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ORIGINAL ARTICLE

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Surgical resection of pulmonary metastases from colorectal carcinoma

Five-year survival and main prognostic factors

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Abstract Between 1986 and 1994, 19 patients underwent pulmonary resection for metastatic colorectal carcinoma. The mean interval between colon resection and appearance of pulmonary metastasis was 41 ± 21 months. All the patients had no more than two metastases. Wedge resection alone or associated with lobectomy was performed in four patients, lobectomy in ten, and pneumonectomy in five. One patient died within the month after surgery. Mean follow-up was 35 ± 26 months. The 5-year survival rate was 38.7%. Repeat thoracotomy for recurrent metastases was performed in one patient. The disease-free interval, the size of metastases, the type of pulmonary resection, and the location and the stage of primary cancer had no apparent influence on survival, but the survival rate at 4 years was 25% for patients with high carcinoembryonic antigen (CEA) level versus 80% for those with low CEA level. We conclude that, at least when the number of metastases is less than two, resection of colorectal lung metastasis is safe and effective. [Eur J Cardio-thorac Surg (1996) 10: 347–351]

Key words Pulmonary metastasis · Colorectal carcinoma · Surgical resection

Introduction

In 1944, Blalock [3] first reported the surgical resection of pulmonary metastasis from colorectal cancer. The results of the first series of patients who underwent resection of a metastatic lesion was reported in 1947 [1]. Since then, the 5-year survival rate documented by different institutions has varied from 9% to 45% [18, 26]. Drawing on our experience and an extensive review of the literature, our purpose is to determine the main 5-year prognostic variables better to define indications for resection of pulmonary metastases from colorectal cancer.

Patients and methods

From May 1986 to March 1994, 19 consecutive patients underwent resection for pulmonary metastases from colorectal carcinoma at our institution. Surgical resection was indicated when such a resection would render the patients free of disease. All patients had been evaluated for local recurrence of their colorectal cancer with endoscopy and abdominal computed tomography (CT) scan. Only patients whose metastatic site was confined to the lung and who had no more than two lesions on the CT scan were included in the study. The preoperative functional status of all patients permitted pulmonary surgery under safe conditions.

The records for each patient were reviewed for age, sex, location and stage of primary colorectal cancer, diameter of the largest resected pulmonary metastases, type of surgery, length of post-thoracotomy survival, and the disease-free interval between the resection of the primary colorectal lesion and the appearance of the pulmonary metastases.

Follow-up data were collected over a 1-month period (August 1994). All patients were traced. Patients not followed up at this institution were contacted through their referring physicians. Mean follow-up was 35 ± 26 months (range, 2–90 months). Survival after pulmonary resection was estimated according to the method of Kaplan and Meier [10]. The influence of variables on survival rates was analyzed with the log rank test [19]. A probability value less than 0.05 was considered significant.

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Results

Table 1 summarizes the location and stage of the cancer, the number of metastases and type of resection for the 19 patients (13 men and 6 women, mean age 63 years with a range of 46–76 years) studied. In all patients, the primary neoplasm was a solitary adenocarcinoma located on the colon in ten (53%) patients and on the rectum in nine (47%) patients. The neoplasm was classified as Dukes' B in 11 (58%) patients and C in 8 (42%) patients. In all patients, the pulmonary metastases were unilateral. Fifteen patients had a solitary metastasis and four had two metastases diagnosed on the chest CT scan and confirmed during the operation. The level of carcinoembryonic antigen (CEA) measured in ten patients at the time of diagnosis of the metastasis was elevated (>5 ng/ml) in four. The mean interval between the colorectal resection and the diagnosis of metastasis was 41±21 months (range, 5–79 months). Thirty-seven percent had a tumour-free interval of less than 2 years.

