Original
Article

Surgical Treatment for Metachronous Second Primary Lung Cancer after Radical Resection of Primary Lung Cancer

Takahiko Ishigaki, MD, Tatsuya Yoshimasu, MD, PhD, Shoji Oura, MD, PhD,
Fuminori Ota, MD, Rie Nakamura, MD, Yoshimitu Hirai, MD, PhD,
and Yoshitaka Okamura, MD, PhD

Purpose: We retrospectively reviewed our experience of surgical resection for second primary lung cancer (SPLC) in our institute. And to clarify whether periodic follow-up after resection of first primary lung cancer (FPLC) is associated with earlier detection of SPLC.

Methods: From January 2003 to March 2011, a total of 386 patients underwent surgical resection for primary lung cancer in our institute. Of these patients, 21 (5.4%) with SPLC were observed during follow-up after surgery. Radiation therapy was selected instead of surgical resection in 7 patients to preserve respiratory function. The other 14 patients are reviewed in this paper.

Results: Histological types were different between FPLC and SPLC in only one patient (FPLC: adenosquamous carcinoma, SPLC: squamous cell carcinoma). The average SPLC tumor size (18 ± 8 mm) was smaller ($P = 0.07$) than the average FPLC tumor size (26 ± 14 mm). Recurrence was not observed in these patients.

The follow-up period after resection of SPLC was 31 ± 30 (5–94) months. During follow-up, 2 patients died of de novo malignancies, and the other 12 patients were alive without recurrence.

Conclusion: Systematic and periodic long-term follow-up after FPLC probably resulted in earlier detection of SPLC and yielded this good prognosis.

Keywords: lung cancer, second primary lung cancer, Noguchi classification

Introduction

Lung cancer is a leading cause of cancer death in Japan. More than 60000 patients die of lung cancer each year. The majority of lung cancer patients have

an advanced stage of disease at the time of diagnosis. This appears to be associated with the poor prognosis of lung cancer.

Surgical resection is the only therapeutic method that guarantees a possibility of cure in most patients with lung cancer. However, a possibility of recurrence remains after surgery. Usually, follow-up in the outpatient clinic is performed periodically.

Patients with lung cancer also have the risk of developing second primary lung cancer (SPLC) after surgery because they still have lung tissue. We frequently see metachronous SPLC during follow-up of these patients. Most of these patients with SPLC have early-stage disease and are thus assumed to be good candidates for surgical resection. In this paper, we retrospectively

Department of Thoracic and Cardiovascular Surgery, Wakayama Medical University, Wakayama, Japan

Received: February 8, 2012; Accepted: May 22, 2012
Corresponding author: Takahiko Ishigaki, MD. Department of Thoracic and Cardiovascular Surgery, Wakayama Medical University, 811-1 Kimiidera, Wakayama 641-8509, Japan
Email: ishigaki_takahiko@yahoo.co.jp
©2012 The Editorial Committee of *Annals of Thoracic and Cardiovascular Surgery*. All rights reserved.

Table 1 Characteristics of SPLC

	FPLC		SPLC	<i>p</i>
Histology	AD	11	→ AD	11
	SQ	2	→ SQ	2
	ADSQ	1	→ SQ	1
Tumor size (mm)		26 ± 14	18 ± 8	0.07
Pathological stage	IA	6	12	0.049
	IB	6	1	
	IIA	0	0	
	IIB	0	1	
	IIIA	1	0	
	IIIB	1	0	

FPLC: first primary lung cancer; SPLC: second primary lung cancer; AD: adenocarcinoma; SQ: squamous cell carcinoma; ADSQ: adenosquamous carcinoma

reviewed our experience of surgical resection for SPLC in our institute.

Materials and Methods

From January 2003 to March 2011, a total of 386 patients underwent surgical resection for primary lung cancer in our institute. The patients were followed every month for the first 6 months after surgery at the outpatient clinic and every 3 months thereafter, at which times plain chest X-rays and serum tumor marker levels were obtained. Brain MRI and chest and abdominal CT scans were performed every 6 months to detect tumor recurrence. PET/CT scans were performed once yearly. We recommended a follow-up period of at least 5 years for each patient. A longer follow-up period was allowed if patients requested it.

