Sleeve Lobectomy as an Alternative Procedure to Pneumonectomy for Non-small Cell Lung Cancer

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Introduction: The aim of this study is to compare the outcomes of sleeve lobectomy (SL) and pneumonectomy (PN) and to determine which one is more acceptable standard procedure for patients with non-small cell lung cancer.

Methods: From 1996 to 2005, 424 patients underwent SL ($n = 157$) and PN ($n = 267$) in our institution. Propensity score matching analysis was performed to compare these two groups for mortality, morbidity, survival, recurrence, and postoperative pulmonary function.

Results: In each group, 105 patients were eligible for analysis. The operative mortality was lower in the SL group (1.0%) than the PN group (8.6%), ($p < 0.0001$). The morbidity was similar (33.4% versus 29.5%, $p = 0.376$). The 5-year survival was lower in the PN group (PN, 32.14% versus SL, 58.43%, $p = 0.0002$). The recurrence pattern (locoregional versus distant) did not differ between two groups ($p = 0.180$). The mean actual postoperative first second forced expiratory volume in the patients underwent SL was 2.05 ± 0.55 liter, which increased by 7.9% compared with the predicted-postoperative first second forced expiratory volume.

Conclusions: Our results showed that the SL can be performed with low operative risk and may offer superior survival and better postoperative pulmonary function compared with the PN in selected patients. If anatomically feasible, a SL must be considered as a favorable alternative to PN in patients with non-small cell lung cancer.

Key Words: Non-small cell lung cancer, Sleeve lobectomy, Pneumonectomy.

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Sleeve lobectomy (SL) was first introduced for patients with lung cancer who were unable to tolerate a pneumonectomy (PN) due to compromised lung function. Initially, the SL was considered only as an alternative procedure, because of the complex surgical technique and the possibility of incomplete resections compared with the PN. Because surgical experience with the SL accumulates, it has been shown that the SL could offer a local tumor control and be a safe operative modality.[1–7] In addition, the PN is associated with several serious medical problems.[8,9] Nevertheless, despite the SL is widely used at present, there are still some debates on the efficacy of this procedure. Points to consider include the following: whether to perform a SL in patients with sufficient lung function, whether the operative procedure is safe, whether the procedure is adequate as a cancer operation, and whether the reimplanted lung functions normally.

The objective of this retrospective study was to compare the outcomes of the SL and PN, focusing on the operative outcomes, recurrence, survival, and postoperative functional aspects of these procedures and to determine whether SL can be accepted as a favorable alternative procedure to PN for patients with non-small cell lung cancer (NSCLC), not only in patients with pulmonary dysfunction but also in patients with sufficient pulmonary function.

PATIENTS AND METHODS

There were 1973 consecutive patients with primary NSCLC, who underwent major lung resection surgery from 1996 to 2005 in Samsung Medical Center, Seoul, Korea. Of the 1973 patients, lobectomy/bilobectomy was performed in 76.6% ($n = 1511$), PN in 14.9% ($n = 294$), and SL in 8.5% ($n = 168$). Eleven patients who received sleeve PN were excluded from study, and finally, 451 patients with PN or SL were listed for analysis.

In our institution, cervical mediastinoscopy was routinely performed in patients with preoperative diagnosis of lung cancer. The patients diagnosed with N2 disease by mediastinoscopy underwent neoadjuvant chemoradiotherapy. After that, restaging of local tumor extension and nodal status were assessed to determine the operative procedures. The predicted postoperative first second forced expiratory volume (FEV1) was calculated using pulmonary function testing and lung perfusion scintigraphy. Among 77 patients (49%) of the patients with SL, the predicted post-PN FEV1 was compared with the actual postoperative FEV1. Postoperative spirometry was performed at a median of 3.9 months after the surgery (mean: 9.8 ± 11.2 months, range: 0.5–45.8 months). We tried to perform SL whenever it was technically feasible in patients who otherwise were candidates for PN, even if they had sufficient functional pulmonary reserve. Sleeve resec-

