The role of hepatic metastases and pulmonary tumor burden in predicting survival after complete pulmonary resection for colorectal cancer

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Objective: Our objective was to investigate the role of clinicopathologic factors as predictors of outcome after complete pulmonary resection for metastatic colorectal cancer.

Methods: Consecutive patients undergoing radical pulmonary resection for colorectal cancer at our institution were included in the study. Clinicopathologic variables including sex, age, site and stage of the primary tumor, disease-free interval, prior hepatic resection, timing of pulmonary metastases, preoperative chemotherapy, type of pulmonary resection, number, size, and location of pulmonary metastases, and thoracic lymph node involvement were retrospectively collected and investigated for prognostic significance. Survival curves were generated by the Kaplan-Meier technique and difference between factors were evaluated by the log-rank test.

Results: A total of 127 patients undergoing pulmonary resection between 1997 and 2009 were included in the study. The median follow-up was 67.1 months. The median overall survival from the time of pulmonary resection was 48.9 months. The 5-year overall survival was 45.4%. Among all investigated prognostic variables, the number of pulmonary metastases (1 vs >1) was the most important factor affecting the outcome after pulmonary resection (5-year overall survival 55.4% vs 32.2%; hazard rate, 1.92; $P = .006$).

Conclusions: In this study, the presence of a single pulmonary metastasis was a favorable predictor of survival after complete pulmonary resection for metastatic colorectal cancer. All the other prognostic variables did not seem to affect survival and should not contraindicate such surgery in clinical practice. However, the study sample size does not allow us to draw any definitive conclusion, and further investigation of the role of these prognostic factors in larger series is warranted. (*J Thorac Cardiovasc Surg* 2013;145:97-103)

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Colorectal cancer (CRC) is the second most common malignancy and the second leading cause of cancer death in Europe.¹ When symptoms first occur, about 20% of CRC patients are diagnosed with metastatic disease. After curative resection of the primary tumor, approximately 25% of patients have a recurrence.²

The recent development of biological agents has drastically enhanced the therapeutic options for patients with metastatic CRC, with better outcome in terms of disease control

and prolonged survival. Moreover, the practice of radical surgery even in the metastatic setting has converted a traditionally unfavorable condition into a potentially curable disease. The number of patients amenable to curative resection of metastases has increased. Higher response rates, owing to new combination regimens, greatly increased the ability to render resectable an initially unresectable disease.³

The most common site of recurrence is the liver, and hepatic resection is a widely established curative option, with survivals approaching 60% in highly selected series.⁴ The lung is less frequently involved, with only 10% of CRC patients having pulmonary metastases.⁵ Curative pulmonary resection has also emerged as a safe and effective procedure. Recent improvements in the perioperative care and surgical techniques have significantly reduced the operative mortality from such surgery to less than 1%. Recent retrospective studies have reported 5-year survivals higher than 50% in patients surgically treated for isolated pulmonary metastases.⁶

Nevertheless, relative to hepatic resection, pulmonary resection is more questioned and less practiced as a routine surgical procedure, with palliative treatments often favored. Indeed, less information is available about its real impact on the outcome of patients with metastatic CRC, and prognostic factors predicting tumor recurrence after pulmonary surgery are still to be completely elucidated.⁶

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Abbreviations and Acronyms

CI	= confidence interval
CRC	= colorectal cancer
HR	= hazard rate

One of the most intriguing topics is the prognostic significance of a history of hepatic metastases.⁷ Few studies specifically addressing this controversial issue have been published.⁸⁻¹³ In most of them, the survival benefit derived from resection of pulmonary metastases does not seem to be negatively affected by a previous surgical procedure. However, the retrospective design and the absence of a comparable comparison group with sufficient statistical power are important limitations.

Through the retrospective analysis of consecutive patients who underwent pulmonary resection at a single center, we aimed to clarify the prognostic impact of a number of clinicopathologic variables on the outcome of patients undergoing radical pulmonary resection for metastatic CRC. We also focused on the prognostic significance of synchronous or metachronous hepatic metastases.