A wedge excision alone or associated with a lobectomy was performed in 4 (21%) of 19 patients, lobectomy alone in 10 (53%), and pneumonectomy in 5 (26%). The mean diameter of the colorectal metastases was 3.6±2 cm (range, 1–9 cm). One (5.3%) patient had lymph-node involvement. Complications are listed in Table 2. One patient died of a myocardium infarction (operative mortality, 5.3%) while in the hospital within 30 days after surgery.

Follow-up was complete in the 18 (94.7%) survivors of surgery. The mean follow-up was 35±26 months (range, 2–90 months). Table 3 lists the location of the tumor for the 12 patients who died from a recurrence of metastic colorectal cancer. The post-thoracotomy survival at 5 years was 38.7% (Fig. 1). When the influence of prognostic variables on survival was studied, age, sex, location, Dukes' stage of the colorectal cancer, size of the metastasis and the disease-free interval had no significant influence on survival. The survival rate at 4 years was 25% for patients with a CEA level greater than or equal to 5 ng/ml and 80% for those with a CEA level less than 5 ng/ml. The small number of patients in these two CEA level groups did not allow statistical analysis of these results. One patient had a second thoracotomy for local recurrence of metastasis. The interval between the first and the second thoracotomy was 35 months. Two wedge excisions were performed during the second operation. This patient was still alive 33 months after the second operation.

Table 1 The characteristics of 19 patients undergoing resection of pulmonary metastases from colorectal cancer

Characteristic	Number of patients
Localization of primary cancer	
– Colon	10
– Rectum	9
Stage of primary cancer	
– Duke'	
B1	1
B2	10
C1	2
C2	6
Number of pulmonary metastases	
– Solitary metastases	15
– Double localizations	4
Type of pulmonary resection	
– Pneumonectomy	5
– Lobectomy	10
– Segmentectomy or wedge	2
– Lobectomy plus wedge	2

Table 2 Postoperative complications

Complication	Number of complications
Arrhythmia	2
Hemorrhage	1
Venous thrombosis	1
Myocardium infarction	1
Phrenic nerve palsy	1

Table 3 Location of the tumour in 12 patients who died of a recurrence of metastic colorectal cancer*

Location of tumor	Number of patients
Peritoneal recurrence	1
Brain metastases	3
Multiple metastases	8

* Mean survival 27 months (range 1 to 69 months)

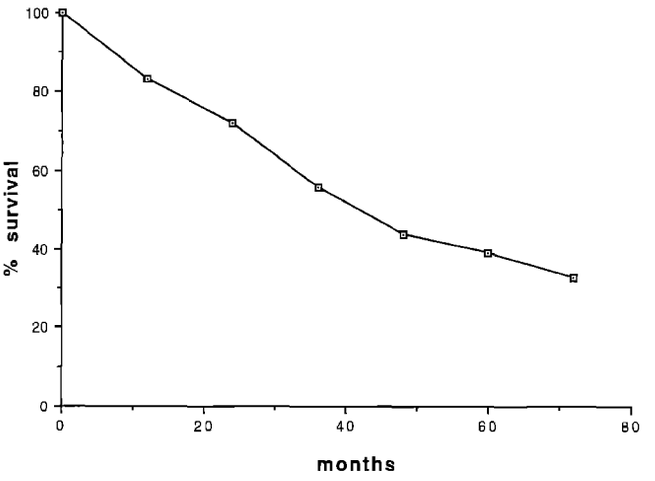

Fig. 1 Survival after resection for pulmonary metastases

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Discussion

In 1991, about 157,500 people were diagnosed with colorectal carcinoma, which is second only to those diagnosed with primary lung carcinoma [4]. McCormack and Attiyeh [12] estimated that 10% of all patients with adenocarcinoma of the colon and rectum develop pulmonary metastases, about 10% of whom (i.e., 1% of the total) will develop solitary pulmonary metastasis. Our data with a small number of patients confirm this impression that solitary pulmonary metastasis is a rare occurrence in patients with metastases from colorectal carcinoma. Although Pihl et al. [20], in a series of 16 patients, found that rectal carcinoma had a higher rate of lung metastases than colon carcinoma because of a difference in the venous outflow, our findings and those of others [15] do not confirm this result.

