

Surgical Outcomes in Small Cell Lung Cancer

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Background: The experience of a single-institution regarding surgery for small cell lung cancer (SCLC) was reviewed to evaluate the surgical outcomes and prognoses. **Materials and Methods:** From July 1990 to December 2009, thirty-four patients (28 male) underwent major pulmonary resection and lymph node dissection for SCLC. Lobectomy was performed in 24 patients, pneumonectomy in eight, bilobectomy in one, and segmentectomy in one. Surgical complications, mortality, the disease-free survival (DFS) rate, and the overall survival rate were analyzed retrospectively. **Results:** The median follow-up period was 26 months (range, 4 to 241 months), and there was one surgical mortality (2.9%). Six patients (17.6%) experienced recurrence, all of which were systemic. Eight patients died during follow-up; four died of disease progression and the other four died of pneumonia or of another non-cancerous cause. The three-year DFS rate was $79.2 \pm 2.6\%$ and the overall survival rate was $66.4 \pm 10.5\%$. Recurrence or death was significantly prevalent in the patients with lymph node metastasis ($p=0.001$) as well as in those who did not undergo adjuvant chemotherapy ($p=0.008$). The three-year survival rate was significantly greater in the patients with pathologic stage I/II cancer than in those with stage III cancer (84% vs. 13%, $p=0.001$). **Conclusion:** Major pulmonary resection for small cell lung cancer is feasible in selected patients. Patients with pathologic stage I or II disease showed an excellent survival rate after surgery and adjuvant treatment. Prospective randomized studies will be needed to define the role of surgery in early-stage small cell lung cancer.

Key words: 1. Lung neoplasms
2. Lung surgery
3. Carcinoma, oat cell

INTRODUCTION

Small cell lung cancer (SCLC) has a poor prognosis because of its rapid growth rate and early metastatic dissemination [1,2]. In general, systemic chemotherapy, with or without radiotherapy, has been recommended as the appropriate therapy, and surgery has had only a limited role [3]. Pulmonary resection has been used as part of a combination therapy [4,5] or for residual lesions following concurrent chemoradiotherapy (CCRT). Pulmonary resection has also been

used for mixed type lesions with non-small cell lung cancer (NSCLC). There have only been a few reports regarding surgical outcomes in patients with SCLC [6-9]. Surgery does have an established role for treating SCLC. We investigated the outcomes and risk factors of surgery in the patients from a single institution who underwent major pulmonary resection for SCLC within the past 20 years.

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MATERIALS AND METHODS

A total of 3,194 patients underwent major pulmonary resection for malignant neoplasm at our institution from April 1990 to December 2009. A pathology review confirmed SCLC in 34 of these patients (0.01%). The pulmonary resections were performed via a posterolateral thoracotomy (n=31) or video-assisted thoracoscopic surgery (VATS) (n=3). Mediastinal lymph node dissections were routinely performed, and all patients who had any component of SCLC seen on histology were included in this study. The Kaplan-Meier analysis was used to plot the survival curves and the rates of freedom from recurrence as well as to compare the survival rates between stage I and II, and stage III disease. Univariate Cox regression analyses were used for risk factor analysis of death or disease recurrence. Statistical analyses were performed using SPSS ver. 16.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was defined as a 2-sided p-value ≤ 0.05 . This study was conducted using a retrospective chart review. The seventh edition of the American Joint Committee on Cancer (AJCC) Cancer Staging was used for the stage classification.

RESULTS

1) Patient characteristics

A total of 34 patients with SCLC underwent major pulmonary resection. There were 28 males (82.4%) and six females (17.6%), and the mean age was 64 years (range, 44 to 76 years). Three patients underwent neoadjuvant chemotherapy. Lobectomy was performed in 24 patients (70.6%), and pneumonectomy was performed in 8 patients (23.5%). A segmentectomy and bilobectomy were both performed in one patient (2.9%) (Table 1). Mediastinoscopic lymph node dissection followed by lobectomy using VATS was performed on three patients. The other thirty-one patients underwent posterolateral thoracotomy.

2) Surgical outcomes

There was one case of surgical mortality (2.9%). This patient died of sudden cardiac arrest, and the cause of shock was thought to be bleeding at the pneumonectomy site. There were no major postoperative complications in any of the oth-

Table 1. Patient characteristics (n=34)

Variables	Values
Gender (male)	28 (82.4)
Age (yr)	61.7 \pm 8.8
Follow-up period (mo)	53.4 \pm 63.8
Clinical stage	
I	21 (61.8)
II	9 (26.5)
III	4 (11.8)
IV	0 (0)
Pathological stage	
I	10 (29.4)
II	16 (47.1)
III	8 (23.5)
IV	0 (0)
Upstaging	13 (38.2)
Downstaging	4 (11.8)
Surgical extent	
Lobectomy	24 (70.6)
Pneumonectomy	8 (23.5)
Segmentectomy	1 (2.9)
Bilobectomy	1 (2.9)
Concomitant resection*	3 (8.8)
Cell type	
Pure SCLC	24 (70.6)
Mixed type	10 (29.4)
Squamous cell carcinoma	4 (11.8)
Adenocarcinoma	3 (8.8)
Large cell carcinoma	2 (5.9)
Other	1 (2.9)

Values are presented as mean \pm standard deviation or number (%). SCLC=small cell lung cancer.

