Pulmonary Resection for Metastases from Colorectal Cancer

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Introduction: The lung is the most common extraabdominal site for metastases from colorectal cancer. Patients with untreated metastatic disease have a median survival of less than 10 months and a 5-year survival of less than 5%. The purpose of this study was to evaluate long-term survival in patients who underwent pulmonary resection for metastases from colorectal cancer.


Results: Median age was 68 years (range: 46–80 years). Median follow-up was 30 months (range: 12–149 months). The 2- and 5-year overall survival rates were 64 and 26%, respectively. Of the 23 patients, 16 patients had a solitary lesion, and seven patients had multiple lesions. The 5-year survival rates were 23 and 33%, respectively (not significant). The median disease-free interval (DFI)—the interval between colon resection and the appearance of lung metastases—was 43 months (1–168). Ten patients had DFIs <36 months, and 13 patients had DFIs >36 months. The 3-year survival rates were 20 and 38%, respectively (not significant). Recurrence of lung metastases was diagnosed in seven patients; three patients underwent second resections. They are alive today, with a median follow-up of 18 months. Patients who did not undergo second resections had a median survival of 12 months.

Conclusions: Pulmonary resection for metastases from colorectal cancer does produce longer survival, even in patients with multiple lesions and recurrent metastases.

Key Words: Lung, Resection, Metastases, Colorectal, Cancer.

(J Thorac Oncol. 2007;2: 652–656)

Colorectal cancer is the second-most commonly diagnosed malignancy in men and women in the Netherlands.

One of the most important predictors of survival in patients with colorectal cancer is lymph node status. In most countries, patients with curatively resected colorectal cancer without nodal tumor involvement do not receive adjuvant chemotherapy because studies have failed to demonstrate a beneficial effect.

Nevertheless, more than 30% of these patients will develop locoregional recurrence or distant metastases.1 The lung is the most common extraabdominal site of metastases in patients affected by cancer of the colon. Patients with untreated metastatic disease have a median survival of less than 10 months and a 5-year survival of less than 5%.2

Conventional treatment of stage IV colorectal carcinoma in most patients is palliative. For a long time, fluoracil-based chemotherapy has been considered the standard treatment, but it seldom has produced long-term survival. Because no effective chemotherapy regimen has been identified for pulmonary metastases of colorectal origin, surgery is the only potentially curative treatment.

Divis3 performed the first resection of a pulmonary metastasis in 1927. Several retrospective studies since then have shown that patients with pulmonary metastases benefit from resection.

The published 5-year survival rates after pulmonary metastasectomy of colorectal origin range from 21 to 62%.4–7

The purpose of this study was to evaluate postoperative mortality, morbidity, and long-term survival in patients who underwent pulmonary metastasectomy for metastases of colorectal cancer.

PATIENTS AND METHODS

Between January 1990 and January 2005, 23 patients underwent 29 operations for resection of lung metastases from colorectal cancer in the Jeroen Bosch Hospital, the Netherlands. Data were collected from the patient records, both electronic and paper. Information was collected on the clinical characteristics of the patients, operative reports, and the reports of the pathologist. The following patient characteristics and data were analyzed: age, gender, carcinoembryonic antigen (CEA) levels, primary site of the tumor, number and type of pulmonary resections, completeness of resection, second resection, disease-free interval (DFI), infiltration of pulmonary or mediastinal lymph nodes, postoperative morbidity, mortality, and long-term survival.

Selection criteria for resection were as follows: (1) controlled primary tumor, (2) controlled or controllable extrathoracic lesion, and (3) computed tomography scan demonstrating that radical resection could be performed regardless of the number of lesions. Tumors in both lungs were not considered a contraindication. Principally, wedge resection...
was the procedure of choice; if this was not possible, a lobectomy or a pneumonectomy was performed.

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. Follow-up was done routinely every 3 months, using CEA levels in blood samples and computed tomography of the thorax/abdomen on indication. Table 1 and 2.

RESULTS

The median age of patients at time of diagnosis of lung metastases was 68 years (range: 46–80 years). Twelve patients were men and 11 patients were women.

In 12 patients, the primary origin of the tumor was the colon, and in 11 patients, the primary origin was the rectum. There were 15 wedge resections, 11 lobectomies, two bilobectomies, and one pneumonectomy.

There were 20 patients with unilateral disease and three patients with bilateral disease. The median number of metastases per patient was one.

