Left sleeve lobectomy versus left pneumonectomy for the management of patients with non-small cell lung cancer

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Keywords
Non-small cell lung cancer; pathological stage; pneumonectomy; sleeve lobectomy; survival.

Abstract

Background: The study was conducted to compare the outcomes of sleeve lobectomy (SL) and pneumonectomy (PN) for management of the left lung in patients with non-small cell lung cancer (NSCLC).

Methods: One hundred and thirty-five patients who underwent left SL (n = 87) or left PN (n = 48) for NSCLC from January 2006 to December 2011 were enrolled in this retrospective study. Left SL was performed when technically possible. The clinicopathological features and treatment outcomes in both groups were compared. Survival was evaluated using the Kaplan-Meier method, and significant differences were calculated using the log-rank test. Multivariate analysis was conducted using the Cox proportional hazards model to analyze significant variables associated with the outcomes of left SL.

Results: There were no significant differences in general clinicopathological features (age, gender, lymph node metastasis, pathological stage, and complications of bronchial fistula) between patients who underwent left SL and left PN. The operation duration was markedly longer and the extent of bleeding was greater for left SL than left PN; however patients who underwent left SL achieved significantly longer overall survival than patients who underwent left PN. The outcomes of left SL were only associated with pathological stage.

Conclusions: Our results indicate that left SL may offer superior survival than left PN in selected patients. If anatomically feasible, left SL may be a preferred alternative to left PN for NSCLC patients. Pathological stage is an important factor to determine the outcome of SL.

Introduction

Lung cancer is the leading cause of cancer-related mortality worldwide,¹ in which non-small cell lung cancer (NSCLC) accounts for up to 85%.² Despite great advances in diagnostic and therapeutic options, the five-year overall survival (OS) rate of patients with NSCLC remains < 15%.³

Surgical resection remains the mainstay of management for localized NSCLC.⁴,⁵ Pneumonectomy (PN) is considered the gold standard for the treatment of centrally located NSCLC; however, PN is accompanied with high risks of postoperative morbidity, mortality, and reduced quality of life.⁷,⁶ Sleeve lobectomy (SL) was first introduced for patients with compromised lung function unable to tolerate PN. SL was initially considered as an alternative procedure to PN because PN has a complex surgical technique and complete resection is not always possible.¹⁰ Nevertheless, SL is widely used at present and is preferred in suitable patients because of the better long-term survival outcomes and fewer incidences of operative complications and postoperative mortality.¹¹,¹² Although accumulating studies have compared the outcomes of SL and PN for the management of patients with NSCLC, little research has been conducted to compare such outcomes for the management of the left lung.

In this retrospective study, we compared left SL and left PN focusing on operative outcomes and survival to further determine which was more favorable for the management of the left lung in NSCLC patients. The significant
clinicopathological features associated with the outcomes of surgery were also determined. The findings of this study provide theoretical guidance for clinical practice.

Methods

Study population and data collection

A total of 135 patients who were diagnosed with primary NSCLC and underwent left lung resection surgery in our hospital from January 2006 to December 2011 were enrolled in this retrospective study. Left SL was performed whenever technically feasible, otherwise left PN was performed. Consequently, 87 patients underwent left SL and 48 underwent left PN for NSCLC. The clinicopathological features, including age, gender, lymph node metastasis, pathological stage, and complications (bronchial fistula), were collected before surgery and the treatment outcomes, such as operation duration, bleeding, length of hospital stay, tumor size, and OS were also recorded. All patients were followed-up annually for five years. The ethics committee of our hospital approved the study and each participant provided written informed consent.

Statistical analysis

The Kolmogorov-Smirnov test was used to test the normal distribution of enumeration data. If data were normally distributed, they were presented as mean \pm standard deviation and significant differences between groups were evaluated using a t-test. If the data were not normally distributed, they were expressed as interquartile range and significant differences were calculated using the Mann-Whitney U test. Differences in qualitative data between groups were analyzed using the chi-squared (\( \chi^2 \)) test. The Kaplan-Meier method was used for univariate survival analysis and significant differences were compared by log-rank test. In order to further analyze significant variables associated with the outcomes of left SL, multivariate analysis using the Cox proportional hazards model was performed and evaluated using hazard ratios (HR) with 95% confidence intervals (CIs). SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses and a two-sided \( P \) value of <0.05 indicated statistical significance.