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tions were performed in the right upper lobe ($n = 70$), right middle lobe ($n = 3$), right lower lobe ($n = 8$), right middle lobe and right lower lobe ($n = 17$), right upper lobe and right middle lobe ($n = 9$), the left upper lobe ($n = 40$), and left lower lobe ($n = 21$). Concomitant pulmonary angioplasty (bronchovascular sleeve resection) was done in 30 patients (17.86%). Right PN was performed in 107 patients, and left PN in 176. Combined procedures with PN included pericardial resection ($n = 9$), chest wall resection and reconstruction ($n = 8$), partial superior vena cava resection ($n = 2$), descending thoracic aorta replacement ($n = 2$), partial pleurectomy ($n = 2$), diaphragm resection and reconstruction ($n = 2$), and partial resection of esophagus and left atrium ($n = 1$). For all operations, the resection margin of the bronchus was confirmed intraoperatively, and routine systematic mediastinal lymph node dissection was carried out. Histologic typing was performed according to the World Health Organization classification. Surgical-pathologic staging was determined according to the New International Staging System for Lung Cancer (International Union Against Cancer, 1997). Operative mortality was defined as any postoperative death within 30 days and in hospital death. Postoperative complications were subdivided into major complications, which included acute respiratory distress syndrome (ARDS), bronchopleural fistula (BPF), bronchovascular fistula, empyema, severe bronchial stenosis requiring completion PN, and chylothorax requiring reoperation. The minor complications included pneumonia based on the chest radiographic findings that required antibiotics, atelectasis, or bronchial stenosis that could be managed by therapeutic bronchoscopy, vocal cord palsy, radiation pneumonitis, a persistent air leak for more than 7 days, chyle leak, wound infection, and cardiac problems that could be treated medically such as atrial fibrillation and heart failure. Among the patients with morbidity or mortality, anastomosis or bronchial stump-related complications including BPF, bronchovascular fistula, atelectasis, and bronchial stenosis were subgrouped to determine the negative effects of the operative procedure itself. A locoregional recurrence was defined as any recurrence in the ipsilateral hemithorax such as bronchial stump or anastomosis, ipsilateral remaining lobe, ipsilateral mediastinal lymph nodes, or ipsilateral mediastinal structures. A distant recurrence was defined as any recurrence at distant organs or in the contralateral lung.

All patients completed follow-up, and all the patients ($n = 451$) were included in the survival analysis. The follow-up period ranged from 1 to 154 months, with a median of 30.73 months (mean: 41.8 ± 36.7 months). The patients were subdivided into two groups, SL group and PN group. To create two comparable groups with common clinicopathologic background, we performed propensity score analysis, using nearest neighbor matching method of covariates, which includes age, sex, neoadjuvant therapy, cell type, and pathologic stage of tumor. Other variables such as tumor size, preoperative pulmonary function, and postoperative adjuvant therapy were compared to verify that these two groups are nearly identical for statistical comparison.

Statistical Analysis

Statistical analysis was performed using statistical software (SAS, version 9.1.3). Data are reported as the mean ± standard deviation or as a proportion. Survival rates were calculated according to the life-table (actuarial) method and were compared between groups with the Wilcoxon test. Time zero was the date of the operation. Other comparisons were made using an unpaired t test or χ^2 test. A p value less than 0.05 was considered to be significant.

RESULTS

Clinical Characteristics

Comparisons of the patients' clinical characteristics in the SL and PN groups are shown in Table 1. By performing nearest available pair matching, 105 patients in each group were eligible for analysis. The match model was favorable for analysis, i.e., area under the curve of receiver operating characteristic curve was 0.74621, and p value was 0.7532 by the Hosmer-Lemeshow test. All the covariates were well balanced, and there were no significant difference in preoperative pulmonary function of patients and performance of postoperative adjuvant treatment. Only the size of tumor was significantly greater in the PN group compared with the SL group (3.74 ± 1.86 in SL group and 5.20 ± 2.66 in PN group, $p < 0.001$).

TABLE 1. Comparison of Patient Characteristics: Sleeve Lobectomy and Pneumonectomy

	Sleeve Lobectomy	Pneumonectomy	*p*
Number	105	105	
Age (yr)	61.25 ± 8.89	62.24 ± 8.42	0.259
Gender (M/F)	99/6	98/7	0.439
Cell type			
Squamous cell carcinoma	91 (77.7%)	89 (71.9%)	0.700
Adenocarcinoma	8 (10.2%)	11 (18.7%)	
Large cell carcinoma	2 (2.5%)	3 (0.7%)	
Others[a]	4 (5.7%)	2 (3.4%)	
p-Stage			
IA/IB	4/40	2/41	0.920
IIA/IIB	2/30	3/33	
IIIA/IIIB	19/7	17/7	
IV	3	2	
Neoadjuvant therapy			
Chemotherapy	10 (9.52%)	10 (9.52%)	1.000
Radiotherapy	8 (7.62%)	6 (5.71%)	0.4795
Adjuvant therapy			
Chemotherapy	13 (12.4%)	6 (5.71%)	0.108
Radiotherapy	26 (24.76%)	16 (15.24%)	0.068
Tumor size	3.74 ± 1.86	5.20 ± 2.66	<0.001
Preoperative FEV1	2.45 ± 0.720	2.38 ± 0.67	0.180