*Major pulmonary resection with surrounding tissues, i.e., chest wall, rib, pericardium, diaphragm, etc.

er cases.

Pure SCLC was confirmed in 24 patients (70.6%), and mixed type tumors with NSCLC was confirmed in 10 patients (29.4%) on the postoperative histological examination. Squamous cell lung cancer was most often accompanied by a mixed histology (n=4, 11.8%). Twenty-six patients had pathologic stage I or II disease, and eight patients had stage III disease (Table 1).

Thirty patients (88.2%) received adjuvant therapy. Nineteen patients (55.9%) received only radio-therapy. Ten patients (29.4%) received CCRT, and one patient (2.9%) received only chemotherapy. Adjuvant therapy was not performed in three patients because of either their poor general condition

Table 2. Treatment combined with surgical resection in patients with small cell lung cancer

Variables	Values
Neoadjuvant therapy	3 (8.8)
Adjuvant therapy	30 (88.2)
Radiotherapy only	19 (55.9)
Chemotherapy+radiotherapy	10 (29.4)
Chemotherapy only	1 (2.9)
None	3 (8.8)

Values are presented as number (%).

Table 3. Surgical outcomes for patients with small cell lung cancer

Variables	Values
Recurrence	6 (17.6)
Local	0 (0)
Systemic	6 (100.0)
Death	9 (26.5)
Operative mortality	1 (2.9)
Disease progression	4 (11.8)
Pneumonia or sepsis	2 (5.8)
Pulmonary thromboembolism	1 (2.9)
Other	1 (2.9)

Values are presented as number (%).

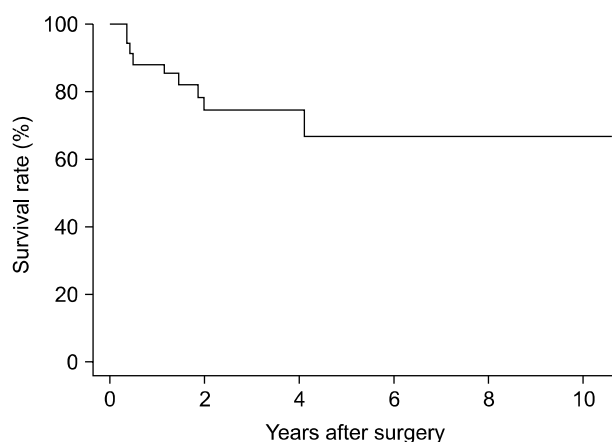
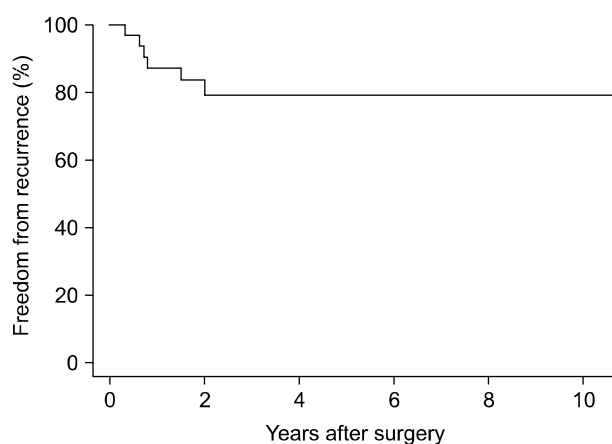
or other complications (Table 2).

The median follow-up period was 26 months (range, 4 to 241 months). There were eight late deaths (26.5%) during the follow-up period; four died of disease progression and the other four died of pneumonia or another non-cancerous cause. The cancer recurred in six cases (17.6%), which were all systemic recurrences (Table 3).

In this study, the overall five-year survival rate was 66.4% (Fig. 1) and the three-year disease-free survival rate was 79.2% (Fig. 2). The three-year survival rate according to the pathologic stage was 84% in patients with stage I and II disease and 13% in patients with stage III disease ($p=0.001$) (Fig. 3).

