignant diseases before the present surgery.

Surgically related factors exhibited no significant differences between the two groups (Table 4). Seven patients had combined resection of the chest wall because of direct invasion with severe pain. A defect on the chest wall was reconstructed with a network using absorbable thread and mesh. One of the 24 survivors underwent left pneumonectomy because of peripheral obstructive pneumonia with a large lung abscess. The patients in the hospital death group tended to have long surgery and massive blood loss due to severe adhesion in the pleural cavity.

The postoperative complications were observed at an incidence rate of 2.5 events per patient on average in the hospital death group and 0.6 events per patient in the sur-

vivor group ( $p < 0.001$ ). Serious respiratory and cardiac complications were observed in the hospital death group, as shown in Table 2.

Single-variable analysis indicated that a preoperative performance status of grade 2 or higher, two or more preoperative concomitant diseases and two or more postoperative complications influence hospital death.

Fourteen of the 24 survivors underwent a postoperative pulmonary function test 2.5 months on average after surgery. In these 14 patients with COPD, the predicted postoperative values were shown to be underestimated for the observed postoperative percent FEV<sub>1.0</sub> and percent maximal ventilatory volume (%MVV), namely  $119 \pm 40\%$  and  $127 \pm 37\%$ , respectively, which were calculated using the following equation: (observed postoperative value / predicted postoperative value)  $\times 100$  (%).

The median follow-up period was 24 months on average (range, 6 to 142) after surgery. The 1- and 5-year survival rates of all the patients were 68 and 32%, respectively. The 5-year survival rate at stage I ( $n=12$ ) was 90%. The 1- and 5-year survival rates at stage II or beyond ( $n=18$ ) were 80 and 0%, respectively.

## Discussion

On the occasion of surgical treatment for an impaired pulmonary function case, a thoracic surgeon must decide the surgical indication after having sufficient evaluation of physical reserves and tumor-related changes of the lungs and pleural cavity. Thus far, we have performed surgical treatment on 30 lung cancer patients with preoperative FEV<sub>1.0</sub>  $< 1.0L$ . This time, we reviewed mainly the causes of the hospital deaths of 6 of the 30 patients.

As for the tumor-related conditions and the changes in the thoracic cavity, in the patient with lung abscess resisting therapy, a surgical approach, instead of chemoradiotherapy by a chemotherapist and a radiologist, was recommended. A thoracic surgeon must decide the surgical procedures after due consideration of the conditions of the thorax, i.e., severe adhesion due to old pleurisy and infection. Cases 1 and 5 were necessary to undergo surgical treatment because of lung abscess, which resisted therapy. Case 2 was suffering from pulmonary emphysema with severe intrapleural adhesion. Long surgery and massive blood loss resulted in severe operation stress for these three patients. Thus, there was a limit to the surgical approach that can be tolerated by these patients considering their clinical conditions. The presence of infection was a problem in the perioperative phase. We recon-

sidered that the deterioration of infection resistance induced by operative stress should be avoided as much as possible.

Reconsideration of a surgical technique is also important to protect postoperative complications. Case 3 had standard radical mastectomy 12 years ago and had received medication for diabetes mellitus. Thirty days after right upper sleeve lobectomy, the patient died of massive hemoptysis. The reinforcement of anastomosis using adjacent tissues should have been performed.

Ischemic heart diseases and the deterioration of hemodynamics are problems in the treatment of patients with poor cardiopulmonary reserves and/or elderly. Generally, we use catecholamine and vasodilator during the perioperative phase for the treatment of elderly patients and/or patients with poor cardiopulmonary functions based on prior studies.<sup>8,10,11</sup> Case 4 underwent limited surgery by VATS. The patient had acute myocardial infarction 60 days after the operation; nevertheless, the patient neither had chest pain nor showed ischemic signs on the preoperative electrocardiogram. Further examination should be performed as in Cases 4 and 6 had bullous pulmonary emphysema of both lungs. The patient underwent limited surgery by VATS. On the 5th postoperative day, the patient suddenly fell into respiratory failure due to tension pneumothorax of the opposite lung. Three of the 6 patients in the hospital death group underwent VATS procedures to minimize operation stress based on prior studies.<sup>9,10,12,13</sup> However, long surgery was the disadvantage of the VATS approach.<sup>14</sup>

In the surgical treatment of a patient with poor pulmonary reserves, the prediction of postoperative pulmonary functions has led to the understanding of the limitation of pulmonary resection for lung cancer patients.<sup>1-4</sup>

The type of ventilatory disturbance is an important factor for deciding the operative procedure. In the present study, the hospital death group had different ventilatory disturbances. In contrast, the patients with COPD revealed the predicted postoperative values to be underestimations of the observed postoperative values, which were reported by several researchers as effects similar to that observed in lung volume reduction surgery for severe pulmonary emphysema.<sup>15-20</sup> Although the patients had different backgrounds, we considered that these suggest the effectiveness of surgery for selected patients even with preoperative FEV<sub>1.0</sub>  $< 1.0L$ .

In this retrospective study, 6 (30%) of 20 patients who underwent lung cancer surgery between 1982 and 1997 died during their postoperative hospital stay. The postop-

erative mortality was too high, so that the reevaluation of preoperative conditions, surgical procedures, postoperative complications, and cause of death has been performed.<sup>9-14)</sup> Between 1998 and 2003, the remaining 10 patients who underwent surgery (i.e., pneumonectomy, 1; lobectomy, 7; and segmentectomy, 2) including combined resection of the chest wall (n=3) showed uneventful postoperative courses.

## Conclusion

To achieve better results of surgical treatment for patients with preoperative FEV<sub>1.0</sub><1.0L, patient selection should be required based on precise evaluation of physical conditions and management of infectious diseases. Moreover, we thought that a preoperative performance status of grade 1 or lower, at most one preoperative concomitant disease, and a COPD are desirable for deciding the surgical indication.

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