Of these patients, 21 (5.4%) with SPLC were observed during follow-up after surgery. Distant metastasis was not detected in any patient. All were diagnosed with operable early-stage disease. Radiation therapy was selected instead of surgical resection in 7 patients to preserve respiratory function (their %VC below 40% after second operation). The other 14 patients are reviewed in this paper.

Included were 11 males and 3 females with a mean age of 71 ± 7 (62–87) years. The criteria of Martini and Melamed with the recent modifications by Antakli and associates¹⁾ were applied to define SPLC.

Values were described as means ± SD (min–max). The unpaired t-test and chi-square test were employed to evaluate the significance of differences between the groups. A value of $P < 0.05$ indicated statistical significance.

Fig. 1 Intervals between first primary lung cancer (FPLC) and second primary lung cancer (SPLC).

Results

Characteristics of the SPLC compared with the first primary lung cancer (FPLC) are summarized in **Table 1**. Adenocarcinoma was the most common pathology. Histological types were different between FPLC and SPLC in only one patient (FPLC: adenosquamous carcinoma, SPLC: squamous cell carcinoma). The average SPLC tumor size (18 ± 8 mm) was smaller ($P = 0.07$) than the average FPLC tumor size (26 ± 14 mm). The pathological stage of SPLC was IA in 12 patients, IB in 1 patient, and IIB in 1 patient. There were more patients with stage IA SPLC than stage IA FPLC ($P = 0.049$).

Intervals between FPLC and SPLC are illustrated in **Fig. 1**. All cases of SPLC were detected during the follow-up period of each patient. The average interval was 60 months. Three patients had intervals longer than 5 years. The longest interval was 246 months.

Surgical procedures for SPLC in association with FPLC are illustrated in **Fig. 2**. Surgical procedures for FPLC were partial resection in 2 patients and lobectomy in 12, while those for SPLC were partial resection in 9 patients, segmentectomy in 1, and lobectomy in 4. Lobectomy was selected in fewer patients with SPLC ($P = 0.0075$).

There were four cases of ipsilateral SPLC. All were right-sided. Partial resection was selected as the surgical procedure for ipsilateral SPLC. Lobectomy was not included. It appears that completion pneumonectomy was intentionally avoided in our institute.

The follow-up period after resection of SPLC was 31 ± 30 (5–94) months. During follow-up, 2 patients died of de novo malignancies, and the other 12 patients were alive without recurrence.

Fig. 2 Surgical procedures for second primary lung cancer (SPLC) in association with first primary lung cancer (FPLC).

Discussion

We observed 21 (5.4%) patients with SPLC during follow-up after surgical resection of FPLC. This prevalence is extremely high compared with that of lung cancer reported in Japan, indicating that after surgical resection for FPLC, patients were at risk for subsequent lung cancers (smoking, accumulation of gene mutation, etc.).

Systematic and periodic follow-up should be performed not only to detect recurrence, but also to detect early-stage SPLC. Shields mentioned that a major reason for follow-up was to find second primaries because these are more amenable to surgical resection than are recurrent diseases.²⁾ SPLC was detected at an earlier stage than was FPLC in our patients. The saturation level of high-resolution CT in Japan is very high, and we usually used high-resolution CT in patient follow-up. This may have resulted in the early detection of SPLC in our patients.

How long and how often we should follow-up our patients after resection of FPLC is a matter in hand. Our patients developed SPLC after an average of 60 months after surgery. Follow-up more than 5 years appears to be needed. We should also notice that periodic follow-up to find SPLC is a kind of cancer screening for the high-risk populations. The guideline of CT screening for lung cancer is not defined in Japan yet. So we recommended the patients to receive CT screening one or

two times a year until the patients could not undergo surgical resection because of their old age.

