

Comparison of the Surgical Results of Pneumonectomy and Lobectomy for Lung Cancer

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Abstract

Objective: Although the preference is to avoid pneumonectomy as much as possible for the surgical resection of Non-small cell lung cancer (NSCLC), in some instances pneumonectomy must be considered among the treatment choices. We aimed to evaluate the surgical results of pneumonectomy and lobectomy for lung cancer. **Methods:** The patients who underwent lobectomy or pneumonectomy for primary NSCLC between January 1995 and June 2004 were studied and compared in the aspects of patients' characteristics, complication, 5-year survival, and recurrence rates. **Results:** Ninety-four percent of 236 patients was male. Mean age was 59.2 (range 37-76). Lobectomy was performed in 68.2% of all patients while the rest had had pneumonectomy. Complete resection was achieved in 95.8%. The cumulative 5-year survival rate was 44.4%. The rates of operative mortality, complications, and recurrences in follow-up were 1.9%, 40.4%, 42.9%, respectively in lobectomy group and 4.0%, 29.3%, 32.0%, respectively in pneumonectomy group. The 5-year survival rates were 40.0% and 58.8%, respectively in lobectomy and pneumonectomy groups. The difference between two groups was significant ($p=0.02$), conversely in complication and total recurrence rates. Local recurrence rate was 19.9% in lobectomy group and 4.0% in pneumonectomy group ($p=0.006$). Survival rate was higher in pneumonectomy for symptomatic, male, T3, N1 and stage IIB cases (p values <0.05). **Conclusions:** By considering higher survival and lower local recurrence rates than lobectomy group, pneumonectomy might be a good choice for the management of highly selected patients such as with stage IIB or N1 diseases, and for the patients who could tolerate pneumonectomy.

Keywords: Lobectomy, Pneumonectomy, Non small cell lung cancer, Resection, Surgery

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INTRODUCTION

Surgical treatment is the most favorable treatment for early stage non-small cell lung cancer (NSCLC) and anatomic lobectomy (LB) with mediastinal lymph node dissection is the standard approach for those resectable and operable cases. However, the anatomic location of the tumor or its enlargement might necessitate pneumonectomy

(PN) or bilobectomy. Although the late survival rates of two procedures are consistent with each other, the operative risk is higher in PN than in LB. Thus, PN is the less preferable method, unless it is technically required (1,2,3). However, it is interesting to know that the first PN was performed for a stage IIB (T2N1) patient successfully and resulted 30 years survival (4).

PN in lung cancer patients might be indicated in N1 involvement as in major fissure or interlobar vessel involvement (2,5). Recently published reports either on the outcomes of sleeve lobectomy (SLB) or comparing the outcomes of SLB and PN came to conclusions against SLB because of higher local recurrence rates (6,7) and lower long-term survival rates (7) related lymph node involvement. In this study, we aimed to evaluate the surgical results of PN and LB for lung cancer. The comparison was made in terms of clinical and histological characteristics, and complication, recurrence and survival rates.

MATERIALS AND METHODS

The study population consisted of the patients with NSCLC who underwent to resection surgery between January 1995 and June 2004. There were 236 patients in total and they were retrospectively divided into two groups as "lobectomy group" and "pneumonectomy group" according to the operation type performed. Related with the new alignments of our principles in the management of primary lung carcinoma, in the last five years of the study, patients having mediastinal lymph adenopathy (short axis >1 cm) were applied mediastinoscopy in preoperative period. Standard posterolateral thoracotomy was performed in all of patients. Between 1995 and 1998, only the mediastinal lymph nodes with pathological appearance were dissected (non-systematic lymph node dissection). After 1998, all mediastinal nodes (Naruke stations 2, 4, 7, 8, 9 and 10 in right sided resections and stations 4, 5, 6, 7, 8, 9 and 10 in left sided ones) were systematically dissected (systematic lymph node dissection). Resected specimens were examined his-

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Table I. Patient Characteristics*

