Original Article

Surgical Results of Lung Cancer Associated with Postobstructive Pneumonia

Shuji Haraguchi, MD,[1,2] Kiyoshi Koizumi, MD,[1,2] Shigeo Tanimura, MD,[1,2]
Tomomi Hirata, MD,[1,2] Kyoji Hirai, MD,[1,2] Iwao Mikami, MD,[1,2]
Hirotoshi Kubokura, MD,[1,2] and Kazuo Shimizu, MD, FACS, FJCS[2]

Purpose: We report surgical results of lung cancer associated with postobstructive pneumonia.
Materials and Methods: We report on morbidity and mortality, and we analyze the risk factors for them and the prognostic factors for overall survival of patients without mortality.
Results: Morbidity developed in 13 of the 38 patients (34.2%). Mortality rate was 10.5%. Hemoglobin concentration before surgery and predicted postoperative forced expiratory volume in one second were significantly low in patients with morbidity and mortality based on the univariate analyses. Predicted postoperative forced expiratory volume in one second was a significant risk factor for morbidity based on a multivariate analysis. Poor prognostic factors for overall survival were serum albumin concentration, hemoglobin concentration, and performance status before surgery, combined resection, and pathological stage. Serum albumin concentration was significant based on a multivariate analysis.
Conclusions: Morbidity and mortality are high in patients with lung cancer associated with postobstructive pneumonia. Morbidity demonstrates significant association with low predicted postoperative forced expiratory volume in one second and hemoglobin concentration, indicating the need for preoperative transfusion in severe anemia or bronchoplasty if possible. Poor nutritional state before surgery possibly derived from cachexia may influence not only morbidity and mortality, but also prognosis. (Ann Thorac Cardiovasc Surg 2009; 15: 297–303)

Key words: lung cancer, postobstructive pneumonia, mortality, morbidity, prognosis

Introduction

Postobstructive pneumonia usually develops because of lung cancer. Most patients with lung cancer associated with postobstructive pneumonia are nonoperable and incurable at the time of initial presentation.[1)] Moreover, severe fibrous adhesion to the adjacent organ system, or cancer invasion of it, sometimes makes surgical procedures difficult. Some cases also have poor general conditions. To our knowledge, there is no information in the literature on the results of surgery for lung cancer associated with postobstructive pneumonia. In the present study, we report morbidity and mortality in such patients and analyze the risk factors for them. We also analyze prognostic factors for overall 5-year survival of patients without mortality.

Materials and Methods

From January 1983 to December 2003, a total of 1,265 patients with lung cancer underwent lung resection at the Division of Respiratory Surgery, Department of Surgery, Nippon Medical School, and the Department of Surgery, Nippon Medical School Musashikosugi Hospital. Forty-one patients had lung cancer associated with postobstructive

From [1]Division of Thoracic Surgery, Department of Surgery, Nippon Medical School; and [2]Department of Biological Regulation and Regenerative Surgery, Graduate School of Medicine, Nippon Medical School, Tokyo, Japan

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Address reprint requests to Shuji Haraguchi, MD: Division of Thoracic Surgery, Department of Surgery, Nippon Medical School, 1–1–5 Sendagi, Bunkyo-ku, Tokyo 113–8603, Japan.

pneumonia in their medical records, but 3 were excluded from the present study because of the lack of a detailed clinical background. Therefore 38 patients, including 33 males and 5 females, were analyzed in the present study. All patients were treated with antibiotics after a diagnosis of postobstructive pneumonia. The mean interval between the onset of postobstructive pneumonia and surgery was 45 days (range, 4–111 days). Thirty-four patients underwent lung resection by posterolateral thoracotomy and 4 by video-assisted thoracoscopic surgery. Fourteen patients (40%) underwent pneumonectomy, 9 (29%) underwent bilobectomy, 8 (25%) underwent lobectomy, and 2 (5%) underwent segmentectomy. A bronchoplasty was performed on 5 patients (sleeve bilobectomy: 2; sleeve lobectomy: 2; and sleeve pneumonectomy: 1). Combined resection was performed on the pericardium in 6 patients, the chest wall in 4, the truncus of the pulmonary artery, left atrium, and aorta in 2, and the diaphragm and innominate vein in 1. Nineteen patients (50%) had pathological stage III disease, 12 (32%) had stage I disease, 6 (16%) had stage II disease, and 1 (2%) had stage IV disease. Twenty-seven patients (71%) had squamous cell carcinoma, 8 (20%) had adenocarcinoma, 1 (3%) had large cell carcinoma, 1 (3%) had carcinoid, and 1 (3%) had mucoepidermoid carcinoma.