[a] Other tumors included pulmonary sarcomas, adenosquamous carcinomas, etc. Low-grade malignant tumors such as mucoepidermoid carcinomas, and adenoid cystic carcinomas were excluded from the analysis.

FEV1, first second forced expiratory volume.

Mortality and Morbidity

As shown in Table 2, the operative mortality was 1.0% (1/105 patients) for the SL and 8.6% (8/105 patients) for the PN group ($p < 0.0001$). In the SL group, death occurred due to ARDS. In the PN group, causes of death included ARDS ($n = 6$), pneumonia ($n = 1$), and sudden cardiac arrest with an undetermined cause ($n = 1$). The rate and pattern of postoperative morbidity was similar in both groups (33.4% in SL group and 29.5% in PN group, $p = 0.376$). The distributions of morbidities in two groups showed no significant difference even when all of the morbidities were subdivided into major and minor complications.

Survival and Recurrence

The overall 3-year survival rates were 71.4% for the SL group and 41.8% for the PN group ($p < 0.0001$). The overall 5-year survival rates were 58.4% for the SL group and 32.1% for the PN group ($p = 0.0002$) (Figure 1). The data showed that patients in PN group had poorer survival than those in SL group ($p = 0.0002$, odd ratio of 3.14).

Locoregional recurrence pattern of the matched patients was showed in Table 3. Although direct comparison of recurrence pattern of two groups was not possible due to the pair-match design of the analysis, the composition of locoregional and distant recurrence was similar in two groups. Nevertheless, in 12 pairs having recurrence in both groups, there was no significant difference in pattern of recurrence ($p = 0.180$), even though the number of included subject was rather small to have statistical significance.

Functional Outcomes

Both the SL and the PN group had similar preoperative lung function. The mean preoperative FEV1 for the patients underwent PN was 2.38 ± 0.67 liter compared with 2.45 ± 0.720 liter for the patients who underwent SL ($p = 0.18$). Additionally, for the entire patients who underwent SL, the mean predicted post-PN FEV1 was 1.90 ± 0.50 liter and the mean actual postoperative FEV1 was 2.05 ± 0.55 liter, which was decreased by 18.5% compared with the preoperative FEV1 and increased by 7.9% compared with predicted post-PN FEV1. The correlation value between the predicted and measured FEV1 was 0.93.

TABLE 2. Postoperative Morbidity and Mortality

	Sleeve Lobectomy ($n = 157$)	Pneumonectomy ($n = 267$)	p
Operative mortality	1 (1.0%)	8 (8.6%)	<0.0001
Operative morbidity	34 (33.4%)	31 (29.5%)	
Major complication	9 (8.6%)	13 (12.4%)	
ARDS	4	7	
Bronchopleural fistula	4	5	
Empyema			
Bronchovascular fistula	1		
Chylothorax		1	
Minor complication	25 (23.8%)	18 (17.1%)	0.376
Pneumonia	2	2	
Atelectasis	3		
Vocal cord palsy	3	4	
Mild bronchial stenosis	3		
Prolonged air leak	7		
Hemothorax		1	
Atrial fibrillation	3	5	
Wound infection	4	6	

ARDS, acute respiratory distress syndrome.