Variable		Lobectomy n=161	Pneumonectomy n=75	Total (%)	p value
Sex	Male	148 (91.9)	74 (98.7)	222 (94.1)	0.04
	Female	13 (8.1)	1 (1.3)	14 (5.9)	
Age (y)	≤60	74 (46.0)	48 (64.0)	122 (51.7)	0.011
	>60	87 (54.0)	27 (36.0)	114 (48.3)	
Symptomatic		131 (81.4)	72 (96.0)	203 (86.0)	0.002
Histology	Squamous	79 (49.1)	54 (72.0)	133 (56.4)	0.001
	Non-squamous	82 (50.9)	21 (28.0)	103 (43.6)	
Differentiation	Well	23 (17.2)	16 (23.5)	39 (19.3)	0.18
	Moderate	63 (47.0)	36 (53.0)	99 (49.0)	
	Poor	48 (35.8)	16 (23.5)	64 (31.7)	
	0	2 (1.2)	1 (1.3)	3 (1.3)	
T status	1	34 (21.1)	0 (0)	34 (14.4)	0.0008
	2	87 (54.1)	50 (66.7)	137 (58.0)	
	3	28 (17.4)	19 (25.3)	47 (19.9)	
	4	10 (6.2)	5 (6.7)	15 (6.4)	
	0	116 (72.0)	48 (64.0)	164 (69.5)	
N status	1	28 (17.4)	11 (14.7)	39 (16.5)	0.10
	2	17 (10.6)	15 (20.0)	32 (13.6)	
	3	0 (0)	1 (1.3)	1 (0.4)	
Lymph Node Dissection	Systematic	106 (65.8)	50 (66.7)	156 (66.1)	0.9
	Non-systematic	55 (34.2)	25 (33.3)	80 (33.9)	

*Figures in parentheses represent percentage values.

topathologically. Surgical-pathologic staging was performed according to the New International Staging System for Lung Cancer (8). The outcome of each resection was assessed as "complete" or "incomplete". The reasons for incomplete resection were surgical margin invasion (bronchial, chest wall or diaphragmatic) or invasion of extracapsular lymph node into adjacent tissues. Postoperative adjuvant treatment was administered when the N2 node was positive or in incomplete resection cases. Local recurrence was defined as any recurrence in the ipsilateral hemithorax.

Operative mortality was defined as death occurring within 30 days of the operation and was excluded from the survival data. The follow-up information could be ob-

tained for each patient as the period between the operation time and date of death or the last visit before December 2004. In addition to other examinations, we performed routine CT scans during the follow-up period to exclude recurrences. Non-cancer related causes of death were excluded from the survival analyses.

For the statistical analysis, "Statistica v5.1, StatSoft, Inc, USA" software was used. For the comparison of frequencies Fisher's Exact Test or "Pearson Chi-Square Test", for survival analyses "Kaplan Meier Survival Analysis" and for comparison of survival rates log-rank test were used. P value less than 0.05 was accepted as statistically significant.

RESULTS

Between January 1995 and June 2004, 236 patients with NSCLC underwent surgical treatment in our department.

Table II. Pathologic stages

Stage	Lobectomy (%)	Pneumonectomy (%)	Total (%)	p value
0	2 (1.2)	1 (1.3)	3 (1.3)	
IA	25 (15.5)	0 (0)	25 (10.6)	
IB	61 (37.9)	31 (41.4)	92 (39.0)	
IIA	3 (1.9)	0 (0)	3 (1.3)	
IIB	35 (21.8)	20 (26.7)	55 (23.3)	0.01
IIIA	19 (11.8)	16 (21.3)	35 (14.8)	
IIIB	10 (6.2)	6 (8.0)	16 (6.8)	
IV	6 (3.7)	1 (1.3)	7 (2.9)	
Total	161 (100.0)	75 (100.0)	236 (100.0)	

Table III. Recurrences

Recurrence	Lobectomy (%) n=161	Pneumonectomy (%) n=75	Total (%) n=236	p value
Local (local alone plus local and distant)	32 (19.9)	3(4)	35(14.8)	0,006
Distant	37 (23.0)	21 (28)	58 (24.6)	0.42
Total	69 (42.9)	24 (32.0)	93 (39.4)	0.12

