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Ipsilateral Lung Resections for Postoperative Recurrent or Second Primary Lung Cancer

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Abstract

Purpose: This study aimed to report our experience with repeated ipsilateral pulmonary resection in patients with local recurrent and second primary lung cancer, and to assess operative mortality and long-term outcomes.

Methods: The medical records of all patients who underwent a second ipsilateral lung resection for local recurrent and second primary lung cancer from 2000 to 2016 were reviewed.

Results: Thirteen (0.9%) patients (group 1) had a local recurrence. The second operation consisted of completion pneumonectomy in three cases, completion lobectomy in two, segmentectomy in three, and wedge resection in five. The remaining eight (0.6%) patients (group 2) had a new primary lung cancer. The second pulmonary resection was completion pneumonectomy in one, completion lobectomy in one, lobectomy in four, and segmentectomy in two. Overall hospital mortality was 4.8%, including one postoperative death. Five-year survival after the second operation was 35% and 85% with a median survival of 29 and 36 months in groups 1 and 2, respectively (p>0.05).

Conclusion: These long-term results justify the need for complete work-up of patients with ipsilateral local recurrent or second primary lung cancer in our hospital. Surgical treatment should be considered when the patients have no distant metastasis and are in good health.

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Introduction

The recurrence of lung cancer after complete resection generally results in a poor prognostic status and short life expectancy. When a single lung nodule is detected during follow-up, it sometimes suggests the possibility of systemic metastasis; however, there is always concern regarding the development of second primary lung cancer. Although there are criteria that can be applied in this situation, it is sometimes very difficult to distinguish between a new lung cancer and a recurrent one. Therefore, some researchers have insisted an aggressive surgical approach, whenever possible, as the survival rate after surgery is quite good [1-4]. On the other hand, many doubts have been expressed concerning the utility of repeated surgery for recurrent lung cancer due to the treatment's poor overall survival [5,6]. In particular, ipsilateral re-operation is technically demanding because of the occurrence of dense adhesions and a high risk of pulmonary artery bleeding. However, the widespread use of video-assisted thoracic surgery for lung cancer has made re-resection of the lung more common. We are convinced of the value of an aggressive surgical approach in all patients whose functional condition makes resection possible. Therefore, the aim of this study was to report the results from ipsilateral re-resection for patients with recurrent or second primary lung cancer, focusing on mortality and survival characteristics of these two groups of patients.

Materials and Methods

From 2000 to 2016, 1,390 patients underwent radical pulmonary resection for non-small-cell lung carcinoma (NSCLC). Of these, 21 (1.5%) consecutive patients underwent repeated ipsilateral surgical resections for recurrent lung cancer after curative resection for lung cancer. The second operation was conducted for local recurrence (n=13, 0.9%; group 1) or second primary lung cancer (n=8, 0.6%; group 2). The second primary lung cancers were defined using the criteria outlined by Martini and Melamed [7]. In cases where the histology was the same as the first surgery, subtypes and the degree of differentiation of the histology were considered to distinguish a new lung cancer from a recurrent one. Patient and surgical characteristics and outcomes are shown in Table 1.

The operations were performed by a group of three thoracic surgeons' at a single hospital. Every

Table 1: Patient characteristics.

	Patients (n=21)
Age (y), median (range)	66 (46-79)
Gender (Male: Female)	14:07
Histology	
Squamous cell carcinoma	4 (19.0%)
Adenocarcinoma	13 (61.9%)
Bronchioloalveolar carcinoma	2 (9.5%)
Large cell carcinoma	1 (4.8%)
Carcinoid	1 (4.8%)
P-Stage (first resection)	
IA	14(66.7%)
IB	2 (9.5%)
IIA	1 (4.8%)
IIB	0 (0%)
IIIA	2 (9.5%)
IIIB	1(4.8%)
IV	1 (4.8%)
Type of pulmonary resection (first resection)	
Wedge resection	1 (4.8%)
Segmentectomy	4 (19.0%)
Lobectomy	14 (58.6%)
Bilobectomy	2 (9.5%)
Pneumonectomy	0 (0%)
Interval from first resection (mo), mean ± SD	20.3 ± 15.0
<12 mo	2 (31.0%)
12-24 mo	1 (41.3%)
24-48 mo	0 (0%)
>48 mo	18 (13.8%)

SD: Standard Deviation. Data are presented as number (percentage), unless noted otherwise

patient was followed-up by the same surgeons on a regular follow-up schedule (every 3 months for 2 years, then every 6 months for the next 3 years). A chest Computed Tomography (CT) was performed every 6 months. When recurrent disease was suspected in the lung, repeated CT scan was performed every 2 months, and Positron Emission Tomography (PET), bronchoscopy and/or percutaneous needle aspiration were also performed. The descriptive statistics are summarized as the median or mean for the continuous variables and as frequencies and percentages for the categorical variables. Survival and the disease free rate were analyzed by the Kaplan-Meier and log-rank methods on SPSS for Windows, Version 22.0 (SPSS Inc., Chicago, IL, U.S.A.). All differences were considered significant at a p value less than 0.05.