Results

Eighty-seven patients who underwent left SL and 48 who underwent left PN for NSCLC were eligible for this study. No significant difference was found in regard to general clinicopathological features, including age, gender, lymph node metastasis, pathological stage, and complications (bronchial fistula), between left SL and left PN patients (all \( P > 0.05 \)) (Table 1).

The outcomes of left SL and left PN in patients with NSCLC were subsequently compared. As shown in Table 2, the operation duration of left SL was markedly longer (\( P = 0.011 \)), and the extent of bleeding of left SL was significantly greater (\( P < 0.001 \)) than left PN. However, patients who underwent left SL achieved significantly longer OS than patients who underwent left PN (\( P = 0.014 \)). No significant difference was observed between the two groups regarding tumor size or length of hospital stay (\( P > 0.05 \)). Notably, Kaplan-Meier univariate survival analysis revealed that OS was longer in patients who underwent left SL than left PN (\( P = 0.031 \)) (Fig 1).

Multivariate analysis was therefore conducted to identify the significant clinicopathological features associated with the outcomes of left SL (Table 3). The results showed that

Table 1 Comparison of the clinicopathological features in patients undergoing sleeve lobectomy and left pneumonectomy

| Clinicopathological features            | Sleeve lobectomy (n = 87) | Left pneumonectomy (n = 48) | Statistic | \( P \) |
|----------------------------------------|---------------------------|-----------------------------|-----------|-------|
| Gender                                 |                           |                             | 0.210†    | 0.646 |
| Male, n (%)                            | 80 (92.0)                 | 43 (89.6)                   |           |       |
| Female, n (%)                          | 7 (8.0)                   | 5 (9.3)                     |           |       |
| Lymph node metastasis                  |                           |                             | 0.339†    | 0.560 |
| No, n (%)                              | 22 (25.3)                 | 10 (20.8)                   |           |       |
| Yes, n (%)                             | 65 (74.7)                 | 38 (79.2)                   |           |       |
| Pathological stage                     |                           |                             |           |       |
| 1, n (%)                               | 20 (23.0)                 | 10 (18.5)                   | 0.278†    | 0.870 |
| 2, n (%)                               | 24 (27.6)                 | 12 (25.0)                   |           |       |
| 3-4, n (%)                             | 43 (49.4)                 | 26 (54.2)                   |           |       |
| Complication (bronchial fistula)       |                           |                             | 2.082†    | 0.149 |
| No, n (%)                              | 87 (100.0)                | 47 (97.9)                   |           |       |
| Yes, n (%)                             | 0 (0.0)                   | 1 (2.1)                     |           |       |
| Age, mean (SD)                         | 57.2 (7.6)                | 56.5 (7.8)                  | 0.537‡    | 0.592 |

†\( \chi^2 \) test; †t-test; SD, standard deviation.
the outcomes of left SL were only associated with pathological stage \((P < 0.001)\). Other clinicopathological features, such as age, gender, lymph node metastasis, and tumor size, had no significant effects on the outcome in NSCLC patients who underwent left SL \((P > 0.05)\).

**Discussion**

In this retrospective study, we compared the outcomes of NSCLC patients who underwent left SL and left PN. The results showed that although operation duration and the extent of bleeding in patients who underwent left SL were significantly greater than in patients who underwent left PN, patients who underwent left SL achieved significantly longer OS than patients who underwent left PN, suggesting that left SL might be a preferred alternative for patients with NSCLC. Significantly, the outcomes of left SL were only associated with pathological stage, implying the important role of pathological stage in determining survival in NSCLC patients who undergo left SL.

Since SL was introduced for the treatment of lung cancer, it has been accepted as a reliable and safe procedure for the management of NSCLC patients who have low-grade, centrally located lesions and cannot tolerate PN as they do not have sufficient pulmonary reserve.\(^1\)\(^1\)\(^3\) SL by single-incision video-assisted thoracic surgery is reportedly feasible and safe for patients with left lower central lung cancer.\(^1\)\(^4\) In centrally located NSCLC, extended SL is considered an alternative approach to avoid PN.\(^1\)\(^5\) Morgant et al. demonstrated that PN and bronchial SL could affect the rates of postoperative death following lung cancer surgery and the odd ratio (OR) range for PN was higher than for bronchial SL.\(^1\)\(^6\) Although the operation duration and extent of bleeding of left SL were significantly greater than for left PN in our study, there were no significant differences regarding postoperative death and length of hospital stay between the two groups. This result may be attributed to the low mortality associated with left PN in our study. In addition, we found that the OS of patients who underwent left SL was significantly longer than those who underwent left PN, which was consistent with previous findings. Ferguson and Lehman demonstrated that better long-term survival was achieved in patients with anatomically appropriate early-stage lung cancer after SL than PN.\(^1\)\(^7\) Ludwig et al. reported five-year OS rates of 39% for SL and 27% for PN, and confirmed that SL should be performed whenever possible.\(^1\)\(^8\) Maurizi et al. concluded that even after induction chemotherapy, SL represented a valid therapeutic procedure providing better long-term survival than PN.\(^1\)\(^9\) Pagès et al. also suggested that SL provided better outcomes than PN and was the preferred technique when technically feasible.\(^2\)\(^0\) Based on our results, we therefore speculate that left SL may offer superior survival over left PN in selected patients, and could be a preferred alternative for NSCLC patients whenever possible.

