Pulmonary Resection for Metastases From Colorectal Cancer*

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Background: We reviewed our experience in the surgical treatment of 47 patients with colorectal pulmonary metastases and investigated factors affecting their survival.

Method: From September 1986 to December 1999, 47 patients underwent 59 thoracotomies for pulmonary metastases from colorectal cancer.

Results: The median interval between colorectal resection and lung resection (disease-free interval [DFI]) was 33 months. Overall, 5-year survival was 48%. Five-year survival was 51% for patients with solitary metastasis (n = 30), 47% for patients with ipsilateral multiple metastases (n = 11), and 50% for patients with bilateral metastases (n = 6), and there were no significant differences. Five-year survival was 80.8% for 14 patients with DFI of < 2 years and 39.7% for 30 patients with a DFI of > 2 years (p = 0.22). Five-year survival for 11 patients with normal prethoracotomy carcinoembryonic antigen (CEA) levels was 70%, and that for 26 patients with elevated prethoracotomy CEA levels (> 5 ng/mL) was 36% (p < 0.05). Eight patients had extrathoracic disease. The median survival time after pulmonary resection was 18.5 months, and the 5-year survival was 60%. A second resection for recurrent metastases was performed in five patients, and a third resection was done in one patient. All six patients are alive. The median survival of five patients who underwent a second thoracotomy was 22 months (range, 2 to 68 months), and one patient is alive 39 months after the third resection.

Conclusion: Pulmonary resection for metastases from colorectal cancer may help prolong survival in selected patients, even with bilateral lesions, recurrent metastases, or extrathoracic disease. Prethoracotomy CEA level was found to be a significant prognostic factor.

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Key words: carcinoembryonic antigen; colorectal cancer; lung metastases; prognosis; surgical resection

Abbreviations: CEA = carcinoembryonic antigen; DFI = disease-free interval

Since no effective chemotherapy regimen has been proposed for pulmonary metastases from colorectal cancer, surgery is the only potentially curative treatment. Thomford and colleagues1 reported the principles for resection of metastatic lung tumors, and these have been accepted by most surgeons. Over a few decades, the indication for metastatic lung tumors has been extended.

Resection of a solitary lung metastasis has been accepted by physicians, while pulmonary resection for multiple lesions or bilateral lesions remains controversial. In addition, the role of repeat thoracotomy for recurrent cancer has not been well defined.

We reviewed our experience in the surgical treatment of 47 patients with colorectal pulmonary metastases and investigated factors affecting their survival.

**Materials and Methods**

From January 1986 to December 1999, 49 patients underwent thoracotomy for metastases from colorectal cancer at our institution. Two patients who underwent exploratory thoracotomy only were excluded from this study. The remaining 47 patients received 59 curative resections, and all resected specimens demonstrated tumor-free margins pathologically. Twenty-nine patients were men, and 18 patients were women. Their age at surgery ranged from 40 to 80 years, and median age was 61 years. The primary tumor site was the colon in 33 patients and the rectum in 14 patients.

Selection criteria for resection were as follows: controlled primary tumor, controlled or controllable extrathoracic lesions, and CT scan demonstrating that radical resection could be performed regardless of the number of the lesions. Tumors in the bilateral thorax were not a contraindication. Principally, wedge resection was the procedure of choice, and...
we tried to preserve normal pulmonary parenchyma as much as possible. Lymph node dissection was not undertaken unless macroscopically positive findings were seen during operation. Surgical procedure was wedge resection in 29 patients, segmentectomy in 10 patients, segmentectomy plus wedge resection in 2 patients, lobectomy in 11 patients, lobectomy plus wedge resection in 6 patients, and pneumonectomy in 1 patient. Bronchoplasty in combination with pulmonary resection was employed for three patients for the purpose of avoiding excessive pulmonary resection. Therefore, 41 operations (69%) involved less than a lobectomy.

Survival was estimated by the method of Kaplan and Meier, using the date of the pulmonary resection as the starting point. The influence of variables on survival was analyzed using the log-rank test for discrete variables.

**Results**

There was one postoperative death due to pulmonary embolism 3 days after a segmentectomy (operative mortality, 1.7%). The follow-up was complete for all patients. Overall, 5-year survival was 48%, and the median survival was 19 months (Fig 1).

**Disease-Free Interval**

Pulmonary resection followed colon resection in 44 patients; 3 patients, however, had initial lung resection that led to the subsequent diagnosis of colorectal cancer. In these three patients, one patient died of multiple lung metastases 55 months after pulmonary resection, and the remaining two patients are alive without relapse 10 months and 28 months after pulmonary resection, respectively. The disease-free interval (DFI) was defined as the interval between colon resection and lung resection. The DFI ranged from 1 to 260 months, and the median DFI was 33 months; 14 patients had a DFI of <2 years and 30 patients had a DFI of >2 years. Five-year survival was 80.8% and 39.7%, respectively, and this observation was not significant (p = 0.22; Fig 2).

**Mode of Pulmonary Metastasis**

Thirty patients had a solitary lesion, 11 patients had multiple and ipsilateral lesions, and 6 patients had bilateral. For bilateral lesions, one patient underwent simultaneous bilateral thoracotomies and the other five patients underwent staged bilateral thoracotomies. Median sternotomy was not performed because of insufficient manipulation of the entire lung. The number of resected lesions by a single thoracotomy was 1 lesion in 42 patients; 2 lesions in 11 patients; 3 lesions in 3 patients; and 4, 6, and 8 lesions in 1 patient each, respectively; the average number of lesions was 1.5. The 5-year survival rate was 51% for solitary metastasis, 47% for ipsilateral multiple metastases, and 50% for bilateral metastases, and there were no significant differences (Fig 3).