Table IV. The comparison of 5-year survival rates

Variable	5-year survival rates (%)		p value	
	Lobectomy group	Pneumonectomy group		
Overall	40.0	58.8	0.02	
Sex	Male	38.8	57.0	0.02
	Female	51.4	ID*	-
Age (y)	≤60	33.4	62.8	0.06
	>60	46.0	55.8	0.15
Symptom	Yes	32.7	54.5	0.009
	No	66.9	100.0	0.28
Differentiation	Well	40.0	52.5	0.87
	Moderate	42.9	58.8	0.09
	Poor	32.7	82.1 (4 year)	0.25
Histology	Squamous	49.6	55.1	0.29
	Non-squamous	31.6	73.5 (4 year)	0.07
	0	100 (2 year)	ID	-
T status	1	64.9	-	-
	2	35.7	55.4	0.06
	3	30.9	86.0 (4 year)	0.02
	4	28.7	0 (2 year)	0.52
N status	0	52.2	63.0	0.09
	1	10.0	75.2 (4 year)	0.003
	2	35.4 (4 year)	22.4	0.95
	3	-	ID	-
Lymph Node Dissection	Systematic	64.3	69.2	0.12
	Non-systematic	36.9	47.4	0.35

*ID: Inadequatedata

The mean age of the patients was 59.2 (range 37-76), and 222 of 236 patients (94.1%) were male. LB was performed in 161 patients (68.2%) of total 236 patients (bilobectomy in 21 of them) and PN in 75 patients (31.8%). The patients' characteristics were as shown in Table I and classification of the patients according to pathologic stages was summarized in Table II. The patients in PN were younger, more frequently symptomatic and mostly with squamous cell carcinoma histology than in LB group ($p < 0.05$). None of the patients who underwent PN was in T1 and stage IA while more patients in stage IIIA had PN.

Resection was assessed as "complete" in 95.8% of the patients and all of the "incomplete" cases were in LB group ($p = 0.03$). For incomplete resection, surgical margin invasions were as bronchial in 4 cases (microscopic invasion in 3 cases and carcinoma insitu in 1 case), chest wall in 3 cases and diaphragmatic in 1 case. Invasion of extracapsular lymph node into adjacent tissues was found in 2 cases.

In this study, operative mortality occurred in 6 cases (2.5%); 3 (1.9%) in LB group and 3 (4.0%) in PN group ($p = 0.39$). In LB group, 1 patient having chest wall resection died 1 day after the surgery due to myocardial infarction; 1 patient underwent bilobectomy died on the 18th day of the postoperative period on account of respiratory failure after bronchopleural fistula and empyema; 1 patient

who underwent LB plus wedge resection died on the first day of the postoperative period due to massive pulmonary embolism. In PN group, 1 patient died on the 30th day of the postoperative period because of sepsis after re-thoracotomy for chylothorax, 1 patient died on the 3rd day of the postoperative period because of congestive cardiac failure and 1 case who had chest wall resection died on the 4th postoperative day due to respiratory failure.

Complication rates were 40.4% in LB group and 29.3% in PN group ($p = 0.11$). The most frequent complications were residual pleural space (15.5%), atelectasis (9.3%), and prolonged air leak (6.8%) in LB group and wound infection (9.3%), atelectasis (8.0%), and arrhythmia (8.0%) in PN group. Two patients in PN group having lymph node dissection developed chylothorax. No independent variable responsible for the development of the complications has been detected in LB group. In PN group, only the extended resections were found responsible for the increase in complication rate ($p = 0.00055$).

The total number for recurrence was 93 patients (39.4%) and the recurrence rate was 42.9% (69 in 161 patients) in LB group and 32.0% (24 in 75 patients) in PN group (Table III). The difference between those two groups was not statistically significant ($p = 0.12$). In both groups, most of the recurrences were occurred in the dis-

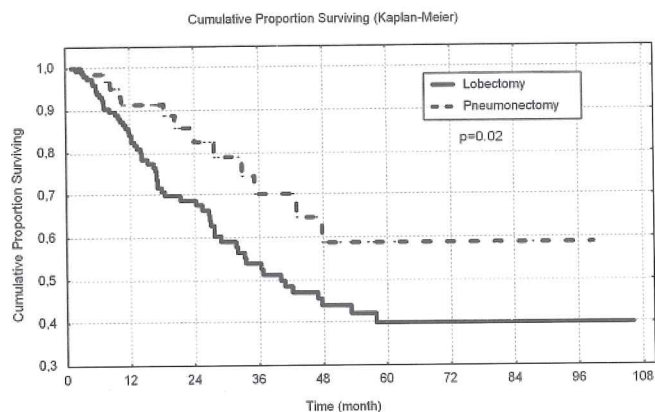


Figure 1. Survival rates according to operation type

tant regions. The places of distant recurrences with decreasing frequency were contralateral lung, bone, and brain in LB group and contralateral lung, brain, and bone in PN group. Local (local alone plus local and distant) recurrence occurred in 32 patients (19.9%) and in 3 patients (4.0%), respectively in LB and PN groups ($p=0.006$).