Results

Cumulative survival curves of all 21 patients with local recurrent and second primary lung cancer are shown in Figure 1. Five-year survival after the second operation was 58.0% with a median survival of 38 months. Overall hospital mortality of all patients was 4.8%.

Group 1: local recurrences

Thirteen patients (male, n=9; female, n=4) underwent a second pulmonary resection for local recurrence. Mean age at the time of the first operation was 60 years (range, 40-70 years). Only one patient was symptomatic at the time of detection. In the other 12 patients, the cancer recurrence was detected at the scheduled examination at 4-6 months. The local recurrences developed at a mean interval of 59 months (range, 3-126 months). The detailed operative characteristics of patients in group 1 are described in Table 2, and the cumulative disease-free survival curve is shown in Figure 2. The 5-year disease-free survival rate for patients with recurrent tumor after the second operation was 43%.

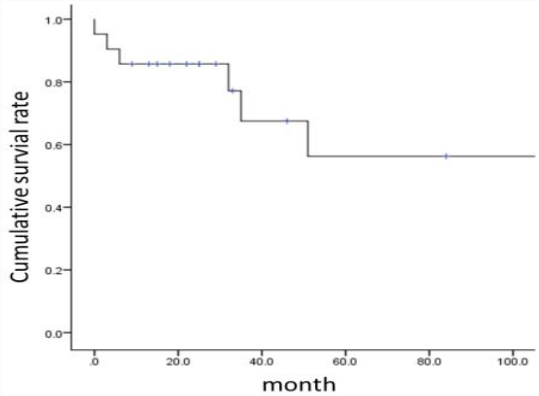

Figure 1: Actuarial survival from the time of the second operation for patients with local recurrent and second primary lung tumor (21 cases).

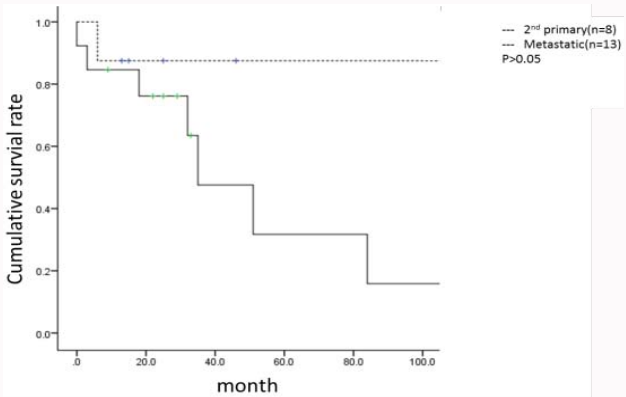

Figure 2: Actuarial survival for recurrent lung cancer with 2nd primary and metastatic tumor after the second operations.

In group 1, the first resection was considered radical for all patients. The second resection was considered radical in all but one patient; of these 12 patients, complications occurred in three patients and included cardiac arrhythmias in one, recurrent nerve paralysis in one, and prolonged air leak in one. No patients died intra operatively. The mean follow-up period of the 13 patients with local recurrence who survived the second operation was 38 months (range, 3-109 months). Currently, six of the 13 patients are alive and are free from any known recurrent cancer after 109, 33, 29, 25, 22 and 15 months from the second operation, respectively. Of the seven patients who died, recurrent lung cancer was known to be present, and was identified as the cause of death in four patients. Five-year survival after the second operation was 35% with a median survival of 29 months (Figure 3).

Group 2: second primary lung carcinomas

Eight patients (male, n=5; female, n=3) underwent a second pulmonary resection for second primary lung cancer. Mean age at

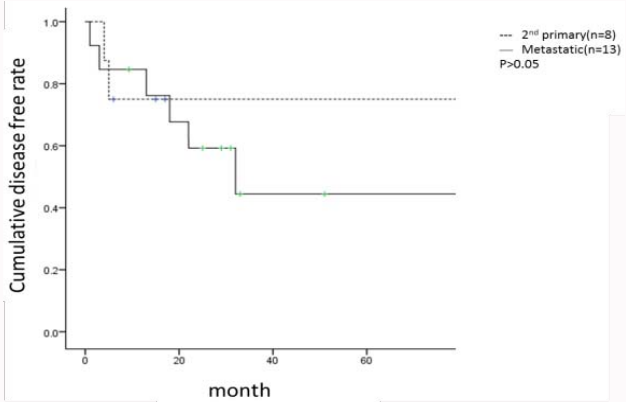

Figure 3: Cumulative disease free rates of recurrent lung cancer with 2nd primary and metastatic tumor.