Anemia was defined according to World Health Organization (WHO) criteria as hemoglobin concentration less than 13.0 g/dl in a male and less than 12.0 g/dl in a female. Twenty-five patients (66%) had anemia before surgery, but only 4 had hemoptyses and hemosputa. Twenty-four of 25 anemic patients had normocytic normochromic anemia, and 1 had microcytic hypochlomic anemia. The mean hemoglobin concentration of all patients with postobstructive pneumonia was 12.4 g/dl (range, 7.9–17.3 g/dl). No patients were transfused before surgery.

The postoperative pulmonary functions were predicted according to a simplified system, which we developed using plain chest roentgenograms of patients with primary lung cancer.[2] The predicted postoperative forced expiratory volume in 1 second ($ppoFEV_{1.0}$) is (42–R)/(42–T) × preoperative $FEV_{1.0}$, where R is the number of subsegments scheduled for lung resection and T is the number of subsegments showing atelectasis or postobstructive pneumonia.[2]

The lung cancers of all patients were staged pathologically according to the International Union against Cancer system.[3]

Mortality was defined as death occurring during the hospitalization period following surgery.[4] Morbidity in this study was defined as complications that occurred during the hospitalization period after surgery[4] and included pneumonia, respiratory failure necessitating mechanical ventilation for more than 48 hours, bronchopulmonary artery fistula, bronchopleural fistula (BPF), a prolonged air leakage of more than 7 days from the chest drain, acute myocardial infarction, and cerebral infarction.

Statistical analyses were performed between patients with and without morbidity and between patients with and without mortality, using the StatView 5.0J software package (SAS Institute, Inc., Cary, NC) and SPSS 10.0 software package (SPSS, Inc., Chicago, IL). Univariate analyses between the groups were performed by means of unpaired two-tailed t tests or the chi-square test, using age, sex, body mass index (BMI), smoking history (smoker and ex-smoker vs. nonsmoker), number of cigarette pack-years, serum albumin concentration and hemoglobin concentration before surgery, performance status (PS) before surgery (PS 0, 1 vs. 2, 3), and partial pressure of oxygen and carbon dioxide at pulmonary artery before surgery (PaO_2 and $PaCO_2$), $ppoFEV_{1.0}$, duration of surgery, volume of blood loss, operative procedures (pneumonectomy or bilobectomy vs. lobectomy or segmentectomy), combined resection of other organs, pathological stage (stage I or II vs. stage III or IV), and histological type of lung cancer (squamous cell carcinoma vs. others). Multivariate logistic regression tests were performed with significant risk factors identified with univariate analyses.

For statistical analyses of prognostic factors for the overall survival of patients without mortality, we partitioned the patients by age (above or below the median of 63 years), sex, BMI (above or below the median of 22.7 kg/m^2), number of cigarette pack-years (above or below the median of 45), serum albumin concentration (above or below the median of 3.6 g/dl), and hemoglobin concentration (above or below the median of 12.5 g/dl) before surgery, PS before surgery (0, 1 vs. 2, 3), partial pressure of oxygen (above or below the median of 83.6 mmHg), and carbon dioxide (above or below the median of 39.0 mmHg) at pulmonary artery before surgery (PaO_2 and $PaCO_2$), $ppoFEV_{1.0}$ (above or below the median of 1.4 L), duration of surgery (above or below the median of 330 minutes), volume of blood loss (above or below the median of 607.5 ml), operative procedures (pneumonectomy or bilobectomy vs. lobectomy or segmentectomy), combined resection of other organs, pathological stage (stage I or II vs. stage III or IV), and histological type of

