Surgical Management in Lung Metastases from Colorectal Cancer


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Abstract. Background: Colorectal cancer is a non-aggressive slow-growing disease. Surgery is often considered for the management of metastases. Chemotherapeutical agents may offer tumor reduction but radical tumor remission can only be achieved by surgery. The aim of the present study was to show the evolution of patients with lung metastases from colorectal cancer, treated with surgery. Patients and Methods: Five hundred and seventy-nine (male 327, female 252, median age 60 years [range 30-87 years], disease stage IV) patients with colorectal cancer were evaluated. Histology showed adenocarcinoma with 94% moderate differentiation. Sixty-six patients (11.40%) had only lung metastasis (single or multiple deposits). Of these 66 patients, 57 were treated with surgery (pneumonectomy, lobectomy or nodule excision) and in 52/57 (91.23%) the tumor was removed. Results: In 29 patients (50.88%) the disease recurred 8 months after surgery, at the earliest; however, no recurrence was observed in 28 patients (49.12%) during 2-8 years of follow-up after the operation. Five-year survival was 32.69%. Conclusion: Metastectomy of lung metastasis from primary colorectal cancer may achieve long-term survival without recurrence in a large percentage of patients.

One of the metastatic sites of colorectal cancer is the lung, although most commonly, metastases appear in the liver. Multiple organ metastases may also be detected. Chemotherapy is the treatment of choice in advanced colorectal cancer (1-4). Chemotherapy may offer a response rate in a percentage of patients which varies from trial to trial and is usually less than 50%. Median and overall survival is prolonged by chemotherapy, particularly with the addition of newer cytotoxic agents (5-8). Patients with metastatic disease may have a long survival (9-11). Chemotherapy does not cure these patients but, given their long survival, there is time for other treatment management such as surgery. Surgical treatment is radical and can be performed when metastatic lesions are considered operable.

Metastatic disease in the liver is often managed by surgery and there are adequate data that show a prolongation of life in these patients (12-21). Lung metastases can also be treated with surgical excision, but data in the literature are sparse (22, 23). Certain criteria should be taken into account for surgical treatment, the most important of which is the nonexistence of metastatic disease in other organs. Other criteria are the number of metastatic nodules and unilateral or bilateral disease. The age of the patients and the respiratory condition (sufficient respiratory reserve) are also criteria for surgery.

In approximately 10-15% of cases, patients with colorectal cancer may have synchronous metastatic cancer at diagnosis, and in some, recurrence will be in the lungs. It has been pointed out that <10% of patients with lung metastases fulfill selection criteria and are amenable to surgery (23). Treatment for advanced colorectal cancer has improved during the last 10 years and patient survival has been prolonged (24). However, the cure rate and 5-year survival remain very low. Long-term survival of advanced colorectal cancer without recurrence can only be achieved by successful metastasectomy. To proceed in metastasectomy for lung metastases there are certain criteria which are mentioned below (preoperative assessment) (24). The data have shown successful and unsuccessful attempts in sarcomas, soft tissues or osteogenic sarcomas, in head and neck, renal, melanomas and colorectal cancers, with lung metastases (25-31). The first lung metastasectomy, which involved a patient who had two metastatic lesions originating from a chest wall sarcoma, was carried out by Weinlechner in 1882 (32). In 1994, Blalock first reported the surgical resection of pulmonary metastasis from colorectal cancer (33).

In the present study, patients with advanced colorectal cancer and lung metastases were reviewed. The material was collected from four hospitals in Athens over a period of twelve years.
Patients and Methods

Eligibility criteria. Patients with histologically-confirmed advanced colorectal cancer were reviewed. Staging by objective imaging methods was performed. Bidimensionally measurable disease was required. Patients who had lung metastases in one or both lungs were eligible. The size of metastatic disease had to be detectable (preferably 1-5 cm in diameter) and the number of lesions to be reasonably small (up to 10, and occasionally more if concentrated in one lung or one lobe). Patients with a secondary malignancy were excluded. Patients who had prior chemotherapy treatment were included in the study.

Preoperative assessment. The preoperative assessment included precise radiographic assessment of the primary site and a thorough metastatic assessment and CT scan of the chest. A single metastasis revealed by CT scan, in fact, will be the sole lesion encountered during surgery in 60% to 75% of cases (34). According to existing data, CT scans under-predict the number of lesions in 27-40% of cases and over-predict in 3% (35, 36). Before any decision was made concerning surgical management, an MRI of the brain, CT scan of the abdomen and a bone scan were performed. Pulmonary function studies, FEV1, and occasionally mediastinoscopy or bronchoscopy were evaluated. These examinations confirm that no mediastinal disease, which occasionally occurs, is found.