PATIENTS AND METHODS

We retrospectively reviewed the medical records of all the patients treated with surgery for pulmonary metastases from CRC at Istituto Clinico Humanitas, Rozzano (Italy). Patients were included in the analysis only if (1) they had undergone colorectal resection before the time of pulmonary resection, (2) pulmonary resection was performed with a curative intent, and (3) pathologic analysis of the resected pulmonary tissue had clearly documented a diagnosis of metastatic deposit from CRC. Patients with residual disease after pulmonary surgery, patients with a history of surgery for metastatic disease other than hepatic and pulmonary, and patients undergoing pulmonary resection in the presence of hepatic metastases not amenable to a simultaneous or staged surgical procedure were excluded from the analysis.

For all patients fulfilling the inclusion criteria and deemed suitable for analysis, we collected the following characteristics: sex, age, site and stage of the primary tumor, presence/absence of pulmonary metastases at diagnosis, disease-free interval from the time of colorectal surgery, previous hepatic surgery, chemotherapy before pulmonary resection, type and aim of pulmonary resection, surgical complications, number, size, and location of pulmonary metastases, thoracic lymph node involvement, hospital stay after surgery, and date of last contact or death.

Given the rising interest in the possible prognostic role of a prior hepatic resection, we also analyzed in detail the baseline characteristics and survival outcome of patients with a history of hepatic metastases. To this aim, all the patients included in the study were separated into 2 groups. Group A included patients who had isolated pulmonary metastases and received pulmonary resection as the first surgical approach to metastatic disease. Group B included patients who had a history of hepatic metastases and received hepatic resection before or concurrent with pulmonary resection. For this subgroup analysis, hepatic and pulmonary resections were considered as synchronous when performed in a 1-stage surgical procedure or, if performed in a 2-stage procedure, when the second metastasectomy was carried out within 3 months from the time of the first metastasectomy.

During the study period, patient selection was carried out individually. In general, the indication for pulmonary surgery was given when preoperative

imaging ruled out extrathoracic and/or unresectable disease and indicated the possibility to achieve clear resection margins and leave sufficient functioning parenchyma so that the patient had adequate pulmonary reserve for planned resection and was fit for surgery. Median sternotomy or sequential thoracotomies were used for patients with bilateral metastases, whereas video-assisted thoracoscopic surgery was essentially used for peripheral metastases. Systematic lymph node dissection was not routinely carried out but was performed according to the surgeon's judgment.

After pulmonary resection, patients were usually given a follow-up program with outpatient visits every 3 months for the first 2 years, every 6 months for the following 3 years, and every 12 months thereafter. At every outpatient visit, chest radiography or chest computed tomography and/or an abdominal ultrasound or computed tomography were carried out for surveillance of thoracic and extrathoracic relapse, respectively. Hematology, biochemistry, and serum carcinoembryonic antigen were routinely checked at every visit.

Statistical Analysis

Objectives of this study were to identify predictive factors of outcome in patients undergoing radical pulmonary resection for metastatic CRC.

Patient demographic and clinical characteristics were reported descriptively. For the analysis of the prognostic role of hepatic metastases, differences between patients in group A and patients in group B were tested by χ^2 or Mantel-Haenszel χ^2 test when appropriate.

Overall survival was calculated from the date of pulmonary surgery to death (if alive, patients were censored at the time of the last contact). In case of bilateral or 2-step pulmonary resections and synchronous hepatic and pulmonary surgery, metrics were calculated from the time of the second resection. In the case of patients lost to follow-up, the survival status was corroborated by using the local registry offices or through a first-degree relative contact.

For the identification of prognostic factors, survival curves were generated by using Kaplan-Meier technique and differences between factors were evaluated by the log-rank test. Statistically significant variables were tested in a multivariate Cox proportional hazards regression model.

RESULTS

From April 1997 to September 2009, a total of 185 patients underwent surgical resection for pulmonary metastases from CRC at our institution. Thirty-six patients were excluded from the study because of the palliative or diagnostic intent of resection and residual disease after thoracotomy. Eleven patients were excluded because they had had a previous operation for a metastatic deposit other than hepatic and pulmonary. Eleven patients were excluded because their first thoracotomy had been performed at a different institution and complete clinicopathologic data were not available. Overall, 127 patients fulfilled the inclusion criteria and were then suitable for the analysis.