In this study, the mean follow-up period was 25.6 ± 24.6 months. At the end point of the study, 107 patients were alive free of disease and 30 with disease, whereas 75 patients died disease-related and 24 disease-unrelated reasons. The overall survival rate of the patients was 44.4%. In LB and PN groups, the rates were found as 40.0% and 58.8%, respectively ($p=0.02$) (Figure 1). In LB group, variables correlating the survival were symptom presence ($p=0.002$), histological differentiation ($p=0.018$), histology ($p=0.045$), N status ($p=0.014$) and disease stage ($p=0.002$). In PN group, only the N status ($p=0.015$) was found in correlation with survival.

In comparison of survival rates for those groups according to sex, age, symptom, differentiation and histology of tumor, T status, N status, type of lymph node dissection and pathologic stage (Table IV and V). In PN group, patients who were symptomatic, male, T3 tumor, N1 disease and stage IIB disease had significant increased survival rate than LB group ($p=0.009, 0.02, 0.02, 0.003, 0.002$, respectively). According to the stages, survival rates for LB and PN groups were found as 49.4% and 61.4% in stage IB, 32.5% and 46.9% in stage IIIA, respectively. All of the stage IA patients underwent LB and their survival rate was 71.2%. There were only 3 patients in stage IIA who both underwent LB. They were respectively in the 16th, 24th and 26th months of their follow-up period and were still alive and free of disease. In stage IIB, 5-year survival rate in LB group was 14.3%. PN patients were just in 5th year of their follow-up period and their 4-year survival rate was found as 46.9%. Six patients who underwent PN in stage IIIB

Table V. The comparison of 5-year survival rates according to pathologic stages

Variable	5-year survival rates (%)		p value
	Lobectomy group	Pneumonectomy group	
0	100 (2 year)	ID*	-
IA	71.2	-	-
IB	49.4	61.4	0.17
IIA	100 (1 year)	-	-
IIB	14.3	70.0 (4 year)	0.002
IIIA	32.5	46.9	0.47
IIIB	28.7	0 (2 year)	0.53
IV	0 (4 year)	ID	-

*ID: Inadequate data

died within 2 years. In stage IIIB patients who underwent LB, survival rate was 28.7%. A patient who underwent PN in stage IV (ipsilateral intrapulmonary metastasis in a different lobe of primary tumor) was in the 6th months of his follow-up period and was still alive free of disease. All of the 6 patients in LB group at stage IV died within 4 years.

DISCUSSION

For primary lung cancer patients with adequate pulmonary function, standard resection currently includes LB, SLB or PN depends on the extension of the disease. PN, which limits pulmonary reserve and results in an increased pulmonary artery pressure, leads to greater long-term cardiopulmonary disability and a worse quality of life than does LB (9,10). Therefore PN is being considered as a disease in itself and should be avoided at all cost (2,9). As a result of careful preoperative assessment in our series, the clinical TNM stage was consistent with the extent of the resection performed.

In surgical treatment of primary lung cancer, the resection of adequate tissue and complete resection in relation with tumor location and enlargement is aimed principally. However, even if the surgeons believe to have resected the lesion completely, residual tumoral tissue might be found in surgical margins during the pathological examination in some cases. Incomplete resection rate was previously reported in range between 1.4%-15.7% (9,11,12,13). In our study, the incomplete resection rate was among the lower rates with 4.2%.

The determining factors in terms of complication development in the postoperative period of PN procedure were reported as elderly patients, comorbidity, right-sided lung cancer, smoking and poor pulmonary function tests (14,15,16,17). Ferguson and co-workers have reported that cardiovascular complications were seen more frequently in PN due to arrhythmia and pulmonary complications were

common in LB due to prolonged air leak (3). Age over 70, performance status, and chronic obstructive pulmonary disease (COPD) have been reported as the most important factors contributing to post-operative complications in PN patients when compared to patients with less extensive pulmonary resections (17). In our series, even though there is no significant difference between two groups, complication rate following the LB was higher than that in PN. The reasons might be frequent appearance of LB-specific complications, like prolonged air leak and space problems as previously reported (3,18), and the higher ratio of younger patients (age \leq 60) in PN group (64% vs. 46%). In recent study, the extended resections were found responsible from the increased complication rate in PN group. Less frequent but more severe complications in comparison with LB caused two fold increased operative mortality.

