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Safety and long-term outcome of sleeve lobectomy for non-small cell lung cancer

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[Abstract] **Background and Objective:** Pneumonectomy has been long term used as the standard surgical procedure for central type non-small cell lung cancer (NSCLC). Sleeve lobectomy has been performed in a small number of patients meeting the indications. This study was to compare the 5-year survival rate, operation related complications and mortality of sleeve lobectomy with pneumonectomy for NSCLC, and evaluate sleeve lobectomy in the surgical treatment for NSCLC. **Methods:** Ninety-three patients with NSCLC undergoing sleeve lobectomy (group A) and 571 patients with NSCLC undergoing pneumonectomy (group B) from January 1997 to December 2007 in Sun Yat-sen University Cancer Center were reviewed. The 5-year survival rate, operation related complications and mortality between the two groups were analyzed. **Results:** The overall 5-year survival for group A and group B were 42.0% and 31.5%, respectively ($P=0.015$). In the subgroup analysis, the 5-year survival of N0 ($P=0.007$) and N1 ($P=0.025$) patients were significant higher in group A than in group B, while the survival were not significantly different between N2 patients ($P=0.073$). The 5-year survival rates for bronchial and pulmonary arterial sleeve resection (the subset of group A) and pneumonectomy were not significantly different ($P=0.092$). There was no significant difference in local recurrences between the groups ($P=0.821$). The postoperative complication rates were 11.8% in group A and 20.7% in group B ($P=0.046$). There was no statistically significant difference in mortality between the two groups ($P=0.259$). **Conclusion:** The operative safety and long term efficacy of sleeve lobectomy are superior to pneumonectomy for NSCLC.

Key words: non-small cell lung cancer (NSCLC), sleeve lobectomy, pneumonectomy, efficacy

Nowadays, surgical resection for patients with non-small cell lung cancer (NSCLC) (from stage I to partial stage III) is still regarded as the most effective method of controlling the tumor. The main ways for surgical resections involve pulmonary lobectomy, pneumonectomy, sleeve lobectomy, and so on. The most common indication for sleeve lobectomy is lymph node metastasis or local tumor invasion, which involves the proximal part of the main stem

bronchus but spares the distal part. Before sleeve lobectomy, pneumonectomy was the main method for those patients mentioned above; but patients with poor lung function could not undergo such an operation. According to related studies, of all the patients with lung cancer, about 5% -13% can receive the sleeve lobectomy.^{1, 2} Compared to pneumonectomy, the so called specific complication and other common complications of sleeve lobectomy are not obviously increased.^{2,5} Moreover, in terms of long term survival, the 5-year survival rate of sleeve lobectomy group is higher than pneumonectomy. 6 Ninty-three patients undergoing sleeve lobectomy and 571 receiving pneumonectomy in our Center between January 1997 and December 2007 were retrospective analyzed to compare the safety and long-term survivals of these two procedures.

Data and Methods

General data. Between January 1997 and December 2007, 93 patients underwent sleeve lobectomy in the Department of Thoracic Oncology of Sun Yat-sen University Cancer Center, among which, 78 received sleeve lobectomy, and 15 received sleeve lobectomy combined with sleeve pulmonary artery resection. In the mean time, 571 patients underwent pneumonectomy. Their median age was 58 years and 56 years, respectively. There was no significant difference in clinical characteristics between the two groups (Table 1).

Radical excision is defined as completely resection of the tumor with systematic mediastinal and hilum lymphadenectomy (not lymph node sampling) with the negative bronchial stump. Sleeve lobectomy was performed for patients whose tumors could not be adequately removed by standard lobectomy, but could tolerate pneumonectomy. All patients had the residual tumor, and those who were confirmed positive bronchial margin or N3 lymph node metastasis by pathological examination were excluded from this study. The perioperative death was defined as: 1) death within 30 days after surgery; 2) death during the

Table 1 General characteristics of 664 patients with non-small cell lung cancer (NSCLC)

	Sleeve lobectomy n=93 [cases(%)]	Pneumonectomy n=571 [cases(%)]	P value
Sex			
Male	74(79.6)	482(84.4)	0.720
Female	19(20.6)	89(15.6)	0.720
Histologic type			
Squamous cell carcinoma	55(59.1)	346(60.6)	0.400
Adenocarcinoma	29(31.2)	182(31.9)	0.460
Adenosquamous carcinoma	4 (4.3)	24 (4.2)	0.620
Other	5 (5.4)	19 (3.3)	0.200
pT factor			
T1	20(21.5)	108(18.9)	0.520
T2	31(33.3)	205(35.9)	0.100
T3	33(35.5)	190(33.3)	0.480
T4	9 (9.7)	68(11.9)	0.540
pN factor			
N0	22(23.6)	114(20.0)	0.060
N1	34(36.6)	195(34.1)	0.240
N2	37(39.8)	262(45.9)	0.540
Pulmonary function			
FEV1(L)	1.81±0.41	1.72±0.39	0.220

hospitalization period after surgery; 3) death caused by operative failure after being discharged from the hospital. Recurrence is defined as: 1) local recurrence, presented as anastomotic recurrence and peripheral bronchial epithelial cancerization; 2) regional recurrence, presented as ipsilateral recurrence in the chest cavity; 3) distant recurrence, presented as the distant metastasis to the lymph node and other organs. The pathological staging was carried out according to the latest international staging of lung cancer in this study.

