

## Results of Surgical Treatment for Small Cell Lung Cancers

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We analyzed the data for patients with small cell lung cancer, especially as regards comparison of the results of surgical treatment before and after the introduction of multimodal chemotherapy treatments.

Sixty cases with small cell lung cancer were admitted in our department between January, 1955 and December, 1993. Among them, 38 cases underwent pulmonary resection. To evaluate the efficacy of the multimodal treatment including cisplatin with surgical therapy, patients were divided whether pulmonary resection was performed before 1983 (Group A) or after 1984 (Group B). There were no differences in sex and stage between two groups, but ages and operative procedures were significantly different ( $p < 0.05$ ). Ages were older in Group B (65.5 years) than in Group A (58.1 years) and operations were lesser in Group B (lobectomy or segmentectomy 87.0 %) than in Group A (pneumonectomy or bilobectomy 53.5 %).

The operative mortality rates were 13.3 % (2/15) in Group A and 4.3 % (1/23) in Group B. Survival rate at 3 years of Group A was only 6.7 % and no patients survived more than 4 years. While, survival rates of Group B at 3 and 5 years were 24.2 %. The 5 years survival rate of patients with Stage I and II of Group B was 46.9 % and that of Stage III and IV was 8.5 %.

It is concluded that surgical resection of limited small cell lung cancer (Stage I and II) with intensive chemotherapy is an efficient therapeutic approach.

**Key words:** small cell lung cancer, pulmonary resection, preoperative chemotherapy, prognosis

Small cell lung cancer (SCLC) is a highly malignant tumor that grows rapidly and spreads by lymphatic or hematogenic routes in the early phase (1). For this reason, surgical treatment has been considered as contra-indicated for SCLC and systemic chemotherapy with or without radiation therapy has usually been performed on patients with SCLC in the past (2). Recently the use of multimodal chemotherapy such as cyclophosphamide, adriamycin and vincristine (CAV), CAV and etoposide or cisplatin and etoposide (PE) has induced complete remission in 33 to 46 % of patients with SCLC and response rates were reported in 80 to 100 % (3, 4, 5). Despite this, many cases had local recurrence including primary lesion after the complete

response, and the 2-year survival rate of patients with the complete response was reported as only less than 20 % (3, 6). These results showed that chemotherapy alone or in combination with x-ray therapy did not improve the longer-term survival of patients with SCLC. For this reason, interest has turned to the use of surgical resection with chemotherapy.

We analyzed our data of patients with SCLC especially in regards to comparison of the results of surgical treatment before and after the introduction of multimodal chemotherapy treatments including CAV or cisplatin.

### Materials and methods

Sixty patients with SCLC were admitted to the First Department of Surgery, Nagasaki University Hospital, between January, 1955 and December, 1993. The patients were divided into two groups (Table 1). The first group covered patients admitted between 1955 and 1983 when no systemic multi-drug chemotherapy was given to the patients, and the second group covered 1984 to 1993 when surgical treatment combined with aggressive chemotherapy was introduced. There were 28 cases in the first group (A) and 32 in the second group (B). There were no differences of the sex or the mean age between the two groups. Stages of the disease were almost the same in the two groups. Over 70 % of the patients had advanced SCLC. The therapeutic regimen of Group A was pulmonary resection in 15 cases (53.6 %), thoracotomy without lung resection in 5 (17.9 %) and no operation in 8 (28.6 %), while that of Group B was lung resection in 23 (71.9 %), exploratory thoracotomy in one (3.1 %) and no surgery in 8 (25.0 %). The resection rate was greater and the rate of exploratory thoracotomy was less in Group B. The reason some patients received no surgical treatment was chiefly due to the advanced stage of the disease such as N2, N3 and/or T4.

To evaluate the effectiveness of surgical treatment, analysis was conducted for only the cases with pulmonary resection for SCLC (Table 2). There were 15 patients with lung resection in Group A and 23 in Group B. All patients were men in Group A, while 17 cases were men and 6 were

**Table 1.** Patients characteristics (all cases).

		Group A (1955-1983)	Group B (1984-1993)	
Sex	Male	25	23	N.S.
	Female	3	9	
Age(years)	Mean	58.2	62.8	N.S.
	Range	(40-80)	(50-78)	
Stage	I	5	7	N.S.
	II	3	1	
	III A	14	14	
	III B	5	6	
	IV	1	4	
Operation	None	8	8	N.S.
	Exploratory thoracotomy	5	1	
	Pulmonary resection	15	23	