The mean survival time of patients with metastatic spread of their colorectal carcinoma is less than 10 months without any treatment; only 5% of these patients will be alive 5 years later [27]. Unfortunately, chemotherapy does not improve this dark prognosis. In this report, the overall 5-year survival rate of our patients was 38.7%, which is similar to that of other studies [5, 6, 8, 11–16, 18, 20, 21, 26, 28] (see Table 4).

A number of factors that could affect survival after resection of pulmonary metastases from colorectal carcinoma have been reported in other series. Age, sex and location of the primary carcinoma have never been reported as significant prognostic factors of survival [8, 11, 28]. We found that the size of the metastasis did not affect the term of survival ($P > 0.05$), like most other series [6, 14–16, 27], with the exception of Goya et al. [8] who reported, in 1989, a 45% 5-year survival rate for patients with a lesion less than 3.0 cm versus 15% for those with a lesion of 3.0 cm or more. Similarly, only McCormack and Attiyeh [12] found that a better prognosis was associated with the stage of the primary carcinoma: they reported a 37.5% 5-year survival rate for patients whose cancer was a Dukes' A lesion compared with 14% for those with a Dukes' C lesion.

The findings of most series [11] concur with ours: the type of resection does not affect the 5-year survival rate. Most series, however, had a higher rate (mean, 51%) of wedge resection than ours (21%). Wedge resection is feasible because of the usual peripheral location of metastases. This surgery permits resection of additional pulmonary nodules that may appear subsequently without compromising function and pulmonary capacity [5]. However, the rate of second thoracotomy is low: 5.3% in our study, 11% in that of Yano et al. [28], and 13.6% in that of MacAfee et al. [11]. Only Mori et al. [15] reported a 20.0% rate of re-thoracotomy. Moreover, Cahan et al. [6], who reported a large number (28%) of secondary regional lymph node metastases in patients with pulmonary metastases from the colon, advocated lobectomy and lymph node removal of these lesions. As a prognostic factor, the presence of mediastinal metastatic lymph node involvement is rarely examined in the literature. Lymph node involvement occurred in 5.3% of our patients and in 19.0% of the patients of Goya et al. [8] who found no significant difference in the survival of the patients who had hilar or mediastinal lymph node metastases and those who did not. However, Regnard et al. [21] recently reported that only 1 of their 22 patients who presented with lymph node involvement was alive at 5 years.

A frequently analysed factor is the median interval between colorectal resection and the appearance of pulmonary metastases. Our 37% rate of patients with a disease-free interval of less than 2 years is the same as that of other publications [14]. Although Brister et al. [5] suggest that

Table 4 Five-year survival rate and prognostic factors after pulmonary resection for metastatic colorectal carcinoma. (*DFI* disease-free interval, *CEA* carcinoembryonic antigen, *Yes* significant factor, *No* insignificant factor, – not available)

Source, year [reference]	Number of patients	Mean 5-year survival (%)	Lung metastases		DFI	CEA
			Number	Size		
Cahan et al. 1974 [6]	20	35.0	–	–	No	–
Mountain et al. 1978 [16]	28	28.0	–	–	No	–
McCormack and Attiyeh 1979 [12]	35	22.0	No	–	No	–
Wilking et al. 1985 [26]	27	9.0	Yes	–	No	–
Mansel et al. 1986 [14]	66	38.0	Yes	No	No	–
Pihl et al. 1987 [20]	16	38.0	–	–	–	–
Brister et al. 1988 [5]	27	21.0	–	–	Yes	–
Goya et al. 1989 [8]	62	42.0	Yes	Yes	No	–
Mori et al. 1991 [15]	35	38.0	No	No	No	–
MacAfee et al. 1992 [11]	139	30.5	Yes	No	No	Yes
Yano et al. 1993 [28]	27	41.1	Yes	No	No	–
Ohata 1993 [18]	23	45.0	–	–	–	–
Maebaya et al. 1993 [13]	14	25.7	–	–	–	–
Regnard et al. 1994 [21]	95	21.0	No	–	No	–
Current series	19	38.7	–	No	No	–
Totals	633	31.5	–	–	–	–

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it is logical that a longer disease-free interval reflects a slower growing primary malignancy and is associated with longer post-thoracotomy survival, most authors [8, 15, 28] have reported that the length of this interval bears no relation to survival.

