Original Article

Short- and Long-Term Outcomes after Pneumonectomy for Primary Lung Cancer

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Purpose: The purpose of this study was to investigate the recent results of pneumonectomy (Pn) for primary lung cancer.

Patients and Methods: Thirty-four patients undergoing Pn and 26 patients undergoing broncho- or angioplastic lobectomy (namely, parenchyma-sparing lung resection) from January 1993 to December 2004 were reviewed. The oncological outcome of Pn was analyzed by disease-free survival (DFS). To assess morbidity and mortality, we compared the outcomes of patients undergoing Pn and parenchyma-sparing lung resection.

Results: Five-year DFS of the Pn group was 43%. DFS of pathological stage I/II patients was significantly better than that of stage III/IV (73.3% vs. 8.5%, P = 0.0001). The occurrence of minor and major postoperative complications was not different between Pn and parenchyma-sparing lung resection (52.9% vs. 61.5%, P = 0.5054; 17.6% vs. 7.7%, P = 0.1675). In the late period, respiratory function after Pn was significantly impaired in comparison with parenchyma-sparing lung resection. Moreover, 4 noncancer-related deaths occurred in the Pn group.

Conclusion: The oncological outcome after Pn for patients with lung cancer of less than stage III was satisfactory. Although operative morbidity was not different between the two groups, the loss of pulmonary reserve after Pn was more severe after than the parenchyma-sparing lung resection. (Ann Thorac Cardiovasc Surg 2008; 14: 289–293)

Key words: lung cancer, pneumonectomy, morbidity

Introduction

Recently, parenchyma-sparing lung resection, such as broncho- or angioplastic lobectomy (Pl-Lob), has been well established as a valuable alternative to pneumonectomy (Pn) in the treatment of centrally located lung cancer.[1] It has been applied to patients with sufficient pulmonary function, instead of Pn, as well as to patients with insufficient reserve whenever the extent of the disease permits. In some situations, however, Pn may be inevitable to achieve the complete removal of a tumor for anatomical and/or technical reasons.

Advocates of parenchyma-sparing lung resection point out the disadvantages of Pn, including a higher occurrence of postoperative complications and a poor quality of life as a result of cardiopulmonary dysfunction.[2–6] However, evidence regarding the effect of Pn on morbidity and mortality is conflicting. The purpose of this study was to evaluate recent results in patients undergoing Pn for primary lung cancer.

Patients and Methods

From January 1993 to December 2004, a total of 762 patients were operated on for primary nonsmall cell lung cancer (NSCLC) at our institution. Among them,

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Table 1. Clinical and pathological characteristics of patients in this study

	Pn (n = 34)	Pl-Lob (n = 26)	P Value
Age (median, range)	59 (45–75)	68 (52–84)	0.0002
Gender (male/female)	30/4	18/8	0.0682
Histology (Sq/Ad/AdSq/La)	27/6/0/1	15/9/1/1	0.2579
Location (R/L)	8/26	18/8	0.0004
P Stage (I/II/III/IV)	7/11/15/1	7/8/11/0	0.7194
Preoperative Tx			0.2030
CxRx	5	2	
Cx	5	2	
Postoperative Tx			0.5798
Cx (platinum-based/UFT)	8 (6/2)	8 (4/4)	
Rx	4	3	
Reason for the procedure			0.4303
Direct extension	21	16	
Metastatic lymph node	11	10	
Others	2	0	

Pn, pneumonectomy; Pl-Lob, broncho- or angioplastic lobectomy; Sq, squamous cell carcinoma; Ad, adenocarcinoma; AdSq, adenosquamous cell carcinoma; La, large cell carcinoma; Tx, therapy; CxRx, combined chemotherapy and local radiotherapy; Cx, chemotherapy; UFT, tegaful-uracil (Taiho, Tokyo, Japan); Rx, radiotherapy.

Pn and Pl-Lob were applied to 34 and 26 patients, respectively. Data were collected retrospectively from clinical records. Patients with small cell lung cancer or a low-grade malignant histological type were excluded from this study.

The indication for Pn was usually extensive cancer invasion of the hilum or fissure. Pl-Lob was employed when the lesion was expected to be removed completely. Systematic mediastinal lymph node dissection was performed routinely, and the tumor was completely excised in all patients. Two patients in the Pn group underwent lung resection combined with part of the left atrium. The Pl-Lob group consisted of 16 bronchoplastic resections (sleeve resection in 13, wedge resection in 3), 9 angioplastic resections (wedge resection in 9), and 1 bronchovascular wedge resection. Some patients received pre- or postoperative treatment according to their disease stage or physical status. Histological typing was determined according to the World Health Organization (WHO) classification,[7] and disease staging was based on the tumor-node-metastases (TNM) classification of the International Union Against Cancer.[8]

When evaluating morbidity, we classified postoperative complications into major and minor. Operative mortality included any death during the hospital stay after surgery. A spirometric pulmonary function test was performed within 1 month before lung resection and repeated 3 or more months after operation. Patients who died, who remained in the hospital because of postoperative complications, or who suffered a relapse within 3 months were excluded from this spirometric analysis. Disease-free survival (DFS) was analyzed by the product limit method of Kaplan and Meier, and curves were compared using the log-rank test. The end point of DFS was defined as a relapse of the lung cancer, and the length was measured from the day of the operation. The observation was censored at the last follow-up when the patient was alive without recurrence or when the patient died from causes other than lung cancer. A comparison of the clinicopathological variables in the Pn and Pl-Lob groups was determined by Student's *t* test, χ^2 test, and Mann-Whitney's U test. Statistical analysis was considered significant when the probability value was <0.05.

