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Clinical Science

# Outcome of surgical resection for recurrent pulmonary metastasis from colorectal carcinoma

**Ryu Kanzaki, M.D.[a,*], Masahiko Higashiyama, M.D.[a], Kazuyuki Oda, M.D.[b], Ayako Fujiwara, M.D.[a], Toshiteru Tokunaga, M.D.[a], Jun Maeda, M.D.[a], Jiro Okami, M.D.[a], Koji Tanaka, M.D.[c], Tatsushi Shingai, M.D.[c], Shingo Noura, M.D.[c], Masayuki Ohue, M.D.[c], Ken Kodama, M.D.[a]**

*[a]Department of Thoracic Surgery, Osaka Medical Center for Cancer and Cardiovascular Diseases, 1-3-3 Nakamichi, Higashinari-ku, Osaka 5378511, Japan; [b]Department of Surgery, Sakai Municipal Hospital, 1-1-1 Minamiyasui-cho, Sakai-ku, Sakai, Osaka 5900064, Japan; [c]Department of Surgery, Osaka Medical Center for Cancer and Cardiovascular Diseases, 1-3-3 Nakamichi, Higashinari-ku, Osaka 5378511, Japan*

**KEYWORDS:**
Pulmonary metastasis;
Colorectal cancer;
Repeat thoracotomy

**Abstract**

**BACKGROUND:** The outcomes after repeat pulmonary resection for colorectal cancer (CRC) and the factors associated with the prognosis of these patients remain uncharacterized.

**METHODS:** Data on 156 patients who underwent curative resection of pulmonary metastasis from CRC were reviewed. Repeat pulmonary resection was performed in 25 patients; the present study examined the outcomes and factors associated with prognosis after repeat pulmonary resection.

**RESULTS:** The 5-year survival rate after the first pulmonary resection was 56.2%. A multivariate analysis identified a histological type other than well-differentiated adenocarcinoma, a high prethoracotomy serum carcinoembryonic antigen (CEA) level, and the presence of hilar or mediastinal lymph node metastasis as poor prognostic factors for the first pulmonary resection. The 5-year survival rate after repeat pulmonary resection was 42.1%. Hilar or mediastinal lymph node metastasis at the time of the repeat resection was significantly associated with poor survival.

**CONCLUSIONS:** Repeat pulmonary resection for metastatic CRC provides satisfactory outcomes. Hilar or mediastinal lymph node involvement is consistently associated with a poor prognosis after the first and repeat pulmonary resections.



Colorectal cancer (CRC) remains one of the leading causes of cancer death in Western countries. More than two thirds of these patients undergo primary curative resection; however, more than half of the resected patients eventually succumb to the disease.[1] The most common sites of recurrence after resection of primary CRC are liver and lung. Patients with untreated metastatic CRCs have a median survival time of less than 10 months and a 5-year survival frequency of less than 5%.[2] Recently, antiangiogenic therapy with bevacizumab combined with oxaliplatin-based chemotherapy was reported to improve the survival time of patients with CRC.[3] However, few patients achieved complete remission using these new treatments, and most patients therefore exhibit disease progression.

Therefore, surgery remains the best treatment for patients with pulmonary metastases from CRC if potentially curative

* Corresponding author. Tel.: +81-06-6972-1181; fax: +81-06-6981-8055.

E-mail address: rkanzaki@tj8.so-net.ne.jp

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resection is expected and is an established treatment modality in patients with metastatic CRCs. The reported 5-year survival rates after pulmonary metastasectomy for CRC are 24% to 71.2%.[2–15]

Repeat pulmonary resection is also effective for recurrent pulmonary metastasis.[16] Several authors[5,9,11,13–15,17] have advocated this treatment for patients with metastatic CRCs; however, the outcomes after repeat pulmonary resection for CRC and the factors associated with the prognosis of these patients remain uncharacterized. The present study examined the outcome of surgical resection for recurrent pulmonary metastasis from CRCs and determined the prognostic factors compared with those of the first pulmonary resection.