Follow-up and statistical analysis.

Out-patient return visits and telephone follow-up were performed regularly once a month along the life-long span. Kaplan-Meier Survival analysis was used, followed by log-rank test, to analyze the 5-years survival rate by SPSS 13.0. The chi-square test was used to analyze the postoperative complications and mortality. $p<0.05$ was considered statistically significant.

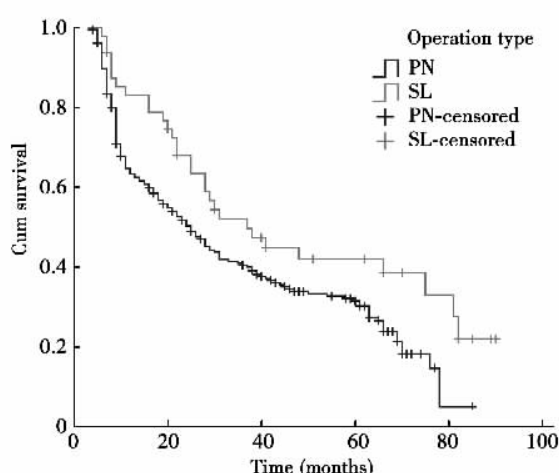


Figure 1 Cumulative survival curves of all patients with non-small cell lung cancer undergoing sleeve lobectomy or pneumonectomy ($P=0.015$).

Results

Comparison of postoperative complications and mortality. Two cases of death occurred in the sleeve resection group (2.1%), which received the double sleeve; 27 cases of death occurred in the pneumonectomy group (4.7%), which did not show significant difference ($p=0.082$). The early complication rate of the sleeve resection group was 11.8% (11/93), including four cases of lung infection, two cases of atelectasis, five cases of arrhythmia. The rate of bronchopleural fistula was 0. However, in the pneumonectomy group, the early complications rate was 20.5% (117/571), including three cases of bronchopleural fistula, 36 cases of lung infection, 21 cases of atelectasis, 41 cases of arrhythmia, six cases of heart failure, and 10 cases of chylothorax. The complications rates of the two group showed significant difference ($p=0.002$).

Difference in the survival rate of the two groups. The one-, three-, and five-year survival rates of sleeve resection was 83.1%, 52.0%, and 42.0%, respectively, and that of pneumonectomy was 63.4%, 40.5% and 31.5%, respectively (Fig. 1). The five-year survival rate between the two groups showed significant difference ($p=0.015$). Stratification research showed that the five-year

survival rate of the sleeve resection with N0 and N1 were 58.2% and 44.3%. But for the pneumonectomy group, the rate was 39.7% and 32.3%. Therefore, the therapeutic effect of sleeve resection was superior to the pneumonectomy ($p=0.007$, $p=0.025$). The five-year survival rate of patients in the stage of N2 showed no significant difference, which was 30.6% and 27.9%, respectively ($P=0.073$).

Comparison of the survival rate of double sleeve and pneumonectomy. Fifteen cases received double sleeve lobectomy in this study. The one-, three-, and five-year survival rate was 64.5%, 39.7%, and 32.5%, respectively. There was no significant difference in the survival rate between double sleeve group and pneumonectomy group ($p=0.092$).

Comparison of the recurrence rate. The recurrence rate of sleeve lobectomy group was 11.8% (11/93), whereas was 11.0% (63/571) in the pneumonectomy group, which showed no significant difference ($p=0.913$).

Discussion

Sleeve lobectomy for lung carcinoma was first described as a compromised operation for patients who were considered inadequate to tolerate pneumonectomy, and also for patients with low-grade malignant tumors and benign ones. When the sleeve lobectomy was first used for the patients, many clinicians raised doubts about the safety of its procedure and the long-term efficacy. As to the operation safety, bronchial end-to-end anastomosis may lead to anastomotic dehiscence and stenosis. With regards to long-term efficacy, bronchial stump from the tumor is relatively close, which may cause the recurrence and the distant metastasis, compared with the pneumonectomy.