Further evaluation of the patients included a detailed medical and physical examination, electrocardiogram (ECG) and cardiac ultrasound.

Surgical procedure. Resections after general anesthesia should be performed conservatively, leaving as much of the lung intact as possible: this enables the patient to undergo subsequent resections in case of recurrence, and also to permit the patient to have a reasonable quality of life. Multiple procedures are recommended for patients who develop further metastases provided that the criteria for surgery continue to be fulfilled. Sternotomy was performed in patients with bilateral disease, as recommended.

A follow-up examination including a CT scan after surgery was carried out after 6-8 weeks and then every 6 to 12 months and pulmonary function tests and clinical examination every 2-3 months during the first year. The cancer markers, carcinoembryonic antigen (CEA) and CA-19-9 were examined every 2-3 months.

Patients’ characteristics. In the present study, the patients reviewed were accrued over the past 12 years. Lung cancer patients may have a long survival after the appearance of metastatic disease, particularly when the metastasis is only at one site. In order to evaluate survival after metastasectomy, a long follow-up period is necessary. The patients’ characteristics are shown in Table I. The number of reviewed patients was 579 from 4 institutions. One hundred and twenty-seven patients had lung metastasis, 66 (51.97%) of whom had no metastatic disease elsewhere. Fifty-seven of the 66 patients had been treated with chemotherapy before any decision was taken for surgery. No patient proceeded to surgical management before a median duration period of 6 months (range 3-12 months) from the time the metastatic lung disease appeared. This was considered necessary in order to confirm that the primary disease was under control and to be sure that no other metastatic disease had, in the meantime, appeared elsewhere.

Chemotherapy given before surgery was initially leucovorin/5-fluorouracil and during the last 8 years irinotecan and/or oxaliplatin were added to the previous regimen.

Patients eligible for surgery. Fifty-seven patients were eligible for surgical excision of the lung deposits. The distribution of lung deposits (unilateral or bilateral [both lungs], single or multiple) is shown in Table II. In the majority of cases, the deposits were single and unilateral. The surgical excision performed in most cases was a lumpectomy. A pneumonectomy was performed in 7% of the patients, bilobectomy in 7%, lobectomy in 41% of the patients and wedge resection or segmentectomy in the remaining 45%.

Statistical analysis. The primary end-point of the study was overall survival which was calculated from the day of the surgical excision for lung deposits until death or the end of the study. The median probability of survival was estimated by the Kaplan-Meier method.
Results

The vast majority of the patients underwent successful surgery with excision of the lung deposits. In Table III, which shows the surgical results, recurrence and 5-year survival are presented: 91.23% of the patients who had surgery had a complete excision of the metastatic nodules. Only in 5 patients was the disease found to be inoperable during the surgery. No operative or postoperative events were observed. In 29 (50.88%) patients, the disease recurred at the earliest, 8 months after the surgery. No recurrence was observed in 28 (49.12%) patients during the 2-8 years of follow-up post surgery. Five-year survival was 32.69%; patients who underwent surgery in less than 5 years (until the end of the study) and who were still without recurrence were considered. Figure 1 shows the Kaplan Meier survival curve. Median survival was 42 months (95% confidence interval (CI) 8-76 months). The great majority of patients (70.58%) who had recurrent disease, presented with it within the first 2 years.

Discussion

The improvement in survival of patients with metastatic colorectal cancer is due to better treatment related to chemotherapy with new cytotoxic agents. Furthermore, survival prolongation has been achieved by the administration of antiangiogenic drugs (bevacizumab) (37). However, the cure rate and 5-year survival have only been affected in a limited number of patients with metastatic operable disease. In our study, 52 out of the 57 patients with lung metastases who underwent surgery had a successful surgical outcome and the 5-year survival was 32.69%. These patients could be considered cured despite the advanced disease.

Several other studies have shown similar results. A trial involving 62 patients operated on for lung metastatic disease from colorectal cancer was published nearly 20 years ago. The cumulative 5-year survival was 42% (31). A more recently published study reviewed 80 patients over 20 years and showed a 41% 5-year survival (38). A higher percentage of 5-year survival, 48%, was documented in another review concerning 47 patients treated with lung metastasectomy over 15 years (39). Four other review studies also dealing with lung metastases excision from colorectal cancer were based on groups of 38 to 159 patients and showed that the 5-year survival was: 31% (40), 43% (41), 40% (42) and 41% (43). Therefore, the 5-year survival in all these studies, including ours, ranges from 31% to 48%. The results of our study show the necessity for metastasectomy of lung deposits from colorectal cancer, as previous studies have also indicated.

Colorectal cancer is a non-aggressive slow-growing disease and the one-organ site of metastases is often not followed by metastases in other organs. This fact allows surgical management to be carried out if necessary.

References