**Table 2.** Patients characteristics (resected cases).

		Group A (1955-1983)	Group B (1984-1993)	
Sex	Male	15	17	N.S.
	Female	0	6	
Age(years)	Mean	58.1	65.5	p<0.05
	Range	(40-76)	(50-78)	
Stage	I	3	7	N.S.
	II	3	1	
	III A	9	10	
	III B	0	2	
	IV	0	3	
Operation	Pneumonectomy	5	1	p<0.05
	Bilobectomy	3	2	
	Lobectomy	4	13	
	Bronchoplasty	1	6	
	Sgmentectomy	2	1	
Adjuvant	None	4	4	N.S.
	Chemotherapy pre	0	1	
	post	7	13	
	pre & post	2	5	
Radiotherapy	5(3)*	2(2)*		

pre : preoperative, post : postoperative,  
pre&post : preoperative and postoperative  
\* : Radiotherapy combined with chemotherapy

women in Group B. The mean age was 58.1 years (range 40 to 76) in Group A and 65.5 (range 50 to 78) in Group B ( $p < 0.05$ ). The stage of lung cancer was Stage I in 3 cases (20.0%), Stage II in 3 (20.0%) and Stage III A in 9 (60.0%) in Group A, while the patients of Group B were Stage I in 7 (30.4%), Stage II in one (4.3%), Stage III A in 10 (43.5%), Stage III B in 2 (8.7%) and Stage IV in 3 (13.0%). There was no significant difference of stage between

two groups and more than 60% of the cases had advanced disease. The operative procedure for the patients in Group A was pneumonectomy in 5 cases (33.3%), bilobectomy in 3 (20.0%), lobectomy in 4 (26.7%), bronchoplastic lobectomy in one (6.7%) and segmentectomy in 2 (13.3%), while for the patients in Group B it was pneumonectomy in only one (4.3%), bilobectomy in one (4.3%), lobectomy in 13 (56.5%), bronchoplastic lobectomy in 6 (26.1%) and segmentectomy in one (4.3%). In Group B, the rates of pneumonectomy or bilobectomy decreased and the rates of lobectomy and/or bronchoplasty increased, compared with Group A ( $p < 0.05$ ).

Eleven cases (73.3%) of Group A and 19 (82.6%) of Group B received the adjuvant therapy pre-or/and postoperatively. Six cases of Group B had preoperative aggressive chemotherapy. The adjuvant therapy for the cases of Group A was radiation in 2 cases, chemotherapy (cyclophosphamide or mitomycin C) in 6 and chemo and radiotherapy in 3, while those of the Group B were chemotherapy in 17 cases and chemo and radiotherapy in 2. Patients received cyclophosphamide 50-100 mg/m<sup>2</sup>, doxorubicin 30 mg/body and vincristine 3 mg/body ( $n = 3$ ) or cisplatin 80-100 mg/m<sup>2</sup> (Day 1), vp-16 100 mg/m<sup>2</sup> (Day 1, 2, 3) ( $n = 5$ ) or carboplatin 350 mg/m<sup>2</sup> (Day 1) and vp-16 75 mg/m<sup>2</sup> (Day 1, 5) ( $n = 4$ ), cisplatin 50 mg/m<sup>2</sup> (Day 1), cyclophosphamide 400 mg/m<sup>2</sup> (Day 1) and vincristine 1 mg/m<sup>2</sup> (Day 1) ( $n = 2$ ) and others ( $n = 5$ ).

The survival rates were calculated by the Kaplan-Meier method and survival data were compared by log-rank test.

## Results

The operative mortality rate (death within 30 days after operation) was 13.3% (2/15) in Group A and 4.3% (1/23) in Group B. One case of Group A died of acute respiratory failure due to contra-lateral bronchial obstruction with a tumorous mass on the operating table and another case died of a pulmonary edema on the first post-operative day. One case of the Group B died of tumorous emboli of the bilateral common iliac arteries on the first post-operative day. Two cases of Group B died of respiratory failure due to pneumonia 37 days and 3 months after operation during the same hospitalization, respectively. Major postoperative complications occurred in 3 cases of Group A (20.0%) and 5 of Group B (21.7%). These results showed that preoperative aggressive chemotherapy did not increase postoperative mortality or morbidity.