Results

Patient characteristics are shown in Table 1. Gender and histology were similar between the Pn and Pl-Lob groups. In the Pn group, most patients underwent left Pn. In contrast, right-sided procedures were predominant in the Pl-Lob group. One patient in the Pn group diagnosed as stage IV had a pulmonary metastasis in the non-tumor-bearing lobe, which was resected simultaneously. All preoperative chemotherapies in this study were based on the platinum regimen. Postoperatively, the regimen included a platinum-based regimen and tegaful-uracil (UFT; Taiho, Tokyo, Japan). The selection of the

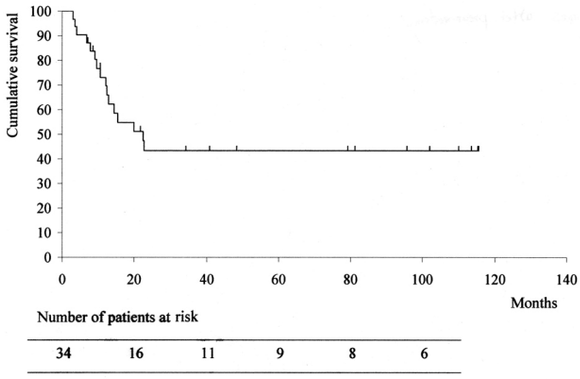

Fig. 1. Cumulative survival in patients undergoing pneumonectomy.

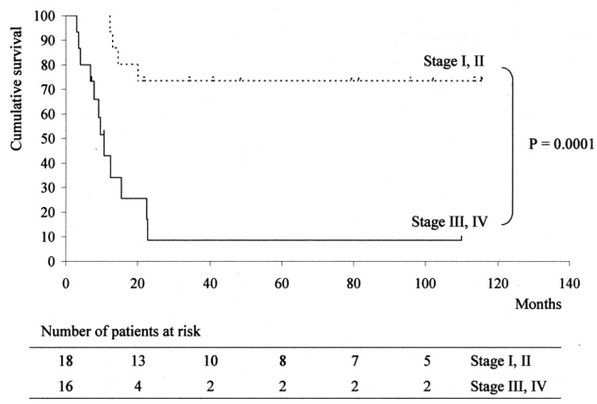

Fig. 2. Cumulative survival by pathological staging (stage I/II vs. stage III/IV, P = 0.0001).

Table 2. Perioperative complications

		Pn (n = 34)	Pl-Lob (n = 26)
Minor	Dysrhythmia	13	6
	Sputum retention	5	12
	Prolonged air leakage	0	3
Major	Pneumonia	2	1
	BPF	2	0
	Empyema without BPF	1	1
	Exploration for bleeding	1	0
	Cardiac failure	1	0

Pn, pneumonectomy; Pl-Lob, broncho- or angioplastic lobectomy; BPF, bronchopleural fistula.

surgical procedure was based on direct proximal extension of the main tumor, metastatic lymph node invasion, or other problems that consisted of a destroyed lung from previous pulmonary tuberculosis in one patient and intraoperative injury of the pulmonary artery in another.

Overall 5-year DFS for patients undergoing Pn was 43%, with a median survival time of 22 months (Fig. 1). In regard to pathological staging, DFS for the patients diagnosed as stage I or stage II was significantly better than that for stage III or stage IV patients (Fig. 2) (73.3% vs. 8.5%, P = 0.0001). The reason for the surgical procedure (direct extension vs. metastatic lymph node) did not affect DFS (P = 0.443).

Operative complications are listed in Table 2. The incidence of complications was not different between the Pn group and the Pl-Lob group (minor, 52.9% vs. 61.5%, P = 0.5054; major, 17.6% vs. 7.7%, P = 0.1675). There was one operative death from bronchopleural fistula (BPF) in a right Pn patient.

Postoperative changes in pulmonary function are shown in Table 3. Preoperative respiratory variables were comparable in both groups. However, postoperative deterioration of spirometric functions in the Pn group was significantly greater than those in the Pl-Lob group. Moreover, postoperative exertional dyspnea developed in the Pn group (Table 3). During the follow-up period, critical events (except for recurrence of lung cancer) developed in 5 patients in the Pn group and in 1 in the Pl-Lob group (Table 4). Four of the 5 Pn patients died of intercurrent disease.