The recurrences in the patients operated for lung cancer were reported with a tendency of being detected mostly in the distant regions, especially in brain, bone, contralateral lung, and liver (19,20,21). Presently, the ratio of overall distant recurrence rates (distant alone plus local and distant) in LB and PN groups were similar, respectively 29.2% and 29.3%. Local recurrence in LB group (19.9%) was significantly higher than in PN group (4.0%). Masard and associates have reported higher local recurrence rate in bilobectomy for stage I lung cancer in comparison with PN while the 5-year survival didn't differ (18). The rates were reported as high as 51% and about 20% also for SLB in previous reports (6,7,9,22,23). The lower rates in the literature were 8% and 10.3% (9,22). Kim et al. have reported local recurrence rates 32.6% in SLB and 8.5% in PN and they have suggested sleeve resection in N0 disease because of the higher locoregional recurrence particularly in patients with N1 positive lymph nodes (6). In particular, in the presence of nodal metastases, a sleeve LB has been reported to result in poor local control (6,7,24).

The age, sex, resection type, histology, tumor size, and pathologic stages have been indicated as important prognostic factors previously (3,11-13,25-27). In our study, the male gender, symptom presence, differentiation of tumor, histology, N status and disease stage are the factors influenced survival in LB group and N status was the only factor for PN group. It is seen that survival was being affected by more parameters in LB than in PN.

In comparison of survival rates of the patients in LB and PN groups, LB patients have had better survival rates (3,26,27). It was possible that patients who underwent PN would have bigger in size and more central tumors or more nodes involved, even if the stage was the same. In other words, the percentage of stage III patients in the PN

group was higher than that of the patients in the LB group. Presently, the proportion of stage IIIA in LB and PN were 11.8% and 21.3%, respectively. In addition, the poor survival of patients with PN has been related to functional or non-cancer-related reasons (9). In contrast to the literature, a better survival rate in PN group was detected in our study. The recent results seem to support the probability of obtaining better results through the resection of as much as possible tissue that been invaded by the disease as a principal of surgery for cancer, i.e. complete resection.

Alexiou and associates have reported in the study which they compared PN and smaller resections than a PN (including bi-lobectomy, LB, sleeve resection, segmentectomy and wedge resection) that PN has a potent, adverse impact on survival for stage I NSCLC (28). By the way, Birdas has criticized that article about the handicaps of such a specific conclusion in the lack of information on disease recurrence and cause of death (29). Ferguson and associates have not detected any significant long-term adverse influence of PN on survival after adjusting for other prognostic factors (such as age, primary tumor status, regional nodal status, and forced expiratory volume in 1 second) in comparison with lobectomy/bilobectomy (3).

In our study, the patients who were male, symptomatic, T3 tumor, N1 disease or stage IIB disease had significant increased survival rate in PN group than in LB group. Since the T3 group has a heterogeneous nature, it would be controversial to make a precise conclusion. There are different opinions on N1 disease. It has been suggested SLB for N1 disease, not for N2 disease (23,30). The opposite ideas have been raised from the studies concluded that the presence of N1 disease would adversely affect the prognosis. A significant difference in the long-term survival between patients with N0 and N1 disease have been reported for SLB (7,24).

A comparison between PN and LB may not be admitted as meaningful since the two groups of patients were inherently different. However, by considering the limitations, it might be helpful to supply the information for decision-making in PN vs. LB. Prospective randomized trials would hopefully resolve the above issue. However, PN, a procedure dedicated for a better complete resection but avoided because of cardiopulmonary dysfunction and postoperative complications, should lead to higher success rates by considering the proper identification of the risk factors for PN. According to our opinion, the advantages and disadvantages have to be determined free from prejudices. Although we agree the preference of avoiding PN as much as possible, our results as higher survival and lower local recurrence rates than LB group are supporting that

PN might be a good choice for the management of selected patients with stage IIB or N1 diseases, especially in the patients who can tolerate PN, with sufficient cardiopulmonary reserve and no accompanying disease, left-sided cancer, and younger age than 60.

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