



Salvage thoracic surgery in patients with primary lung cancer



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ABSTRACT

Background: Patients with advanced non-small cell lung cancer (NSCLC) continue to have a poor prognosis. The majority of patients are not indicated for surgery for a radical cure, and systemic chemotherapy is the mainstay of treatment. However, long-term survival is rare due to the resistance to therapy. On the other hand, surgery is performed only under certain conditions for colon cancer and esophageal cancer. Few reports are available about salvage thoracic surgery in patients with primary lung cancer. The purpose of this study was to show the outcomes of salvage surgery for lung cancer, and we discuss possible future treatment strategies based on our findings.

Methods: Three hundred and fifty-two patients with primary lung cancer underwent surgical resection, and we evaluated those who underwent salvage operations. We also examined the relationships between the performance of a salvage operation and the clinicopathological characteristics of the patients. The clinical outcomes of salvage surgery for lung cancer were assessed.

Results: Salvage thoracic operations were performed in eight (2.3%) of the 352 patients. The surgical procedures were lobectomy in four patients, segmentectomy in two, and pneumonectomy and wedge resection were each performed in one patient. There was no postoperative mortality. All patients were alive at the time of the analysis. The mean follow-up period for the salvage operation cases was 14.0 months. No significant correlation was identified between the incidence of salvage surgery and the age, gender, histology, postoperative stay or hospital stay. The incidence of advanced stage disease was higher in the salvage cases than in the overall cases.

Conclusions: Salvage thoracic surgery was possible, and moderately improved the prognosis, without prolongation of the postoperative stay or hospital stay. A salvage operation might be considered a reasonable and proper treatment for carefully selected patients.

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1. Introduction

Lung cancer remains a leading cause of death worldwide [1]. However, advanced NSCLC, which is the most prevalent type of lung cancer, is not generally indicated for surgery as a radical cure, and systemic chemotherapy is the mainstay of treatment [2]. However, long-term survival is rare due to the resistance of the disease to therapy [3]. In general, stage IIIB and IV NSCLC are considered

to be contraindicated for surgery, the same as for breast cancer [4]. However, salvage operations are sometimes performed under certain conditions in patients with advanced colon cancer [5] and esophageal cancer [6]. However, there are few reports currently available about salvage surgery in patients with primary lung cancer, and the efficacy and safety of salvage thoracic operations have not been fully elucidated. We herein report the results of a retrospective study performed to evaluate the performance of salvage surgery for primary lung cancer.

2. Materials and methods

2.1. Patients and their characteristics

This study was approved by the University of Occupational and Environmental Health Ethics Committee (H125-119). The characteristics and clinicopathological factors were evaluated retrospectively. The preoperative investigations included chest radiographs and a high-resolution computed tomographic (CT)

Abbreviations: NSCLC, non-small cell lung cancer; PS, performance status; CT, computed tomographic; RFS, relapse free survival; FVC, forced vital capacity; FEV1, forced expiratory volume in one second; EFS, event-free survival; CRF, chronic renal failure; AS, aortic valve stenosis; CDDP, cisplatin; CBDCA, carboplatin; PEM, pemetrexed; SBRT, stereotactic body radiation therapy; PFS, progression-free survival; DTX, docetaxel.

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Table 1
Characteristics of the cases treated by salvage operations.

Case	Sex	Age	Stage ^a	Histology ^b	Previous treatment ^c	Duration of previous therapy (mos)	Effect of previous treatment	y-Stage ^d
1	F	66	IIIA	AD	Gefitinib	3	PR	IIIA
2	M	69	rec ^e	AD	Gefitinib	12	SD	rec
3	M	53	IV	SQ	None	–	–	–
4	M	64	IV	AD	None	–	–	–
5	F	72	IIIB	SQ	CBDCA/PTX and S1	5 and 10	SD	IB
6	F	81	IIIB	AD	None	–	–	–
7	M	70	IV	AD	Cyberknife for brain metastasis	0.5	Not evaluated	IV
8	F	38	IV	ADSQ	Tacrolimus ^f	6 ^f	–	IV

^a Clinical stage.

^b SQ: squamous cell carcinoma, AD: adenocarcinoma, ADSQ: adenosquamous cell carcinoma.

^c CBDCA: carboplatin, PTX: paclitaxel.

^d Clinical stage after previous treatment before surgery.

^e rec: recurrence after surgery.