Table 1. Clinical characteristics of 13 patients with lung cancer associated with postobstructive pneumonia developing morbidity

Patient No.	Age/Sex	Stage	Pathology	Tumor location	Procedures	Albumin (g/dl)	Hg (g/dl)	PpoFEV$_{1.0}$ (L)	PS	Morbidity	Survival (M)
1	72M	III	Ad	Rt. B2	Bilobectomy	2.4	10.7	0.96	2	Pneumonia	22D
2	65F	III	Sq	Rt. B1	Sleeve bilobectomy	2.4	8.6	0.58	3	Broncho-PA fistula	1D
3	66M	II	Sq	Rt. B6	Bilobectomy	4.0	12.6	1.39	1	AL and AMI	0.5D
4	54M	II	Sq	Rt. B6	Bilobectomy	3.7	10.1	1.19	2	Bilateral pneumonia	1.8D
5	63M	III	Sq	BUD	Pneumonectomy	2.9	10.3	1.60	2	Pyothorax	8D
6	47M	III	Sq	Rt. IB	Pneumonectomy	3.1	10.8	1.46	3	BPF	37D
7	83M	III	Sq	Rt. B10	Lobectomy	3.0	7.9	0.73	3	Pneumonia and CI	0.4D
8	73M	I	Sq	Lt. B9	Lobectomy	4.4	16.0	0.90	0	Pneumonia	60A
9	57M	III	Sq	BUD	Pneumonectomy	3.5	11.2	1.48	1	BPF	41A
10	68M	I	Sq	Rt. B6	Bilobectomy	3.6	11.5	1.30	1	BPF	20A
11	76F	I	Sq	Lingula	Lobectomy	3.9	11.5	1.22	1	Pneumonia	60A
12	47F	III	Ad	Lt. B1 + 2	Pneumonectomy	4.1	10.5	1.40	3	Pneumonia	10D
13	61M	II	Sq	Lt. B6	Lobectomy	3.6	13.1	0.76	2	Pneumonia	18A

Hg, hemoglobin; ppoFEV$_{1.0}$, predicted postoperative forced expiratory volume in 1 second; M, male; F, female; Ad, adenocarcinoma; Sq, squamous cell carcinoma; Rt, right; B, bronchus; BUD, bronchus of upper division; IB, intermediate bronchus; Lt, left; AL, air leakage; AMI, acute myocardial infarction; BPF, bronchopleural fistula; CI, cerebral infarction; D, dead; A, alive.

lung cancer (squamous cell carcinoma vs. others). For the univariate analyses, the overall survival for subgroups described above was statistically analyzed using Kaplan-Meier estimated survival curves, and the significance of the difference was analyzed by the log-rank test. For a multivariate analysis, the Cox proportional hazards model was used to examine the effect of significant risk factors based on the univariate analyses on survival. A $p < 0.05$ was considered significant.

Results

Morbidity developed in 13 of the 38 patients (34.2%); pneumonia in 7, BPF in 3, and cerebral infarction, pyothorax, bronchopulmonary artery fistula, prolonged air leakage, and acute myocardial infarction each in 1 (Table 1). Treatment of BPF comprised 1 bronchial stump coverage with pedicled lattisimus dorsi flap after fenestration (patient 6), 1 bronchial stump resuture with pedicled omental flap (patient 9), and 1 bronchial stump resuture with pedicled intercostals muscle flap (patient 10). Of these, 1 patient died of lung cancer 37 months after surgery (patient 6). The other 2 patients were alive without tumor 20 and 41 months after surgery, respectively. The characteristics of 13 patients with morbidity and 25 without morbidity are shown in Table 2. Four patients (10.5%) died during hospitalization caused by massive hemoptysis because of bronchopulmonary artery fistula 31 days after surgery (patient 2), acute myocardial infarction 16 days after surgery (patient 3), bilateral pneumonia 56 days after surgery (patient 4), and pneumonia and cerebral infarction 13 days after surgery (patient 7).