The number of pulmonary metastases has been reported as the main important prognostic variable. In 1986, Mansel et al. [14] reported that the cumulative survival rate for patients with a solitary pulmonary metastasis was 49%, whereas that for patients with two or more pulmonary metastases was 8%. Goya et al. [8] and Yano et al. [28] concur with their results. For this reason we limited our study to persons with only one or two metastases. However, MacAfee et al. [11], who observed a 5-year survival rate of 25% after surgery for patients with multiple metastases in the later period of their study (1980–1987), do not consider this factor a contraindication to resection.

The CEA level has been studied only once, with very interesting results. MacAfee et al. [11] reported that the 5-year survival for patients with a pre-thoracotomy CEA level of less than 5 ng/ml was significantly higher (46.8%) than that for those with a CEA level of 5 ng/ml or greater (16.0%; $P<0.01$). Moreover, those with a high CEA level all developed recurrent colorectal cancer after thoracotomy. *This report and our results will certainly incline us to pay more attention to the CEA level before the treatment of these metastases.* However, MacAfee et al. [11] do not consider an elevated CEA level an absolute contraindication to pulmonary resection, since the 5-year survival rate after this procedure was still 16%.

At the time of the diagnosis of lung metastases, other metastases are frequently found, especially hepatic ones. Actually the liver is the organ most commonly affected by hematogenous metastases in colorectal cancer. As many as 35% of the patients have already had hepatic metastases at the time of exploration for resection of primary colon cancer [2]. After surgical resection of hepatic metastases, the 5-year survival rates range from 25% to 42% [9, 17, 25], comparable to those after resection of lung metastases. So far, we have not considered the association of different sites of metastases as a surgical indication, but recent reports [23, 25–28] that refer to the 5-year survival rate of patients after pulmonary resection in the presence of controlled hepatic metastases should lead us to reconsider the indications for surgery. Yano et al. [28] reported a 5-year survival rate of 68.7% in seven patients who had this association of metastases; Smith et al. [23], 52.0% in ten patients. Similarly, the 20 such patients reported by MacAfee et al. [11] had a 30.0% 5-year survival rate, which does not differ significantly from the 30.7% 5-year survival observed in the same study in the 119 patients without metastases in other locations.

Few have studied the effect of adjuvant chemotherapy on survival. Among the ten patients reported by Smith et al. [23], five underwent adjuvant chemotherapy without effect on survival; however, because of the small number of patients studied, no conclusion can be drawn about the effectiveness of their adjuvant therapy. By contrast, chemotherapy has been extensively studied to prevent the metastatic spread of colorectal carcinoma. Three protocols have been found effective: combined intravenous 5-fluorouracil (5-FU) and levamisole in the case of colorectal carcinoma with lymph node involvement [22], combined 5-FU and folinic acid in the same situation [7], and 5-FU given in the portal vein during the week after surgical resection of the colorectal carcinoma through a catheter placed during the surgical procedure [24].

In summary, surgical resection of a pulmonary metastasis from colorectal cancer is associated with very low mortality and morbidity and a significant 5-year survival rate. From the literature, the main prognostic factors seem to be the number of metastases and perhaps the pre-thoracotomy CEA level. Further studies must be undertaken to identify the exact frequenc of lymph node involvement and the influence of this factor on the 5-year survival rate. Currently, since no effective chemotherapy for such lesions is available, aggressive surgery for pulmonary metastases should be pursued.

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