^f Tacrolimus for systemic lupus erythematosus was stopped for lung cancer, and the tumor shrunk.

scan of the thorax. Three hundred and sixty-two patients with primary lung cancer underwent surgical resection between January 2011 and March 2013 in the Second Department of Surgery at the University of Occupational and Environmental Health, Kitakyushu, Japan. Ten of these patients underwent incomplete resection. As a result, 352 patients were excluded from the further analysis. The remaining subjects included 213 males and 139 females in this series, with a mean age of 69.0 years (range 18–89 years). All but one of the patients was Japanese. The histological types included 236 adenocarcinomas, 80 squamous cell carcinomas and 36 other types. The pathological stages were diagnosed as stage IA in 162 patients, IB in 73, II in 65, III in 46 and stage IV in five patients, and one patient had recurrent disease after surgery according to the international pathological staging system [7]. Salvage thoracic surgery was defined as the surgical resection of persistent or recurrent primary lung tumors after previous local treatments in a narrow sense, a matter of urgency such as hemoptysis (palliative intent), and in cases judged to be contraindicated for chemotherapy or definite radiation due to severe comorbidities, despite a clinical diagnosis of stage IIIA, IIIB or IV disease initially [8,9]. We calculated the predicted residual pulmonary function using the following formula: Predicted residual pulmonary function = pulmonary function \times (1 – the resected pulmonary segments/number of pulmonary segments on the actual state). In case 3, a pulmonary function test was not conducted due to hemoptysis. Surgery is indicated for patients with a predicted postoperative forced vital capacity (FVC) of >800 ml/m², a forced expiratory volume in one second (FEV1) of >600 ml/m² and a FEV1 >40% [10,11].

2.2. Postoperative management and follow-up

The data were collected retrospectively for all patients and included a detailed history, age, sex, clinical staging, pathological staging, histology, treatment modalities and the surgical details. The postoperative variables assessed included the postoperative complication(s), postoperative hospital stay and the total length of the hospital stay. The patients were discharged from the hospital after surgery, and the follow-up data were collected via the outpatient department. The patients were evaluated every three months by a physical examination, chest roentgenography an analysis of blood chemistry, and measurements of the tumor marker levels. Chest and abdominal CT scans, brain MRI, and a bone scintiscan were obtained every six months for the first two years after surgery, and annually thereafter in most cases. Additional examinations were performed if any symptoms or signs of

recurrence were detected. The relapse-free survival (RFS) was calculated from the date of registration to the date of recurrence. The event-free survival (EFS) was calculated as the time from surgery to recurrence, or to progression in salvage cases. A follow-up was conducted in all patients. The mean follow-up period was 456 days.

2.3. Statistical analyses

Categorical variables were evaluated using the chi-square test, and the *t*-test was utilized to analyze continuous variables between the two groups. Differences were considered to be statistically significant for values of $p < 0.05$. The data were analyzed using the StatView software package (Abacus Concepts, Inc., Berkeley, CA).

3. Results

3.1. Characteristics of the salvage operation cases

Salvage operations were performed in eight (2.3%) of the 352 patients. A summary of the details of all of these cases is given in Table 1. The cases were evenly split between males and females. The mean age of the patients was 64.1 years old. Five cases had adenocarcinoma. There were various reasons why the operation was performed. Previous chemotherapy or radiotherapy had been administered in three cases, and all had pathological proof of residual disease (Table 2). The PS of these eight patients was 0–1 except for one case. The mean predicted postoperative FVC, FEV1 and percentage of the FEV1 in all cases except for case 3 was 1734 ml/m², 1431 ml/m² and 69%, which exceeded the afore mentioned limits by a large margin. The surgical procedures were lobectomy in four patients, segmentectomy in two and pneumonectomy and wedge resection in one patient each. Every tumor was resected with negative margins. There was no postoperative mortality, and postoperative complications occurred in two cases. The mean postoperative stay and total hospital stay were 14.5 and 19.4 days. All patients were alive at the time of the analysis. The mean follow-up period of the salvage operation cases was 14.0 months. The mean EFS of the salvage operation cases were 5.9 months (Table 3). In case 4, we initially judged the patient to be contraindicated for chemotherapy due to chronic renal failure (CRF) and severe aortic valve stenosis (AS), because cisplatin (CDDP) requires hydration to prevent renal toxicity, which also adds a risk for lung edema in the presence of both cardiac and renal failure. However, carboplatin (CBDCA) and pemetrexed (PEM), which have more favorable

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