Hemoglobin concentration before surgery and ppoFEV$_{1.0}$ were significantly low in patients with morbidity based on the univariate analyses ($p = 0.0071$ and $p = 0.0056$, respectively). PpoFEV$_{1.0}$ (odds ratio, 0.034; 95% confidence intervals, 0.001–0.832; and p value, 0.0381) was the significant risk factor based on a multivariate analysis.

Hemoglobin concentration before surgery and ppoFEV$_{1.0}$ were significantly low in patients with mortality based on the univariate analyses ($p = 0.03$ and $p = 0.0398$, respectively). But neither reached a significant level based on the multivariate analyses.

During the follow-up period, 14 patients (12 males and 2 females) and 8 patients (7 males and 1 female) of 34 patients died of lung cancer and other diseases. Eight patients (7 males and 1 female) were alive, and 4 male patients were unknown.

Univariate analyses of prognostic factors for the overall survival of patients without mortality revealed significant risk factors to be low serum albumin concentration, hemoglobin concentration, and PS before surgery, combined resection of other organs, and pathological stage (Table 3). Low serum albumin concentration before surgery was significant, based on a multivariate analysis (Table 4).

Discussion

Recent advances in operative techniques, anesthesia, and postoperative care have remarkably decreased the mor-

Table 2. Clinical characteristics of patients with or without morbidity

	With morbidity	Without morbidity	P value
Number of patients	13	25	
Age[a]	64.0 ± 11.0	62.2 ± 14.3	0.6872
Sex			
Male	10 (77)	23 (92)	
Female	3 (23)	2 (8)	0.1921
Number of cigarette pack-years[a]	53.4 ± 34.3	54.5 ± 36.8	0.9270
Smoker or ex-smoker	12 (92)	23 (92)	
Nonsmoker	1 (8)	2 (8)	0.9734
Serum albumin (g/dl)[a]	3.4 ± 0.6	3.7 ± 0.4	0.0860
Hemoglobin (g/dl)[a]	11.2 ± 2.1	13.0 ± 1.7	0.0071*
BMI (kg/m^2)[a]	21.2 ± 3.2	22.9 ± 2.7	0.0643
PaO_2 (mmHg)[a]	81.7 ± 19.0	83.5 ± 11.4	0.7128
$PaCO_2$ (mmHg)[a]	39.8 ± 4.2	40.0 ± 2.9	0.9244
$PpoFEV_{1.0}$ (L)[a]	1.1 ± 0.3	1.5 ± 0.4	0.0056*
Performance status			
0, 1	7 (54)	20 (80)	
2, 3	6 (46)	5 (20)	0.0917
Operative procedures			
Pneumonectomy	4 (31)	11 (44)	
Other	9 (69)	14 (56)	0.4286
Duration of surgery (min)[a]	380.6 ± 122.1	348.4 ± 111.7	0.4192
Volume of blood loss (ml)[a]	1064.2 ± 1091.3	1024.0 ± 1233.5	0.9217
Combined resection	4 (31)	9 (36)	0.7471
Bronchoplasty	3 (23)	2 (8)	0.1921
Pathological stage of lung cancer			
I, II	5 (38)	12 (48)	
III, IV	8 (62)	13 (52)	0.5748
Histological type of lung cancer			
Squamous cell carcinoma	10 (77)	17 (68)	
Others	3 (23)	8 (32)	0.5650

BMI, body mass index; PaO_2, partial pressure of oxygen at pulmonary artery; $PaCO_2$, partial pressure of carbon dioxide at pulmonary artery; $ppoFEV_{1.0}$, predicted postoperative forced expiratory volume in 1 second; *, statistical significance.