Patient characteristics are listed in Table 1. There were 79 (62%) men and 48 (38%) women. The median age was 65.5 years. More than 25% of patients originally had metastatic disease (half of them with pulmonary metastases); in the other 53% metastases developed more than 1 year after colorectal surgery. At least 1 chemotherapy regimen was administered to 43% of patients before the time of pulmonary resection (range, 0-4). Ten (8%) patients had preoperative systemic therapy, 28 (22%) had postoperative therapy, and only 3 (2%) received a perioperative treatment. Wedge resection was more frequently used than anatomic resection

TABLE 1. Patient characteristics

	n (%)
All	127 (100)
Sex	
Male	79 (62)
Female	48 (38)
Median age (y) (range)	65.5 (33.4-80.6)
Primary site	
Colon	78 (61)
Rectum	48 (38)
Colon and rectum	1 (1)
Stage of primary	
1-2	35 (28)
3	40 (31)
4	35 (28)
Unknown	17 (13)
Pulmonary metastases at diagnosis	
Yes	23 (18)
No	104 (82)
Disease-free interval (mo)	
0-12	60 (47)
>12	67 (53)
Chemotherapy lines before resection	
0	69 (54)
≥1	55 (43)
Unknown	3 (3)
History of hepatic metastases	
Yes	39 (31)
No	88 (69)
Surgical technique	
Anatomic resection*	48 (38)
Wedge resection	79 (62)
No. of pulmonary metastases	
1	71 (56)
>1	56 (44)
Site of pulmonary metastases	
Unilateral	97 (76)
Bilateral	30 (24)
Size of pulmonary metastases (mm)	
0-10	18 (14)
>10	109 (86)

*Include pneumonectomy, (bi)lobectomy, and segmentectomy.

(62% vs 38%), and in 61% of cases a lymph node dissection was carried out. A solitary pulmonary lesion was diagnosed in 56% of patients, and a predominance of unilateral pulmonary involvement was observed in 76%. The median size of pulmonary metastases was 20 mm (range, 5-80 mm) and most of them (86%) had a maximum diameter greater than 10 mm.

Median follow-up was 67.1 months (0.4-159.1 months). At the time of data collection, 74 (58%) of 127 patients had died. The postoperative morbidity rate was 12% and included only minor self-limiting complications. Two patients died within 60 days of pulmonary resection, for an overall postoperative mortality rate of 1.5%. Thirty-three (30%) patients were alive 5 years after pulmonary

TABLE 2. Univariable analysis of potential predictive factors of outcome after pulmonary resection

Variable	No. of events (N)	Five-year overall survival (95% CI)	P value
Sex			.157
Male	49 (79)	39.0 (26.6-51.4)	
Female	25 (48)	56.4 (40.6-72.3)	
Age			.204
<70 y	51 (86)	52.5 (41.0-64.0)	
≥70 y	23 (41)	23.1 (5.1-41.1)	
Primary site			.611
Colon	48 (78)	47.5 (35.2-59.8)	
Rectum	26 (48)	41.0 (24.3-57.7)	
Stage of primary			.153
1-2	18 (35)	54.1 (35.8-72.5)	
3	25 (40)	44.2 (26.2-62.1)	
4	19 (35)	41.9 (23.3-60.4)	
Lung metastases at diagnosis			.225
Yes	23 (10)	53.4 (30.6-76.3)	
No	104 (64)	43.8 (32.9-54.7)	
Disease-free interval (mo)			.370
0-12	33 (60)	46.1 (31.8-60.4)	
>12	41 (67)	44.7 (30.9-58.5)	
Chemotherapy lines before resection			.035
0	37 (69)	56.1 (42.5-69.7)	
≥1	36 (55)	29.6 (15.6-43.5)	
Surgical technique			.630
Anatomic resection*	28 (48)	49.2 (33.2-65.3)	
Wedge resection	46 (79)	43.2 (30.6-55.7)	
No. of lung metastases			.004
1	36 (71)	55.4 (42.2-68.3)	
>1	38 (56)	32.2 (17.9-46.5)	
Site of lung metastases			.152
Unilateral	52 (97)	48.7 (37.0-60.4)	
Bilateral	22 (30)	35.6 (17.5-53.8)	
Size of lung metastases (mm)			.046
0-10	5 (18)	55.9 (25.6-86.2)	
>10	69 (109)	43.5 (33.1-54.0)	
Thoracic lymph nodes			.118
Normal	38 (67)	46.9 (33.3-60.4)	
Metastatic	10 (12)	19.4 (0.0-43.3)	

Boldface indicates predictive factors that were statistically significant at univariable analysis. CI, Confidence interval. *Include pneumonectomy, (bi)lobectomy, and segmentectomy.

resection. The median overall survival was 48.9 months. The 5-year overall survival was 45.4%.