The particular complications of bronchoplastic surgery involve anastomotic dehiscence, bronchovascular fistula and anastomotic stenosis. According to related studies, the incidence of anastomotic dehiscence and anastomotic stenosis is 0% -6%^{1,4,8,9} and the incidence of bronchovascular fistula is 3% -9%^{1,4,9,10}. In this study, none of the 93 cases occurred anastomotic

dehiscence. The early postoperative complication rate was 11.8%, mainly caused by lung infection and arrhythmia. Compared with the pneumonectomy, the early postoperative complication rate of the former one is fairly low. The death rate of sleeve lobectomy was reported 1.3%-7%,^{6,8,11,12} while the pneumonectomy was 4.1%-10%.^{6,8,9} The death rate of the two groups shows no significant difference. As compared to pulmonary lobectomy and pneumonectomy, sleeve lobectomy requires higher surgical skills. Improper handling of the anastomotic stoma would lead to special complications, which confine the practice of sleeve lobectomy only to patients whose pulmonary reserve were considered inadequate to tolerate pneumonectomy. However, with the development of the surgical technique, sufficient blood supply for the bronchi, proper tense for the anastomotic stoma and other ways to promote the healing of bronchi have decreased the complications of the this surgery. When the indication is appropriate, sleeve lobectomy is safer than pneumonectomy.

Patients received pneumonectomy will apparently affect the quality of life due to the decreased pulmonary reserve. Long-term complications of pneumonectomy include pulmonary hypertension and respiratory failure. It is also known that pneumonectomy is a kind of chronic disease.¹⁴ The use of sleeve lobectomy can maximize the retention of the lung tissue. It not only can raise the chances for patients who failed to receive pneumonectomy, but also increase the quality of life after the surgery. In the mean while, it can decrease the incidence of the long-term complications. According to many studies, sleeve lobectomy also achieved a better five-year survival rate. Ferguson et al.¹³ revealed that the five-year survival rate of sleeve lobectomy is 3.5%, higher than that of the pneumonectomy group in a meta-analysis of a 14 year (1990-2002) review. And also the quality of life and cost-effectiveness analysis are superior to whole-lung resection. Deslauriers et al.⁸ obtained similar results in a study, which compared 184 cases of sleeve lobectomy with 1046 cases of pneumonectomy.

Many scholars believe that, patients should receive the sleeve lobectomy whenever a radical excision is allowed.^{3,12,14} Some scholars suppose that patients with N1 disease can undergo the sleeve lobectomy; but for patients with N1 and N2 disease, pneumonectomy is a better choice. At present, it remains great controversy about the application of these procedures in patients with N2 disease. Some authors suppose that pneumonectomy does not show any superiority compared with the sleeve lobectomy, because many patients died from distant metastasis rather than local recurrence. Okada et al.¹⁴ reported that the three-, five- and 10-year survival rates of sleeve lobectomy wer significantly higher (61%, 48%, 36%) than those of the pneumonectomy group (36%, 29%, 19%). In patients with N0 and N1 disease, the survival rate of sleeve lobectomy group was higher than that of the pneumonectomy group, but showed no statistically significant difference. In this study, we analyzed the N0, N1 and N3 group separately, the results were similar with those in the study mentioned above.

Although a large number of studies of lung cancer sleeve resection affirm the long-term effect, there is still some controversy. Kim et al.⁶ reported that there was no statistically significant difference ($p=0.509$) after comparing the three-, five- and 10-years survival rates in a study of 49 cases of sleeve lobectomy and 200 cases of pneumonectomy. Further stratified study showed that the three- and five-year survival rate of sleeve lobectomy were 94.1% and 88.2%, whereas they were 78.6% and 74.8% in the pneumonectomy group ($p=0.118$). The sleeve lobectomy group had a better survival rate, but showed no statistical difference. In the patients with N1 and N2 disease, it showed no statistical difference. Otherwise, the tumor-free survival rate of pneumonectomy was superior to that of sleeve resection ($p=0.017$).

According to the report, compared with the pneumonectomy group, the local recurrence rate of sleeve lobectomy did not increase. The local recurrence rate of sleeve lobectomy was 11.8%, and the pneumonectomy group was 20.5% . Tedder et al.¹ reported that the recurrence rate of

sleeve lobectomy was 13% . Mehran et al.⁹ reported it was 23%, Van Schil et al.¹² reported it was 20%, and Okada et al.¹⁴ showed the lowest rate of 8%. Compared with the pneumonectomy group, the rate did not increase. The occurrence of regional recurrence and distant metastasis is due to the tumor staging and the effect of the radical systematic lymphadenectomy regardless the selection of the surgical procedure.

Currently, sleeve lobectomy is widely used as a standard procedure in the surgical treatment of lung cancer. This study shows that sleeve lobectomy is a safer procedure than pneumonectomy, and does not increase the incidence of complications. In the long-term effect, the five-year survival rate and the quality of life are superior to the pneumonectomy. Additionally, the study of the double sleeve procedure shows no advantage as compared to the pneumonectomy. Therefore, thoracic surgeon should know the indication for the disease, improve the operation skills and increase perioperative management in order to offer the patient a better treatment.

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