We believe that patients with early-stage SPLC are good candidates for surgical resection when respiratory function allows for surgical resection. Indeed, there are reports of long-term survival in patients undergoing resection of a SPLC after previous lung resection.³⁻⁶⁾

Metachronous lung cancer appears to be increasing.⁷⁾ However, there is no definitive guideline of surgical therapy for SPLC. Generally, lobectomy is now recommended as the standard treatment of early-stage primary lung cancer.⁸⁾ However, lobectomy for ipsilateral SPLC often results in completion pneumonectomy. We believe that the risk of completion pneumonectomy is not sufficiently low.⁹⁾ Thus, we intentionally avoid completion pneumonectomy and choose partial resection for treatment of ipsilateral SPLC.

We agree that lobectomy should be performed in patients with good pulmonary function reserve to decrease recurrence rates. Several prospective non-randomized studies have reported favorable long-term survival following partial resection or segmentectomy among patients with peripheral lung cancers of ≤ 2 cm.¹⁰⁻¹³⁾ Tumors in nine (64.3%) of our patients were ≤ 2 cm. The average follow-up period after partial resection of SPLC in our series was 31 (5-88.4) months. Recurrence was not observed in these patients. We believe that either partial resection or lobectomy is acceptable for treatment of early-stage SPLC.

Conclusion

Aggressive surgical resection, including partial lung resection, for SPLC showed a good prognosis. Systematic and periodic long-term follow-up after FPLC probably resulted in earlier detection of SPLC and yielded this good prognosis.

Disclosure Statement

The authors report to that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

References

- 1) Antakli T, Schaefer RF, Rutherford JE, et al. Second primary lung cancer. *Ann Thorac Surg* 1995; **59**: 863-6; discussion 867.
- 2) Shields TW. Postoperative lung cancer surveillance. Who, what, when, and why? *Chest* 1997; **111**: 11-2.
- 3) Kittle CF, Faber LP, Jensik RJ, et al. Pulmonary resection in patients after pneumonectomy. *Ann Thorac Surg* 1985; **40**: 294-9.
- 4) Spaggiari L, Grunenwald D, Girard P, et al. Cancer resection on the residual lung after pneumonectomy for bronchogenic carcinoma. *Ann Thorac Surg* 1996; **62**: 1598-602.
- 5) Terzi A, Furlan G, Gorla A, et al. Lung resection on single residual lung after pneumonectomy for bronchogenic carcinoma. *Thorac Cardiovasc Surg* 1997; **45**: 273-6.
- 6) Haraguchi S, Koizumi K, Hirata T, et al. Surgical treatment of metachronous nonsmall cell lung cancer. *Ann Thorac Cardiovasc Surg* 2010; **16**: 319-25.
- 7) Haraguchi S, Koizumi K, Hirata T, et al. Surgical treatment of metachronous nonsmall cell lung cancer. *Ann Thorac Cardiovasc Surg* 2010; **16**: 319-25.
- 8) Ginsberg RJ, Rubinstein LV. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Lung Cancer Study Group. *Ann Thorac Surg* 1995; **60**: 615-22.
- 9) Chataigner O, Fadel E, Yildizeli B, et al. Factors affecting early and long-term outcomes after completion pneumonectomy. *Eur J Cardiothorac Surg* 2008; **33**: 837-43.
- 10) Aziz TM, Saad RA, Glasser J, et al. The management of second primary lung cancers. A single centre experience in 15 years. *Eur J Cardiothorac Surg* 2002; **21**: 527-33.
- 11) El-Sherif A, Gooding WE, Santos R, et al. Outcomes of sublobar resection versus lobectomy for stage I non-small cell lung cancer: a 13-year analysis. *Ann Thorac Surg* 2006; **82**: 408-15; discussion 415-6.
- 12) Kodama K, Doi O, Higashiyama M, et al. Intentional limited resection for selected patients with T1 N0 M0 non-small-cell lung cancer: a single-institution study. *J Thorac Cardiovasc Surg* 1997; **114**: 347-53.
- 13) Lee W, Daly BD, DiPetrillo TA, et al. Limited resection for non-small cell lung cancer: observed local control with implantation of I-125 brachytherapy seeds. *Ann Thorac Surg* 2003; **75**: 237-42; discussion 242-3.