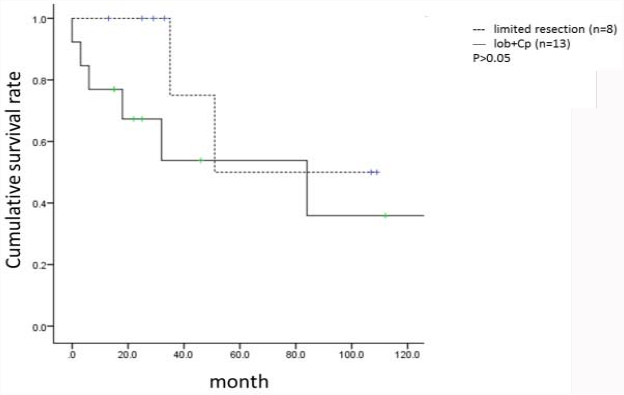

Figure 4: Acturial survival of recurrent lung cancer with 2nd primary and metastatic tumor according to the surgical procedure.

the time of the operation for the first primary cancer was 60.0 years (range 48-74 years). The criteria that were used to distinguish that the second lung tumor was a new primary cancer included different cell type in two patients and location in a different ipsilateral lobe in six. Type of resections, histology, postoperative staging, and the second operations are shown in Table 3. The second cancer was symptomatic in only one patient. The mean interval between the initial and second treatment was 88 months (range, 54-144 months). Resection of the tumor was complete in all cases. The 5-year disease-free survival rate for patients with second primary lung cancer after the second operation was 74% (Figure 2).

One patient died during the follow-up period because of a third recurrence of the cancer, which were multiple brain metastases. The mean follow-up for the seven patients who survived the second operation was 75 months (range, 13-144 months). Currently, all seven patients are alive with three patients who have evidence of recurrent cancer. Five-year survival after the second operation was 85% with a median survival of 36 months (Figure 3).

Actuarial survival of all 21 patients according to the surgical procedure is shown in Figure 4. No significant difference was detected in survival between the limited resection group (n=8) and lobectomy/completion peumonectoy group (n=13) in this study.

Discussion

Recent improvements in diagnostic tools, such as high-resolution CT scan and PET scan, allow physicians to detect recurrent lung cancer much earlier than before. Westeel et al. [8] reported that intensive follow-up may improve patient survival through the detection of recurrences at an asymptomatic stage after surgery for NSCLC. For the detection of residual or recurrent NSCLC, Haberkorn et al. reported that, PET had a sensitivity of 100% and a specificity of 61.5% to 92.0%, showing the superiority of PET scan compared to conventional CT scan [9]. The early detection of recurrences may be more effective in improving patient outcomes compared to therapy that is administered when the patient becomes symptomatic from the tumor [10]. Moreover, early detection of the tumor enables the use of limited resection, thereby avoiding riskier surgeries, such as completion lobectomy or completion pneumonectomy.

The Lung Cancer Study Group reported that for primary lung cancer [11], a resection is less extensive than lobotomy, which places the patient at an increased risk of local recurrence, and subsequently decreases the chances of long-term survival. The limited resections

Table 2: Operative characteristics of patients with recurrent lung cancer.

	First disease			Recurrence				
No.	Procedure	Histology	Stage	Interval (mo)	Location	Procedure	Re-relapse	Result
1	LLL	Squamous cell carcinoma	IA	3	central	LP	yes	dead
2	LLL	Squamous cell carcinoma	IIIA	60	peripheral	W- LS1+2	no	alive
3	RLL	Carcinoid	IA	60	central	RML	yes	dead
4	RUL	Adenocarcinoma	IIIA	57	peripheral	RS8 Seg	no	dead
5	LUL	Large cell carcinoma	IIIB	4	central	LP	yes	dead
6	LUL	Adenocarcinoma	IA	126	peripheral	LP	yes	dead
7	RUL	Adenocarcinoma	IA	24	peripheral	W- RS4	no	dead
8	W-LS10	Bronchioloalveolar carcinoma	IA	100	peripheral	W- LS1+2	no	alive
9	LUL	Bronchioloalveolar carcinoma	IB	60	peripheral	W- LS8	no	alive
10	RS7,10 Seg	Adenocarcinoma	IA	63	intermediate	c-RLL	yes	alive
11	LUL	Squamous cell carcinoma	IA R	64	peripheral	LS8,9 Seg	no	alive
12	RS2 Seg	Adenocarcinoma	IA	65	intermediate	c-RUL,W- RS5	yes	dead
13	RML	Adenocarcinoma	IA	77	central	RLL	yes	alive