## Patients and Methods

### Patient selection

From January 1980 to December 2008, a total of 156 patients with previous CRCs underwent curative pulmonary resection at the Osaka Medical Center for Cancer and Cardiovascular Diseases. Curative resection was defined as follows: no additional extrapulmonary sites of metastatic disease or already resected if present, no locoregional recurrence, and no residual macroscopic tumor tissue after the resection. Histopathological evaluations of the resected lung specimens confirmed CRC metastases in all patients.

Patients were selected for resection of pulmonary metastases after meeting the following criteria: (1) pulmonary metastases were deemed to be completely resectable by preoperative radiological examination, (2) absence of apparent hilar or mediastinal lymph node metastases determined by preoperative radiologic examination, (3) metastatic disease limited to the lungs or extrapulmonary distant metastasis(es) that was controlled or controllable if present, (4) locoregional control of the primary CRC was achieved or achievable, and (5) good general condition and adequate respiratory function to tolerate lung resection.

Before 2006, lymph node involvement was generally assessed by computed tomography (CT) scanning, with lymph nodes diagnosed as positive if they extended more than 10 mm across the short-axis diameter. Since 2006, lymph node involvement is generally assessed by F18-fluorodeoxyglucose positron emission tomography/CT (FDG-PET/CT) in our hospital.

### Patient characteristics

Clinical information was obtained from the medical records in our hospital. The median time interval between resection of primary CRC and first pulmonary resection was 27 months (range, 0–109 months). The mean age at the time of first pulmonary resection was 62 years (range, 39–83 years of age). Thirty-eight patients had previously undergone resection for extrapulmonary metastases or local recurrences before the pulmonary resection. Of these, 29 patients underwent liver metastasectomy, 6 patients underwent resection of a local recurrence of the primary tumor, 2 patients underwent inguinal lymph node metastasectomy, and 1 patient underwent resection of a para-aortic lymph node metastasis. Three patients underwent simultaneous resection of metastatic CRCs to the lung and either to an extrathoracic site or local recurrence: thyroid metastasis in 1 patient, brain metastasis in 1 patient, and local recurrence of primary tumor in 1 patient. Perioperative chemotherapy at thoracotomy, including preoperative and/or postoperative adjuvant therapy, was performed in 76 patients as follows: 5-fluorouracil or its derivatives were administered in 61 patients; tegafur in 23 patients; doxifluridine in 21 patients; fluorouracil in 4 patients; carmofur in 3 patients; UFT in 9 patients; and S-1 in 1 patient. Cisplatin-, irinotecan-, and oxaliplatin-based chemotherapy were administered to 6, 4, and 5 patients, respectively. Table 1 summarizes the patient characteristics.

### Repeat pulmonary resection

If new nodules had evolved after the first pulmonary resection, a second resection was defined as a repeat pulmonary resection. Planned staged thoracotomy for bilateral metastases was counted as a single operation and was therefore excluded from this study definition. In the survival analysis of patients who underwent a planned staged thoracotomy, the date when the earlier surgery was performed was recognized as the starting point. Repeat pulmonary metastasectomies were also performed if the patient met the criteria for the first pulmonary resection as described earlier. Repeat pulmonary resections were performed in 25 patients; 24 of these patients underwent second pulmonary resections, and 1 patient underwent a third pulmonary resection.

### Follow-up schedule

Follow-up generally involved a chest x-ray or a chest and abdominal CT scan, a physical examination, and blood chemistry performed every 6 to 12 months after the first pulmonary resection. Follow-up information was obtained from the medical records in our hospital, letters from the patient's general practitioner, or from the death certificates of the Osaka Cancer Registry. Patients or their families were contacted by phone or by letter if necessary.

### Statistical analysis

The statistical analyses were performed using the StatView 5.0 software program (SAS Institute, Berkley, CA). The overall survival after the first and repeat pulmonary resections was analyzed by the Kaplan-Meier method using the dates of the first and second pulmonary resections, respectively, as the starting points. Significance of differ-