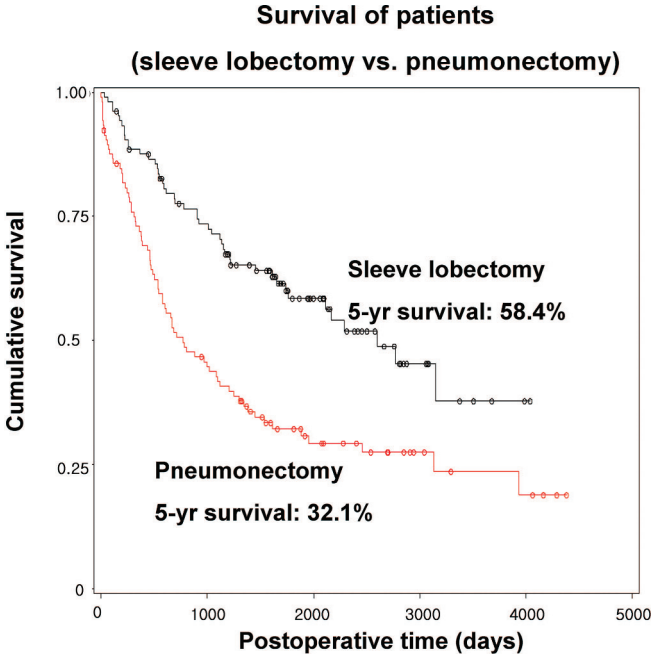

FIGURE 1. Cumulative survival curves of patients.

TABLE 3. Recurrence Pattern After Sleeve Lobectomy and Pneumonectomy

	Sleeve Lobectomy	Pneumonectomy	p
Total recurrence	32 (30.5%)	40 (38.1%)	0.180[a]
Locoregional	15 (14.3%)	17 (16.2%)	
Bronchial anastomosis or stump	2	3	
Distant	12 (11.4%)	23 (21.9%)	

[a] The comparison of recurrence pattern was conducted for only 12 pairs in which recurrence was occurred in two groups.

DISCUSSION

Sleeve resections have gained in popularity regardless of the preoperative pulmonary function status of patients.[1,4–6,10] The preservation of lung function is closely associated with the quality of life and low cardiopulmonary morbidity. On the other hand, the PN is associated with significant morbidity and mortality, including ARDS, BPF, and the post-PN syndrome. In our series, the SL was performed in patients who could have tolerated a PN, if only it was technically possible, hence both the SL and PN groups had a similar preoperative FEV1.

In recent reports, the SL has been performed in 3.4 to 13% of the patients diagnosed with a resectable lung cancer.[1,11] In our series, the SL was performed in 8.5% of the patients with lung cancer. Martin-Ucar et al.[12] reported that the increased use of bronchoplastic techniques decreased the need for a PN. As surgical experience accumulates, centrally located NSCLC may have a higher probability of being treated by bronchoplastic surgery.

SL should achieve certain oncological, operative, and functional requirements to be accepted as a standard procedure. The results of recent studies suggest that the long-term survival after SL is as favorable as that after PN, with a lower mortality and better quality of life, mainly due to the preservation of lung function.[1,7,12,13] In addition, local tumor control, which is a major concern with bronchoplasty, has been found to be acceptable.[1–4,6,7]

The major and minor complications were similar in both the SL and the PN group ($p = 0.376$) in our series. In particular, there were no significant differences in complications related with bronchial anastomosis or bronchial stump between the two groups. Nevertheless, the operative mortality was significantly lower after the SL (1.0%) compared with that after the PN (8.6%). Our results suggest that SL is a safer operative procedure, when compared with PN, even though bronchial anastomosis is performed.

The main reason for the hesitation in performing the SL is the concern about local recurrence. The local recurrence rate after SL ranges from 8 to 23%, whereas the local recurrence after the PN is reported to be 10 to 14%.[1,14] There was no significant difference in recurrence pattern between SL group and PN group in our study ($p = 0.180$). These results are consistent with other studies that showed a similar local recurrence rate between SL and PN. In most recent reports, the long-term survival after a SL, in stage I/II or N0/N1 disease, was similar to that after a PN.[1,5–7] Okada et al.[1] noted that the most important factor for survival after a SL was the nodal status; the patients with N2 disease showed poor survival compared with those with N0 and N1 disease. In our study, patients were stratified according to pathologic substage from the design of the study. Considering that, it could be said that the patients in the SL group had higher 5-year survival rate compared with those in the PN group.

In a recent prospective study, Balduyck et al.[15] reported that patients who had a SL returned to their baseline quality of life in less than 1 month after the surgery. By contrast, the PN patients had decreased physical and functional endurance during the first year of follow-up. Gaissert et al.[4] reported that the perfusion and ventilation of the reimplanted lung was compatible with that of the predicted lung function after a SL. In our study, the postoperative FEV1 after the sleeve resection was decreased by only 18.5% compared with the preoperative FEV1. These data show a complete recovery of the reimplanted lung after a SL.

In conclusion, SL is a safe and effective operation in the treatment of NSCLC. If anatomically feasible, SL is recommended as a favorable alternative to PN in the patients even with good pulmonary function.

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