Discussion

If a cure is to be attempted for NSCLC, surgical treatment is the most important strategy. The completeness and extent of lung resection directly affect the prognosis oncologically and physiologically. Pn has been the standard approach in patients with centrally located lung cancer. In contrast, to conserve respiratory reserve, Pl-Lob has been offered as a surgical alternative. Accord-

Table 3. Changes in respiratory variables after surgery

	Pn (n = 27)	Pl-Lob (n = 16)	P Value
FEV1 (mean ± SD)			
Preoperative value	2,079 ± 641	2,183 ± 719	0.6262
Postoperative value	1,310 ± 301	1,736 ± 533	0.0017
FVC (mean ± SD)			
Preoperative value	2,976 ± 682	3,122 ± 897	0.5506
Postoperative value	1,793 ± 337	2,398 ± 689	0.0004
H-J classification (I/II/III)			
Preoperative value	27/0/0	15/1/0	0.7345
Postoperative value	3/18/6	13/3/0	<0.0001

Pn, pneumonectomy; Pl-Lob, broncho- or angioplastic lobectomy; FEV1, forced expiratory volume in one second; SD, standard deviation; FVC, forced vital capacity; H-J, Hugh-Jones.

Table 4. Intercurrent events, except for those related to lung cancer

Patient	Procedure	Pre- or postoperative treatment	Event	Interval (months)
1*	Pn	Preoperative CxRx	BPF/empyema	2.5
2*	Pn	—	Pneumonia	8.4
3*	Pn	Preoperative CxRx	ARDS	34
4†	Pn	—	Occurrence of RCC	21.8
5*	Pn	Postoperative Cx	Pneumonia	110
6	Pl-Lob	Postoperative Rx	BPF	9

Pn, pneumonectomy; Pl-Lob, broncho- or angioplastic lobectomy; CxRx, combined chemotherapy and local radiotherapy; Cx, chemotherapy; Rx, radiotherapy; BPF, bronchopleural fistula; ARDS, acute respiratory distress syndrome; RCC, renal cell carcinoma; *, died of the intercurrent disease; †, died of RCC.

ing to previous analyses, survival after parenchyma-sparing lung resection is comparable to that after Pn if the tumor is completely removed.[3,5,6] However, if the entire tumor is removed, Pn is essential in some patients.

In our analysis, oncological outcome after Pn was satisfactory for patients with pathological stage I or II diseases. Most patients with pathological stage III or IV disease relapsed early after surgery in spite of the complete removal of the tumor. These observations correlate with previous reports, which revealed that the pathological nodal status of the disease affected survival.[5,6,9] To confirm local control, the application of Pn may be acceptable to disease classified as less than stage III, i.e., stages I and II.

In terms of operative mortality and morbidity, some of the previous reports indicated that after Pn they were significantly higher than after parenchyma-saving resection.[2,5] However, others either found no difference between the two groups[3,6] or reported a higher operative risk in the sleeve lobectomy group.[9] In our analysis, surgical morbidity in the Pn group was comparable to that in the Pl-Lob group. This may explain our results: First, whereas a right-sided procedure is one of the risk factors for Pn,[10] left Pn was predominant in our Pn group. Second, the surgical outcome for NSCLC is improving through advances in pre- and postoperative management.[11]

Long after lung resection (i.e., >3 months), spirometric respiratory function and exertional dyspnea in the Pn group were significantly impaired compared with those in the Pl-Lob group. Previous studies reported a difference between lobectomy and Pn in the recovery of respiratory function and exercise capacity.[12,13] An early loss of respiratory function occurred after lobectomy, followed by significant improvement with time. After Pn, however, there was a greater functional loss, which was sustained without improvement. Nezu et al. suggested that expansion of the remaining lung on the operated side played an important role in the improvement in respiratory function after lobectomy.[13] Furthermore, Kushibe et al. showed that the "volume

reduction effect" of lobectomy resulted in the amelioration of respiratory function.[14] Such effects cannot be anticipated after Pn.

In our study, 4 deaths unrelated to lung cancer were observed in the Pn group, but no deaths from this cause occurred in the Pl-Lob group. Three of the 4 patients died from respiratory complications. Alexiou et al. emphasized the importance of monitoring for non-cancer-related deaths after Pn as a result of the high incidence of deaths unrelated to lung cancer in their series.[4] According to a meta-analysis, Pn patients more often die of intercurrent disease than do sleeve lobectomy patients.[15] Although a definite relationship between Pn and non-lung cancer deaths could not be demonstrated in our series, we speculated that cardiopulmonary overloading after Pn increased the incidence of the fatal intercurrent disorders.

In summary, the oncological outcome after Pn in patients with a pathological stage of less than III was satisfactory. Although there was no difference in operative morbidity or mortality between Pn and parenchyma-sparing lung resection, in the late period the loss of pulmonary reserve after Pn was greater than after parenchyma-sparing lung resection. Any impairment of respiratory status after Pn may influence decisions regarding adjuvant therapy and the treatment of recurrent tumor, and it may also be a factor in the occurrence of lethal intercurrent disease. These results may adversely affect the long-term outcome after Pn.

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