At operation, no mediastinal lymph node dissection was done routinely.

Only “lymph node picking” was done if there were pathological lymph nodes during surgery. This procedure was performed in 11 of the 23 patients. The mean number of lymph nodes was two. There were no patients with metastases in these lymph nodes, and all operations were radical.

None of the operated patients died after surgery.

Five patients developed postoperative complications (17.9%). One patient had a postoperative hemorrhage after a wedge resection, necessitating rethoracotomy; one patient had a wound infection after a wedge resection (sternotomy); one patient developed pneumonia after a lobectomy; one patient developed an abscess of the superficial thorax wound after a wedge resection; and one patient developed an empyema after a bilobectomy.

Pulmonary Metastasectomy and Survival

Median follow-up for the whole group was 30 months (range: 12–149 months). The 2-, 5-, and 10-year overall survival rates were 64, 25, and 12%, respectively. The 2-, 5-, and 10-year cancer-free disease survival rates were 52, 18, and 5%, respectively (Figure 1).

Combined Liver/Lung versus Lung Metastases and Survival

One of 23 patients underwent a hemihepatectomy for liver metastases before lung surgery. Originally, this patient underwent a right hemicolectomy for a Dukes B colon carcinoma. After 2 years, the patient developed liver metastases.

One year after the hemihepatectomy, he developed metastases of the right lung, for which he underwent a bilobectomy. Two years after the bilobectomy, the patient developed recurrent lung metastases and bone metastases. He died 6 years after the bilobectomy.

DFI and Survival

DFI was defined as the interval between colon resection and the appearance of lung metastases. DFIs ranged from 1 to 168 months, and the median DFI was 43 months. Ten patients had a median DFI <36 months, and 13 patients had DFIs >36 months. The 3-year survival rates were 20 and 38%, respectively ($p = 0.32$) (Figure 2).

Solitary versus Multiple Lung Metastases and Survival

Of the 23 patients, 16 patients had a solitary lesion and seven patients had multiple lesions. The 2-year overall sur-

| TABLE 1. Survival Rates of 23 Patients Who Underwent Pulmonary Resection |
|---------------------|---------------------|
| Survival Rates      | 2 yr (%) | 5 yr (%) |
| Overall survival    | 64       | 25       |
| Cancer-free disease survival | 52       | 18       |
| Disease-free interval <36 months | 79       | 0        |
| Disease-free interval >36 months | 78       | 38       |
| Solitary lesions    | 70       | 23       |
| Multiple lesions    | 50       | 33       |

| TABLE 2. Number of Lesions and Type of Surgery |
|---------------------|---------------------|
| Type of lesions     | No. of Patients |
| Solitary lesions    | 16               |
| Multiple lesions    | 7                |
| Recurrence          | 7                |
| Type of surgery     | No. of Patients |
| Wedge resection     | 15               |
| Lobectomy           | 11               |
| Bilobectomy         | 2                |
| Pneumonectomy       | 1                |

FIGURE 1. Kaplan-Meier survival curve for 23 patients who underwent pulmonary resection for metastases from colorectal cancer. Black solid line, overall survival; black dotted line, cancer-free disease survival.
vival rates for these groups were 70 and 50%, respectively. Five-year survival rates were 23 and 33%, respectively ($p = 0.404$) (Figure 3).

Nevertheless, after 6.5 years, survival was 23% for solitary lesions and 0% for multiple lesions.

Recurrence of Lung Metastases and Survival
Seven patients (30.4%) had a recurrence of lung metastases, for which three underwent second resections. The other four patients did not undergo second resections, be-

cause of extrathoracic disease (two patients) or because of deteriorating physical condition (two patients). The median DFI for patients with recurrence was 11 months (range: 4–31 months).

All surgically treated patients with recurrent lung metastases are alive today, with a median follow-up of 18 months. Patients who did not undergo second resections had a median survival of 12 months (Figure 4).

CEA Levels and Lung Metastases
In 11 of the 23 patients (48%), CEA levels were determined both before and after surgery. The median CEA level before surgery was 3 (range: 1.2–94), and the median CEA level after operation was 1.8 (range: 0.5–170).

DISCUSSION
Almost 30 to 40% of patients with colorectal carcinoma develop metastases despite curative resection of the primary tumor. Of these patients, about 10% will develop lung metastases. In addition, the majority of patients have recurrent extrathoracic disease.