All cases in Group A died of recurrent disease within 39 months with a mean survival of 14 months. In group B, 17 cases have died of diseases from one month to 7 years and 6 months, and 6 are alive without recurrence from 4 months to 8 years after operation. The three-year survival rate of all cases of Group A was 6.7% and three and five-year survival rates of patients of Group B were 24.2%

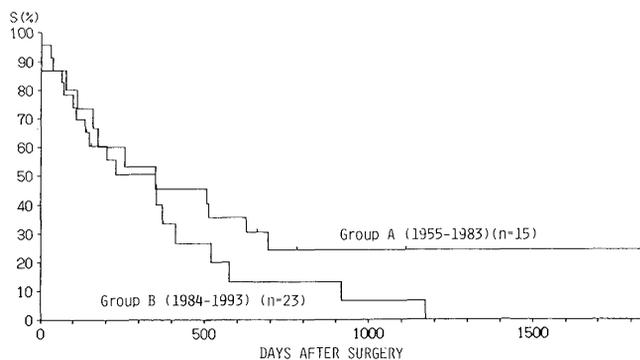


Fig. 1. A comparison of survival of patients with SCLC who had pulmonary resection from 1955 to 1983 (Group A) or from 1984 to 1993 (Group B).

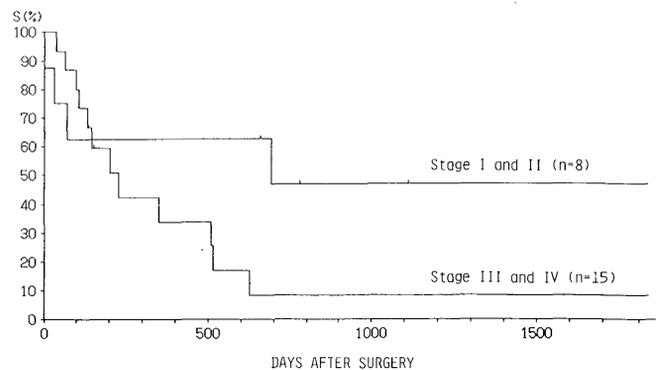


Fig. 2. A comparison of survival of patients of the Group B who had pulmonary resection for stage I and II or for stage III and IV.

(Fig. 1). The five-year survival rate of patients of Group B with Stages I and II (46.9%) was better than that of cases with Stages III and IV (8.5%) (Fig. 2), but there was no statistically significant difference between two groups ( $p = 0.099$ ).

## Discussion

Small cell lung cancer is a highly malignant tumor with rapid growth and frequent lymphatic and hematologic metastasis. In early 1970s, operative treatment was discarded for SCLC as the initial treatment because no better survival was shown in surgical cases than in those with radiation therapy (2). After this study, systemic chemotherapy with or without radiation therapy was the main modality of treatment for SCLC. Recent advances of chemotherapy for small cell lung cancer including CAV or PE have achieved a high response rate (3, 4, 5), but long term survivors were few and the 2-year survival rate was less than 20% (6). Even if cases had a complete response after aggressive chemotherapy, local recurrence including primary lesions occurred with high frequency (7), and a low response rate of chemotherapy for recurrent SCLC and non-small cell lung cancer was found histologically in the recurrent lesions after a complete response was observed (8, 9), therefore, interest has turned to surgical treatment for cases with limited SCLC. Recently, Shepherd et al. (10) reported an 86% local control rate in patients with lung resection for limited SCLC. In our department, only 5 cases with SCLC were resected during 10 years from 1974 to 1983, but resected cases for SCLC have increased since 1984 and 23 have been resected during the last 10 years. In recent reports, five-year survival rates of cases with surgery combined with aggressive chemotherapy have reached above 50% for Stage I and II SCLC (10, 11). Surgical treatment for Stage III A SCLC has also been

reported (11, 12, 13). Salzer et al. (11) reported the results of the surgical treatment for Stage III A SCLC and good results were obtained in cases with no metastasis or only hilar metastasis and the survival of cases with mediastinal node involvement was the same as for non-SCLC. However, the role of operation for Stage III A SCLC remains undefined (14). In our study, prognosis for the cases in Group A were poor regardless of the stage and no patients survived more than 4 years. Poor prognosis was attributed to inaccurate preoperative staging and insufficient adjuvant chemotherapy. In Group B, long-term survivors appeared with surgery combined with chemotherapy. They were cases with no metastasis or only hilar node metastasis, but cases with mediastinal node metastasis and/or metastasis into adjacent organs had poor prognosis. Careful preoperative assessment of staging of the disease for surgery and sufficient adjuvant chemotherapy are important to achieve good results.

As operative procedures, pneumonectomy or bilobectomy were frequent in Group A, but pulmonary preserving operations such as lobectomy or bronchoplastic operations increased in Group B. This reflects early detection of the disease and the advance of operative techniques.

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