C: Completion; LLL: Left Lower Lobectomy; LP: Left Pneumonectomy; LUL: Left Upper Lobectomy; RLL: Right Lower Lobectomy; RML: Right Middle Lobectomy; RP: Right Pneumonectomy; RUL: Right Upper Lobectomy; Seg: Segmentectomy; W: Wedge resection

Table 3: Operative characteristics of patients with metachronous lung cancer.

	First disease			Recurrence						
No	Procedure	Histology	Stage	Time (mo)	Location	Procedure	Histology	Relapse	Result	Comment
1	RUL	Squamous cell carcinoma	IA	144	central	RLL	Adsq	yes	dead	
2	RUL	Adenocarcinoma	IA	120	intermediate	RS6+8 Seg	Adenocarcinoma	no	alive	
3	RLL	Adenocarcinoma	IA	92	intermediate	c-RP	Adenocarcinoma	no	alive	
4	RML	Adenocarcinoma	IA	54	peripheral	RUL	Adenocarcinoma	no	alive	
5	RLL	Adenocarcinoma	IA	86	peripheral	RML	Adenocarcinoma	no	alive	
6	LUL	Squamous cell carcinoma	IIIA	61	intermediate	LS6 Seg	Adenocarcinoma	yes	alive	Adenocarcinoma relapse
7	LS1+2 Seg	Adenocarcinoma	IA	69	intermediate	c-LUL	Adenocarcinoma	no	alive	
8	LS1+2 Seg +W-LS9	Lymphepicelloid carcinoma	IIIA	79	peripheral	LLL	Adenocarcinoma	yes	alive	Adenocarcinoma relapse

C-RP: Completion Right Pneumonectomy; LLL: Left Lower Lobectomy; LUL: Left Upper Lobectomy; RLL: Right Lower Lobectomy; RML: Right Middle Lobectomy; RUL: Right Upper Lobectomy; Seg: Segmentectomy; W: Wedge resection

that were completed in the second primary lung cancer group (group 2) might have increased the risk for locoregional recurrence, but our study did not show that the extent of the resections influenced the survival, as was reported in other studies [12,13]. Major complications occurred in 14% of our patients after the second resection, which is comparable to the previously reported results of pulmonary resection for recurrent lung cancers [14,15].

Voltolini et al. [14] investigated the type of surgical treatment used in cases of metachronous second primary lung tumor, and reported that wedge resection was a reasonable and safe alternative to the standard resections in elderly patients or in those patients with a poor respiratory reserve and after a pneumonectomy.

Some reports have suggested that patients with a second primary lung cancer have a more favorable prognosis than patients with locally recurrent disease [3,5]. However, other studies did not reveal a significantly different survival between patients surgically treated for a second primary lung cancer or those surgically treated for locally recurrent disease [14]. Similarly, our data showed that the 5-year survival rates were not significantly different between patients with second primary lung cancer and those with recurrent lung cancer. Overall, our 5-year survival of 74% for second primary lung cancers and 43% for recurrent lung cancers was far better than what would be expected for local recurrent disease.

Although we did not show a statistically significant positive association of sublobar resection on survival rate, sublobar resection was not inferior to lobar and completion pneumonectomy. From our experience with surgical treatment of second primary or recurrent lung cancer, we conclude that sublobar resection and wedge resection, when feasible, are the treatments of choice. Neither anatomical lobectomy nor completion lobectomy yielded a significant overall survival advantage compared with these limited resection methods. Therefore, segmentectomy is an ideal surgical procedure to minimize recurrence in situations where a parenchymal-sparing technique is indicated or recommended. Completion pneumonectomy should only be performed in carefully-selected patients.

The main limitation of this study was its retrospective nature and lack of randomization, which may have led to potential bias in patient selection and surgeon's choice of operative approach. Prospective, randomized studies are necessary to further understand the feasibility of ipsilateral re-resection for second primary or recurrent lung cancer.

Conclusion

The long-term patient outcomes of this study justify the need for complete work-up of patients with ipsilateral local recurrent and ipsilateral second primary lung cancer at our hospital. Surgical treatment should be considered when patients have no distant metastasis and are in good health.

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