Resection of Pulmonary Metastasis of Non-small Cell Lung Cancer

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Introduction: Management of pulmonary metastasis of non-small cell lung cancer (NSCLC) remains controversial. We reviewed our surgical treatment for pulmonary metastasis of NSCLC.

Methods: Seventy-six patients with pulmonary metastasis of NSCLC underwent pulmonary resections in two institutes during the past 10 years. Eighteen patients with simultaneous same lobe metastasis as the primary lesion underwent mostly lobectomies. Sixteen patients with simultaneous different lobe metastasis underwent combined margin-free resections. Forty-nine pulmonary metastasectomies were performed in 42 patients with recurrent lung cancer. Overall survival and disease-free survival in each group were examined, and factors affecting survivals were investigated.

Results: In the patients with the same lobe metastasis 5-year survival was 79.6%, and median and 5-year disease-free survivals were 39.1 months and 41.3%. In the patients with simultaneous different lobe metastasis median survival and 5-year survival were 37.7 months and 30.7%, and median and 5-year disease-free survivals were 13.3 months and 12.5%, respectively. Multiple pulmonary metastasis and mediastinal node metastasis were identified as significant factors affecting survivals. In the patients with recurrent pulmonary metastasis median survival and 5-year survival were 40.0 months and 34.8%, and median and 5-year disease-free survivals were 23.7 months and 14.4%, respectively. Node metastasis, higher age, and shorter interval from the prior resection were identified as significant factors affecting survivals.

Conclusions: These findings suggest that the simultaneous same lobe metastasis is under the same indication for the primary lesion, and that the simultaneous different lobe metastasis and recurrent pulmonary metastasis should be removed in selected patients.

Key Words: Non-small cell lung cancer, Surgery, Pulmonary metastasis, Recurrence, Metastasectomy.

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Standard treatment for pulmonary metastasis of non-small cell lung cancer (NSCLC) is not well defined. Simultaneous intralobar metastasis can be removed with an anatomic resection when the primary lesion is indicated for surgical treatment, resulting in a favorable outcome in the literature.[1,2] Simultaneous different lobe metastasis of the lung cancer is not indicated for resection in the current clinical guideline.[3] Furthermore, surgical treatment for recurrent pulmonary metastasis has been controversial.[4] To reveal the outcome of surgical treatment for pulmonary metastasis of NSCLC, we reviewed our 10 years experience of pulmonary metastasectomy of NSCLC.

PATIENTS AND METHODS

From 1997 to March 2007, 76 patients with pulmonary metastasis of NSCLC underwent 83 pulmonary resections for curative intent in two institutes, Kyoto University Hospital and Gifu National Hospital, Japan. The indication for presumable pulmonary metastasectomy was a solitary or limited number of pulmonary lesions, completely resectable, without other organ metastasis, and tolerable for the surgery. During the same period 1638 thoracotomies for primary lung cancer were performed in the two institutes, indicating that the resections of pulmonary metastasis were 5.1% of the surgeries for lung cancer. Fifty-eight patients were men and 25 were women with the mean age of 65.9 years (ranging 40–83 years). Thirty-four patients had simultaneous pulmonary metastases at the time of primary resection for lung cancer: 18 were in the same lobe as the primary lesion and 16 were in the different lobe. Forty-nine patients had recurrent pulmonary metastases after the previous pulmonary resection for lung cancer. We also performed 28 pulmonary resections for synchronous multiple lung cancers and 35 pulmonary resections for metachronous primary lung cancers during the period. Diagnosis of pulmonary metastasis was based on the pathologic findings; standard hematoxylin-eosin staining was examined in all specimens and additional immunohistochemical staining of p53 was mostly examined in the later period of the study. Based on the similarity of morphology and immunohistochemical staining, diagnosis of the pulmonary metastasis was done by our pathologists. When the definitive diagnosis was not obtained with the pathologic findings, the criteria for diagnosis of multiple primary lung carcinoma by Martini and Melamed[5] was applied to differentiate metastasis

from multiple primary lung cancer. When multiple pulmonary nodules were identified pathologically similar, the largest nodule was defined as the primary lesion and the other(s) were defined as metastatic lesion(s). According to the lung cancer staging system,[6] the simultaneous same lobe metastasis, different lobe metastasis, and metachronous pulmonary metastasis were classified to T4-stage IIIB, M1-stage IV, and recurrent lung cancer, respectively; therefore, we examined these patients for survival analysis separately.