Furthermore, the results of multivariate analysis showed that the outcomes of left SL were only associated with pathological stage, implying the important role of pathological stage on determining survival for NSCLC patients. In a previous study, Matsuoka et al. demonstrated that pathological stage is a key factor to determine survival for NSCLC patients.\(^2\)\(^1\) In addition, Hanagiri et al. found that the five-year survival rates of SL patients with different pathological nodal status \((N0, N1, \text{and} \ N2)\) were 100.0%, 87.5%, and 41.7%, respectively,\(^2\)\(^2\) indicating that survival in SL patients can be affected by pathological nodal status. Given the similar results obtained in this

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**Table 2** Comparison of the outcomes of sleeve lobectomy and left pneumonectomy in NSCLC patients

| Clinicopathological features | Sleeve lobectomy \((n = 87)\) | Left pneumonectomy \((n = 48)\) | Statistic | \(P\) |
|-----------------------------|-------------------------------|-------------------------------|-----------|------|
| Operation duration (min)    | 261 (57.5)                    | 234 (60.0)                    | 2.579‡    | 0.011|
| Tumor size (cm)             | 3.4 (1.7)                     | 3.8 (1.7)                     | −1.474‡   | 0.143|
| Bleeding (mL)               | 90 (80-100)                   | 30 (20-50)                    | −8.185‡   | < 0.001|
| Length of hospital stay (days) | 11 (9-14)                   | 12.5 (9-14)                   | −0.593‡   | 0.553|
| Overall survival (months)   | 46 (24-63)                    | 30 (10-58)                    | −2.463‡   | 0.014|

\(^{†}\)Mann-Whitney U test; \(^{‡}\)Mann-Whitney U test; NSCLC, non-small cell lung cancer.
study, we speculate that pathological stage is an important factor affecting the outcome of SL in NSCLC patients.

In conclusion, this retrospective study indicates that left SL may offer superior survival than left PN in selected patients. If anatomically feasible, left SL should be performed to provide greater long-term survival benefits to NSCLC patients. Pathological stage is an important factor to determine the outcome after left SL. Despite these promising results, further prospective studies with larger sample sizes are required to verify our observations.

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Disclosure

No authors report any conflict of interest.