**Prethoracotomy Carcinoembryonic Antigen Level**

Prethoracotomy carcinoembryonic antigen (CEA) level was measured in 37 patients. Five-year survival for 11 patients with normal prethoracotomy CEA levels was 70%, and that for 26 patients with elevated prethoracotomy CEA levels (>5 ng/mL) was 36% (Fig 4). Patients with normal prethoracotomy CEA levels had a better prognosis than those with elevated prethoracotomy CEA levels (p < 0.05). In the 26 patients with elevated prethoracotomy CEA levels, postthoracotomy CEA levels were measured in 16 patients. Although the number to be evaluated was insufficient, the postthoracotomy CEA level did not appear to influence the prognosis.
Eight patients had extrathoracic disease. Six patients underwent a resection of extrathoracic disease before pulmonary metastasectomy. Pulmonary metastases were detected after liver metastasectomy in four patients, brain in one patient, and local in one patient. In two patients, pulmonary and liver metastases were detected at the same time and both were resected during the same hospitalization. Two patients died of systemic metastases 10 months and 16 months after pulmonary metastasectomy, respectively, but the remaining six patients continue to survive from 3 to 85 months after lung resections. The median survival time was 18.5 months, and the 5-year survival rate was 60%.

Repeated Thoracotomy

A second resection for recurrent metastases was done in five patients, and a third resection was done in one patient. Two of six patients had extrathoracic disease. There were no major postoperative complications. The interval between colon resection and first thoracotomy ranged from 14 to 145 months, and the median interval was 63.5 months. The interval between first thoracotomy and second thoracotomy ranged from 7 to 26 months, and the median interval was 15 months. The interval between second thoracotomy and third thoracotomy was 5 months.

All six patients are alive to date. The median survival of five patients who underwent a second thoracotomy was 22 months (range, 2 to 68 months) after the second resection, and one patient is alive 39 months after the third resection.

Discussion

Traditional criteria by Thomford and colleagues\(^1\) excluded patients having bilateral intrathoracic lesions and/or extrathoracic lesions. However, recently the criteria have been widened. We retrospectively analyzed the data as to whether our criteria were feasible for candidates for pulmonary resection. Although a longer DFI seems to be a favorable prognostic indicator, our study demonstrated that the DFI was not a significant prognostic factor, which was supported by other authors.\(^4\)\(^–\)\(^9\) Many authors\(^4\)\(^–\)\(^7\),\(^10\) reported that patients with solitary metastasis had a better prognosis than those with multiple metastases. Our data did not indicate a significant difference between solitary metastasis and multiple metastasis. It is possible that there may be bias in selecting patients with multiple lesions, because only 6 of 59 thoracotomies were performed for more than three lesions. In the largest series from a single institute at Memorial Sloan-Kettering Cancer Center, McCormack and Ginsberg\(^8\) reported that 287 patients underwent pulmonary resection from colorectal cancer, and the 5-year survival in 66 patients with ipsilateral multiple metastases did not differ significantly from 57 patients with bilateral single or multiple lesions. Therefore, patients with not only ipsilateral multiple but also bilateral lesions may benefit from surgery. With regard to extrathoracic disease, especially liver metastasis, to our knowledge, almost all authors\(^4\)\(^–\)\(^12\) did not contraindicate pulmonary metastasectomy in patients who had previously received liver metastasectomy. The 5-year survival for patients with
hepatic metastasis before pulmonary resection ranged from 11 to 44%. Our study demonstrated similar results.

We consider wedge resection the procedure of choice, and resection greater than a lobectomy should be avoided whenever possible. Pulmonary metastasis with subsequent lymph node metastasis is in advance of the first step in the metastatic cascade. Okumura and colleagues reported that in the 100 patients who underwent pulmonary resection from colorectal cancer with exploration of hilar and/or mediastinal lymph nodes, 15 patients were positive for lymph node metastasis and their 5-year survival was 6.7%. Therefore, systematic hilar or mediastinal lymph node dissection does not improve prognosis and is meaningful only for predicting survival.

Local recurrence after pulmonary metastasectomy is a crucial problem during follow-up, and the indication for operation is controversial. McAfee and associates reported that 5-year survival for 19 patients who underwent a second thoracotomy was 30.2% from the date of the second thoracotomy, which was similar to the overall 5-year survival of 120 patients undergoing a first thoracotomy. Kandioler and associates reported similar result. In our series, all six patients who underwent repeated metastasectomies are alive to date.

In these settings, avoiding excessive lung resection, even if tumors are located centrally, can allow for the chance of surgical treatment for intrathoracic recurrence, if that should occur.

Our study demonstrated that the prethoracotomy CEA level was the only significant prognostic factor. A few authors reported similar results: elevation of CEA implies a worse prognosis. CEA itself participates in intercellular recognition and attachment and may promote adhesion of tumor cells to each other or to host cells. Therefore, prethoracotomy CEA level can be taken into account in selecting patients for pulmonary resection, especially if tumors are multiple or bilateral.

Because of the small number of patients who are candidates for pulmonary metastasectomy, a prospective, randomized trial is hard to conduct and the usefulness of resecting multiple pulmonary metastases may not be accepted by all physicians. However, survival following surgery in patients with poor prognostic indicators is still superior to that of those after any other form of treatment.

In conclusion, we believe that pulmonary resection for metastases from colorectal cancer may help prolong survival even in selected patients with bilateral lesions, recurrent metastasectomy, or extrathoracic disease. The prethoracotomy CEA level was found to be a significant prognostic factor.

References