[a]Data are shown as mean ± standard deviation; percentage given in parentheses.

bidity and mortality after surgery for lung cancer in Japan.[5] However, the present study revealed that surgery for lung cancer associated with postobstructive pneumonia still had high morbidity and mortality, and that $ppoFEV_{1.0}$ was the significant risk factor for morbidity based on a multivariate analysis. Lung cancer located at the proximal bronchus usually needs major lung resection, and in the present study, pneumonectomy and bilobectomy were performed in 40% and 29% of the patients, respectively. The morbidity and mortality in the pneumonectomy group were equivalent or higher than those in the lobectomy with bronchoplasty.[6–9] Although it is recognized that patients with pneumonectomy most likely have more advanced stage disease, long-term survival and local control are significantly better when complete resection can be achieved by sleeve lobectomy.[8,9] We performed bronchoplastic procedures in 5 cases. Recently, therapeutic bronchoscopy has been used for relieving large airway obstructions caused by tumors.[1,10] It is reported to be a complementary tool in the combined bronchoscopic and surgical management of malignant airway obstruction before curative lung surgery and may permit parenchyma-sparing surgery.[11] Postobstructive pneumonia possibly could be improved early if the obstructed bronchus is recanalized. Therapeutic bronchoscopy could not only restore $FEV_{1.0}$, but it makes PS before surgery better. Direct intratumoral injection with 5-fluorouracil for tumor regression is reported to reduce the size of tumors in most cases and increase the diameter of the airway lumen.[12] Future studies using various therapeutic modalities are expected to clarify the effectiveness in reducing morbidity and mortality after surgery for patients with lung cancer associated with post-

Table 3. Statistical analyses of prognostic factors for overall survival of patients without mortality

Groups		Overall survival rates (%) at 1	2	3	4	5 years	P value (log-rank)
Age <63	(n = 17)	63	63	63	49	49	
≧63	(n = 17)	75	45	45	45	45	0.6532
Sex Male	(n = 33)	65	50	50	42	42	
Female	(n = 5)	40	40	40	40	40	0.4431
Body mass index <22.7	(n = 16)	63	47	47	39	39	
≧22.7	(n = 18)	76	62	62	55	55	0.6604
Pack-years <45	(n = 18)	71	64	64	52	52	
≧45	(n = 16)	66	41	41	41	41	0.6364
Albumin < 3.6 (g/dl)	(n = 14)	47	16	16	16	16	
≧3.6	(n = 20)	84	84	84	71	71	0.0007*
Hemoglobin < 12.5 (g/dl)	(n = 16)	55	31	31	31	31	
≧12.5	(n = 18)	82	75	75	62	62	0.0436*
PS 0, 1	(n = 27)	70	61	61	52	52	
PS 2, 3	(n = 7)	42	14	14	14	14	0.0142*
PaO_2 < 83.6 (mmHg)	(n = 17)	75	53	53	45	45	
≧ 83.6	(n = 17)	63	56	56	49	49	0.8406
$PaCO_2$ < 39.0 (mmHg)	(n = 16)	74	44	44	37	37	
≧39.0	(n = 18)	65	65	65	58	58	0.3846
$ppoFEV_{1.0}$ < 1.4 (L)	(n = 16)	56	48	48	40	40	
≧1.4	(n = 18)	82	61	61	55	55	0.1155
DOS < 330 (min)	(n = 15)	86	60	60	51	51	
≧330	(n = 19)	57	50	50	44	44	0.2652
VBL < 607.5 (ml)	(n = 17)	81	57	57	57	57	
≧607.5	(n = 17)	57	51	51	38	38	0.3036
Lobectomy	(n = 19)	83	55	55	49	49	
Pneumonectomy	(n = 15)	50	50	50	43	43	0.6853
Combined resection −	(n = 22)	85	73	73	67	67	
+	(n = 12)	42	25	25	17	17	0.0076*
Pathological stage I, II	(n = 15)	93	77	77	70	70	
III, IV	(n = 19)	50	36	36	29	29	0.0315*
Squamous	(n = 23)	71	60	60	49	49	
Others	(n = 11)	63	42	42	42	42	0.1371

PS, performance status; PaO_2, partial pressure of oxygen at pulmonary artery; $PaCO_2$, partial pressure of carbon dioxide at pulmonary artery; $ppoFEV_{1.0}$, predicted postoperative forced expiratory volume in one second; DOS, duration of surgery; VBL, volume of blood loss; *, statistical significance.