All eighteen patients with the simultaneous same lobe metastasis were diagnosed after the pulmonary resection. Histology was adenocarcinoma in 10, squamous cell carcinoma in seven, and large cell carcinoma in one. Clinical staging without additional nodes was stage 1A (T1N0) in five, 1B (T2N0) in eight, 2B (T2N1) in two, and 3A (T1–2N2) in three. Surgical procedures were 16 lobectomies including one sleeve lobectomy and two segmentectomies. All tumors were completely removed. Pathologic node staging was N0 in 12, N1 in two, and N2 in four. Sixteen patients had solitary pulmonary metastasis and two patients had two metastatic nodules in the same lobe. Eight patients received postoperative intravenous platinum-based chemotherapy and six patients received postoperative uracil-tegafur (UFT) administration, whereas seven patients did not receive any adjuvant therapy.

Sixteen patients with the simultaneous different lobe metastasis underwent combined pulmonary resections. Four patients were clinically diagnosed as pulmonary metastasis preoperatively, whereas the other patients were diagnosed after the pulmonary resections. Histology was adenocarcinoma in 12, squamous cell carcinoma in three, and large cell neuroendocrine carcinoma in one. Clinical staging without additional nodules was T1N0 in seven, T2N0 in three, T2N1 in one, T1N2 in two, and T2N2 in three. Surgical procedures were 11 lobectomies with wedge resections/segmentectomies, two segmentectomies with wedge resections, one bilobectomy, and two pneumonectomies. All tumors were completely removed. Ten patients had ipsilateral lung metastasis and six patients had contralateral lung metastasis. Thirteen patients had solitary metastasis, and three patients had two metastatic nodules, one of which was the same lobe metastasis in each patient. Pathologic T-factor was T1 in seven, T2 in six, and T4 (pm 1) in three. Pathologic N-factor was N0 in nine, N2 in five, and N3 in two. Four patients received preoperative intravenous platinum-based chemotherapy. Nine patients received postoperative intravenous chemotherapy and four patients received UFT, whereas six patients did not receive any postoperative chemotherapy.

Forty-nine pulmonary resections for recurrent pulmonary metastasis were performed in 42 patients. Seven patients underwent a repeated pulmonary metastasectomy for recurrence again. Histology of the recurrent lung cancer was adenocarcinoma in 30 and squamous cell carcinoma in 19. Thirty-nine resections were for solitary pulmonary lesion and 10 resections were for multiple (2 ~ 4) pulmonary lesions. Staging of the lung cancer at the time of initial resection was stage I in 25, stage II in seven, stage III in eight, and stage IV in two. The interval from the prior pulmonary resection was 9.1 to 112 months (median 28.0 months). Surgical procedures were essentially margin-free resections; 31 wedge resections, 10 segmentectomies with or without wedge resections, four lobectomies including one sleeve lobectomy, and four completion pneumonectomies. Complete resection was obtained in all patients except one who underwent a pneumonectomy with cancer-positive bronchial stump. Lymph node metastasis along with pulmonary metastasis was identified in four patients. Three patients received preoperative intravenous chemotherapy. Fifteen patients received postoperative intravenous chemotherapy and 14 patients received UFT, whereas 25 patients did not receive any postoperative therapy.

The survival and the date of tumor recurrence after the pulmonary resection were examined in each patient. In the patients with simultaneous pulmonary metastasis, overall survival was defined as the duration from the pulmonary resection to the last follow-up or the death with any reason, and disease-free survival was defined as the duration from pulmonary resection to the date of recurrence or the death with any reason. In the patients with recurrent lung cancer, overall survival was defined as the duration from the first metastasectomy to the last follow-up or the death with any reason, and disease-free survival was defined as the duration from the each pulmonary resection to the date of recurrence or the death with any reason. Continuous data are presented as means, and categorical data are presented as exact numbers. Survival estimates were derived by Kaplan-Meier analysis. Factors including age, sex, histology, T and N factors, number of pulmonary metastasis, operative procedure, and adjuvant chemotherapy were analyzed. Stratified log-rank analysis and Cox proportional-hazard modeling were used to investigate and adjust for major prognostic and stratification factors. A two-sided probability value of less than 0.05 was considered statistically significant. The study was performed in accordance with the Declaration of Helsinki. Kyoto University institutional review board approved this study and waived the requirement for individual patient consent for this retrospective study.

RESULTS

Overall Survival and Disease-Free Survival

Median follow-up of all patients was 29.6 months after the resection of pulmonary metastasis. Forty-one patients (53.9%) were completely followed until their death or more than 5 years after the resection.

Overall survival curve and disease-free survival curve of patients with the same lobe metastases are shown in Figure 1. The 5-year survival rate was 79.6%. Median disease-free survival was 39.1 months and the 5-year disease-free survival rate was 41.3%. Overall survival curve and disease-free survival curve of patients with the different lobe metastasis are shown in Figure 2. Median survival was 37.7 months and the 5-year survival rate was 30.7%. Median disease-free survival was 13.3 months and the 5-year disease-free survival rate was 12.5%. Overall survival curve and disease-free survival curve of 42 patients with recurrent pulmonary metastasis are shown in Figure 3. Median survival was 40.0 months and the 5-year survival rate was 34.8%. Median