In the literature, treatment of lung metastases was considered debatable for a long time. Nonsurgical treatment is still of only limited benefit to the patients; patients with untreated metastatic disease have a median survival of less than 10 months and a 5-year survival of less than 5%.

In a highly selected group of patients, surgical intervention is the current therapy of choice; the reported 5-year survival rates range from 21 to 62%. In a study from Lee et al., 59 patients underwent curative resection for pulmonary metastases of colorectal cancer. The 5-year overall survival rate of all patients who received pulmonary resection
was 50%. In a study by Yedibela et al.,\textsuperscript{10} 159 patients with pulmonary metastases from colorectal cancer underwent 180 thoracotomies. The 2- and 5-year survival rates after the first thoracotomy were 64 and 37%, respectively.

In our population, the actuarial 5-year survival for the 23 patients who underwent pulmonary resections for colorectal metastases was 25%, and the 5-year DFS was 18%. With regard to extrathoracic disease, especially liver metastases, almost no authors contraindicated pulmonary resection in patients who had previously received liver metastasectomy.\textsuperscript{11,12,23} In a study from Murata et al.,\textsuperscript{13} 30 patients had undergone resection of both hepatic and pulmonary metastases from colorectal cancer. Actuarial 3- and 5-year survival rates were 49 and 44%, respectively. In a study from Shah et al.,\textsuperscript{14} 39 patients underwent both lung and liver resections for metastatic colorectal cancer. The median DFI and overall survival after initial metastasectomy were 20 and 87 months, respectively.

In a study from Lizzasa et al.,\textsuperscript{15} among patients with pulmonary metastasectomy with sequential resection after partial hepatectomy, the 5-year survival rate was 32% after pulmonary resection and 67% after colorectal resection.

In our study, only one patient received pulmonary resection after a hemihepatectomy; he died 6 years later.

Although a longer DFI seems to be a favorable prognostic factor in our study, it was not a significant prognostic factor; this is supported by other authors.\textsuperscript{11,12,16} Patients with DFIs <36 months had a 3-year survival of 20%, and patients with DFIs >36 months had a 3-year survival of 38%.

In a study from Yedibela et al.,\textsuperscript{10} a DFI >36 months was a predictor of longer survival duration by univariate analysis but not by multivariate analysis.

In a study from Vogelsang et al.,\textsuperscript{17} DFI >10 months was identified as the most important prognostic factor in patients with smaller metastases (<3.75 cm), but not in the whole study group. This might explain why DFI has not been shown consistently to be a prognostic factor in previous studies.

Nevertheless, in a study from Rena et al.\textsuperscript{6} and Roberts et al.,\textsuperscript{18} patients with DFIs >36 months had significantly better survival rates than patients with DFIs <36 months.\textsuperscript{6,18}

Many authors have reported that patients with solitary metastases had better prognoses than those affected by multiple lesions.\textsuperscript{11,12,16} In a study from Lizzasa et al.,\textsuperscript{15} the number of pulmonary metastases was found to be a significant predictor for survival in both univariate and multivariate analysis. In a study from Girard et al.,\textsuperscript{19} a limited number (fewer than two) of pulmonary metastases was a predictor of longer survival duration by univariate analysis, but not with multivariate analysis. In a study from Inoue et al.,\textsuperscript{20} the number of metastases was a considerable prognostic factor. In our study, patients with a solitary lesion had a 2-year survival of 70%, and patients with multiple lesions had a 2-year survival of 50%. The difference, nevertheless, did not reach significance.

Recurrent pulmonary disease after pulmonary metastasectomy is a crucial problem; indication for reoperation is still controversial. McAfee et al.\textsuperscript{12} have reported a 5-year survival rate of 30.2% for 19 patients who underwent second thoracotomies.

In our small study, seven patients had recurrent pulmonary disease (30.4%), and three patients underwent second resections for their metastases. All three patients are alive today, with a median follow-up of 18 months. In the literature, survival of patients after a recurrent thoracotomy for pulmonary metastases is comparable with the primary thoracotomy patients; thus, patients should be offered surgery.

Our data support the results of McAfee et al. and Kandioter et al.\textsuperscript{12,21}

In our study, none of the 23 patients died after surgery. Five patients developed complications.

In conclusion, we believe that pulmonary resection for metastases of colorectal cancer does produce longer survival, even in patients with multiple lesions and recurrent metastases. It is a safe procedure, with low mortality and morbidity.

\textbf{REFERENCES}


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