Table 4. A multivariate prognostic factor analysis in patients with lung cancer associated with postobstructive pneumonia

Factors	Hazard ratio	95% CI	P value
Performance status 0, 1 vs. 2, 3	1.000	0.279–3.583	>.9999
Combined resection – vs. +	0.346	0.096–1.245	0.1043
Pathological stage I, II vs. III, IV	0.742	0.214–2.572	0.6383
Serum albumin < 3.6 (g/dl) vs. ≧3.6	6.200	1.301–29.541	0.0220*
Hemoglobin < 12.5 (g/dl) vs. ≧12.5	0.727	0.197–2.683	0.6324

*, statistical significance.

obstructive pneumonia.

Preoperative hemoglobin concentration was the other risk factor for morbidity. Twenty-five patients (66%) had anemia before surgery. Twenty-four of them had normocytic normochromic anemia and 1 patient had microcytic hypochromic anemia. Only 4 patients had hemoptyses and hemosputa. Twenty-one patients had exacerbation of general conditions because of postobstructive pneumonia and lung cancer. There were no differences in volume of blood loss or transfusion during surgery between patients with and without morbidity (data not shown). Even patients with severe anemia were not transfused before surgery in the present study. It is suggested that a thorough treatment of postobstructive pneumonia with the antibiotics and transfusion for patients with severe anemia early before surgery are necessary for making general conditions better and reducing morbidity and mortality.

BPF developed most frequently after surgery in patients with lung cancer associated with postobstructive pneumonia. Three developed after pneumonectomy (2 after right pneumonectomy and 1 after left). We previously analyzed the risk factors predisposing to postpneumonectomy BPF in patients with lung cancer and found that right pneumonectomy, preoperative infection, and metastasis to a subcarinal lymph node were the risk factors for postpneumonectomy BPF (PBPF).[13] We further reanalyzed the risk factors for PBPF in a larger series, adding some risk factors reported recently, and found that preoperative infection, right pneumonectomy, and pathological N2 and N3 significantly contributed to the development of PBPF.[14] The lung is a common site of infection in patients with lung cancer, and postobstructive pneumonia, lung abscess, and occasionally empyema of mixed bacterial etiology are frequent.[15] Bronchial stump coverage with pedicled thymus and pericardial flaps are reported to be effective in preventing BPF.[16,17] Treatment with the antibiotics and bronchial stump coverage are expected to clarify effectiveness in preventing BPF in patients with lung cancer associated with postobstructive pneumonia.[13,14]

In the present study, low serum albumin concentration, hemoglobin concentration, PS before surgery, combined resection of other organs, and an advanced pathological stage were poor prognostic factors. A combined resection was performed in all cases because of cancer invasion to the adjacent organ system. Combined resection of other organs and an advanced pathological stage were reported to have poor prognosis.[18] Busch and his colleagues reported that combined resection involving chest wall, poor nutritional status as measured by a history of weight loss and preoperative serum albumin levels, and the use of neoadjuvant chemotherapy were associated with an increased risk of any pulmonary complication, but they did not comment whether these risk factors influenced prognosis.[19] Combined resection of other organs, low serum albumin concentration, and PS before surgery were not significant risk factors for morbidity and mortality, and low serum albumin concentration, hemoglobin concentration, and PS before surgery were poor prognostic factors in the present study. It is suggested that low serum albumin concentration, hemoglobin concentration, and PS before surgery were caused mainly because of cachexia more than by postobstructive pneumonia, and compromised immunology against lung cancer led to poor prognosis.

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