References

1 Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin 2015; 65: 87-108.
2 García-Camplayo R, Bernabé R, Cobo M et al. SEOM clinical guidelines for the treatment of non-small cell lung cancer (NSCLC) 2015. Clin Transl Oncol 2015; 17: 1020-9.
3 Tsai MF, Wang CC, Chen JJ. Tumour suppressor HLJ1: A potential diagnostic, preventive and therapeutic target in non-small cell lung cancer. World J Clin Oncol 2014; 5: 865-73.
4 Gorenstein LA, Sonett JR. The surgical management of stage i and stage ii lung cancer. Surg Oncol Clin N Am 2011; 20: 701-20.
5 Faris N, Smeltzer MP, Lu F et al. Evolution in the surgical care of non-small cell lung cancer (NSCLC) patients in the mid-south quality of surgical resection (MS-QSR) cohort. Semin Thorac Cardiovasc Surg 2017; 29: 91-101.
6 Ma QL, Guo YQ, Shi B, Tian YC, Song ZY, Liu DR. For non-small cell lung cancer with T3 (central) disease, sleeve lobectomy or pneumonectomy? J Thorac Dis 2016; 8: 1227-33.
7 Fell SC. A history of pneumonectomy. Chest Surg Clin N Am 1999; 9: 267.
8 Cusumano G, Marra A, Lococo F et al. Is sleeve lobectomy comparable in terms of short- and long-term results with pneumonectomy after induction therapy? A multicenter analysis. Ann Thorac Surg 2014; 98: 975-83.
9 Bernard A, Deschamps C, Allen MS et al. Pneumonectomy for malignant disease: Factors affecting early morbidity and mortality. J Thorac Cardiovasc Surg 2001; 121: 1076-82.
10 Park JS, Yang HC, Kim HK et al. Sleeve lobectomy as an alternative procedure to pneumonectomy for non-small cell lung cancer. J Thorac Oncol 2010; 5: 517-20.
11 Shi W, Wei Z, Sun H, Shao Y. Sleeve lobectomy versus pneumonectomy for non-small cell lung cancer: A meta-analysis. World J Surg Oncol 2012; 10: 1-9.
12 Andersson SEM, Rauma VHS, Rääsänen JV, Ilonen IK, Salo JA. Bronchial sleeve resection or pneumonectomy for non-small cell lung cancer: A propensity-matched analysis of long-term results, survival and quality of life. 2015; 7: 1742-8.
13 Nagayasu T, Yamasaki N, Tsuchiya T et al. The evolution of bronchoplasty and broncho-angioplasty as treatments for lung cancer: Evaluation of 30 years of data from a single institution. Eur J Cardiothorac Surg 2016; 49: 300-6.
14 Fan JQ, Yao J, Chang ZB, Wang Q, Zhao BQ. Left lower sleeve lobectomy and systematic lymph node dissection by complete video-assisted thoracic surgery. J Thorac Dis 2014; 6: 1826-30.
15 Berthet JP, Paradelo M, Jimenez MJ, Molins L, Gómezcaro A. Extended sleeve lobectomy: One more step toward avoiding pneumonectomy in centrally located lung cancer. Ann Thorac Surg 2013; 96: 1988-97.
16 Morgant MC, Pagès PB, Orsini B et al. Time trends in surgery for lung cancer in France from 2005 to 2012: A nationwide study. Eur Respir J 2015; 46: 1131-9.
17 Ferguson MK, Lehman AG. Sleeve lobectomy or pneumonectomy: Optimal management strategy using

Table 3 Multivariate analysis of key variables associated with the outcomes of sleeve lobectomy

| Variables                                | B   | SE   | Wald | P    | HR  | 95% CI         |
|------------------------------------------|-----|------|------|------|-----|---------------|
| Pathological stage (vs. 1)               |     |      |      |      |     |               |
| 2                                        | 2.138 | 0.441 | 75.341 | < 0.001 | 8.482 | 3.571-20.145  |
| 3                                        | 4.169 | 0.502 | 23.466 | < 0.001 | 64.658 | 24.157-173.062 |
| Age                                      | −0.014 | 0.013 | 1.231 | 0.267 | 0.986 | 0.962-1.011   |
| Gender (female vs. male)                 | −0.358 | 0.532 | 0.454 | 0.501 | 0.699 | 0.247-1.982   |
| Lymph node metastasis (Yes vs. No)       | 0.076 | 0.757 | 0.010 | 0.919 | 1.079 | 0.962-1.146   |
| Tumor size (cm)                          | −0.006 | 0.073 | 0.007 | 0.934 | 0.994 | 0.862-1.146   |

Cl, confidence interval; HR, hazard ratio.
decision analysis techniques. Ann Thorac Surg 2003; 76: 1782-8.

18 Ludwig C, Stoelben E, Olschewski M, Hasse J. Comparison of morbidity, 30-day mortality, and long-term survival after pneumonectomy and sleeve lobectomy for non-small cell lung carcinoma. Ann Thorac Surg 2005; 79: 968-73.

19 Maurizi G, D’Andrilli A, Anile M et al. Sleeve lobectomy compared with pneumonectomy after induction therapy for non-small-cell lung cancer. J Thorac Oncol 2013; 8: 637-43.

20 Pagès PB, Mordant P, Renaud S et al. Sleeve lobectomy may provide better outcomes than pneumonectomy for non-small cell lung cancer. A decade in a nationwide study. J Thorac Cardiovasc Surg 2017; 153: 184-95.

21 Matsuoka H, Nishio WT, Harada H, Tsubota N. Survival of resected non-small cell lung cancer patients according to pathological stage. Jpn J Lung Canc 2002; 42: 181-6.

22 Hanagiri T, Baba T, Ichiki Y et al. Sleeve lobectomy for patients with non-small cell lung cancer. Int J Surg 2009; 8: 39-43.