3) Risk factors for death or recurrence

The risk factors for death or disease recurrence were analyzed using the univariate Cox-regression hazard model. As the number of the deaths and patients with disease recurrence

**Fig. 1.** Overall survival rate determined using the Kaplan-Meier method. The overall survival rate was $66.4\pm 10.5\%$ at five years after surgery.**Fig. 2.** Freedom from recurrence rate after surgical resection, determined using the Kaplan-Meier method. The freedom from recurrence rate was $79.2\pm 2.6\%$ at five years after surgery.

was too small for statistical analysis, we analyzed the risk factors for death or disease recurrence. Lymph node metastasis ($p=0.001$) and the absence of adjuvant chemotherapy ($p=0.008$) were shown to be risk factors for death or recurrence (Table 4).

DISCUSSION

In general, the role of surgery in SCLC is limited as SCLC is usually treated using chemotherapy or CCRT [3,10]. The important role of chemotherapy in SCLC has been

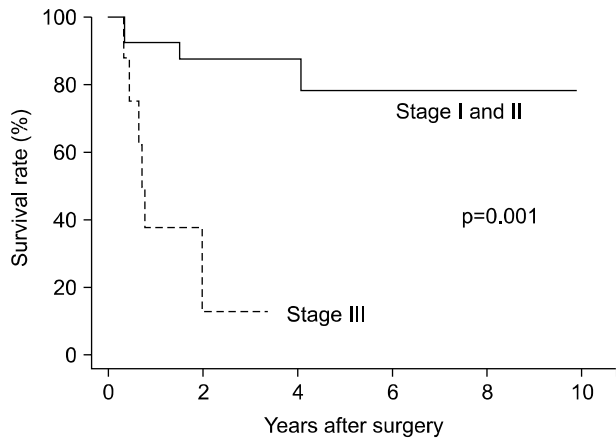


Fig. 3. Comparison of the survival rates in the stage I, II, and III groups. The stage I and II groups showed a significantly higher survival rate than the stage III group ($p=0.001$).

well-established by clinical trials [9,11,12]. Despite the development of new chemotherapeutic agents for decades, SCLC remains a disease with a high mortality rate and a low cure rate, even in limited stage groups [11]. Despite their initial responses to therapy, most patients with SCLC develop local recurrence [12].

There have been some previous reports regarding the role of surgery and its outcome in patients with SCLC. Shah et al. [13] reported that the five-year survival rate was 43% when treated with only surgery in 28 patients with SCLC. Schreiber et al. [14] indicated that the use of surgery, particularly lobectomy, was associated with favorable survival outcomes. There were other reports regarding the surgical outcome using adjuvant therapies [1,15-17]. In these reports, in the majority of cases, the use of surgery as part of multi-modality therapy had more successful outcomes than those of conventional therapies. As seen in previous reports, current CCRT protocols have demonstrated local failure rates of approximately 50% [18]. Complete surgical resection after induction CCRT has shown control of local relapse in almost 100% [19]. This was particularly noticeable in the early stage groups (T1-2, N0, M0). In our study, 84% of the stage I and II group and 13% of the stage III group patients showed a three-year survival rate. Histologically mixed tumors with both SCLC and NSCLC components may fail to meet CCRT protocol requirements since there is less sensitivity of the NSCLC component to chemotherapy. It has been shown that

Table 4. Risk factor analysis for death or disease recurrence

Variables	HR	95% CI	p-value
Age (> 60 yr)	0.97	0.90–1.04	0.347
Gender (male)	0.60	0.16–2.25	0.445
Neoadjuvant therapy	0.89	0.11–7.03	0.908
Tumor size (> 3 cm)	0.93	0.66–1.33	0.666
T stage	1.87	0.92–3.80	0.085
N stage	5.72	2.17–15.61	0.001*
TNM stage	11.19	2.85–44.04	0.001*
Tumor location (right)	1.05	0.31–3.48	0.941
Extent of surgery*	0.73	0.19–2.75	0.896
Adjuvant therapy	0.16	0.04–0.63	0.008*

HR=hazard ratio; CI=confidence interval; TNM=tumor-node-metastasis.

*Comparison of the risk of the extent of surgery by scoring (1=wedge resection, segmentectomy, lobectomy; 2=bilobectomy; 3=pneumonectomy).

the final histological findings for tumors that were initially reported as SCLC indicated that they contained NSCLC components in 11% to 25% of patients [20]. In our study, 29.4% of the patients had NSCLC components according to the pathology review.

CONCLUSION

Overall, the five-year patient survival rate was 66.4% in this study. Lymph node metastasis and the absence of adjuvant chemotherapy were risk factors for patient death or tumor recurrence. Our study had some limitations. It was a retrospective investigation with only a small number of subjects. Despite these factors, according to our study results, major pulmonary resection for SCLC was feasible in selected patients. Prospective, randomized studies will be needed to determine the role of surgery in early-stage SCLC.

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