The univariate analysis of the prognostic factors investigated indicated the number ($P = .004$) and size ($P = .05$) of pulmonary lesions and the number of prior chemotherapy lines ($P = .03$) as predictors of outcome after pulmonary resection (Table 2).

In a multivariate model including these 3 variables of interest, only the number of pulmonary lesions retained its prognostic significance, with a 5-year overall survival of 55.4% in case of a solitary pulmonary lesion versus 32.2% in case of multiple pulmonary lesions (hazard rate [HR],

FIGURE 1. Overall survival after resection of pulmonary metastases from colorectal cancer according to the number of pulmonary metastases (1 = dotted line; >1 = solid line).

1.92; 95% confidence interval [CI], 1.201-3.069; $P = .006$) (Figure 1).

Given the limitations resulting from the relatively small study sample size, a multivariate model including all variables presenting a P value $< .2$ was set. Consistent with the main analysis, we found that only the number of pulmonary metastases was a statistically significant predictor of outcome. Furthermore, in the attempt to use clinically meaningful variables as potential risk adjusters, disease-free interval (reported in some studies as a statistically significant prognostic factor) and size of pulmonary metastases were included in the multivariate model despite nonsignificant P values in the univariate analysis. In this model the number of pulmonary metastases retained its significance (HR, 1.64; 95% CI, 1.01-2.67; $P = .044$) but, more interestingly, also the number of chemotherapy lines before pulmonary resection was found to be a statistically significant predictor of outcome (HR, 1.70; CI 95%, 1.04-2.80; $P = .036$).

When the entire study population was analyzed according to the presence or absence of a history of hepatic resection, we observed the following findings. In 88 (69%, group A) patients, lung was the first site of recurrence after colorectal surgery and pulmonary metastasectomy was the first surgical procedure for metastatic disease. In 39 (31%, group B) patients, pulmonary resection followed (or was synchronous to) a radical operation for hepatic disease. Owing to their comparable clinical history, 3 patients who actually had not received a curative hepatectomy were included in the latter group. They were treated with systemic chemotherapy and had complete response in hepatic metastases. In 1 case, no signs of hepatic disease were appreciable at the time of pulmonary surgery,

TABLE 3. Patient characteristics according to the presence/absence of a history of hepatic resection

	Group A: n (%)	Group B: n (%)	<i>P</i> value
All	88 (100)	39 (100)	
Sex			.92
Male	55 (63)	24 (61)	
Female	33 (37)	15 (39)	
Median age (y) (range)	65.5 (34.7-80.6)	65.2 (33.4-80.2)	.30
Primary site			.16
Colon	51 (58)	27 (70)	
Rectum	37 (42)	11 (28)	
Colon and rectum	0 (0)	1 (2)	
Stage of primary			.04
1-2	26 (30)	9 (23)	
3	30 (34)	10 (26)	
4	18 (20)	17 (43)	
Unknown	14 (16)	3 (8)	
Pulmonary metastases at diagnosis			.38
Yes	18 (20)	5 (13)	
No	70 (80)	34 (87)	
Disease-free interval (mo)			.001
0-12	33 (37)	27 (69)	
>12	55 (63)	12 (31)	
Chemotherapy lines before resection			<.001
0	64 (75)	5 (13)	
≥1	21 (25)	34 (87)	
Surgical technique			.28
Anatomic resection*	36 (41)	12 (31)	
Wedge resection	52 (59)	27 (69)	
No. of pulmonary metastases			.94
1	49 (56)	22 (56)	
>1	39 (44)	17 (44)	
Site of pulmonary metastases			.92
Unilateral	67 (76)	30 (77)	
Bilateral	21 (24)	9 (23)	
Size of pulmonary metastases (mm)			.79
0-10	12 (14)	6 (15)	
>10	76 (86)	33 (85)	
Thoracic lymph nodes			.73
Normal	48 (55)	19 (49)	
Metastatic	8 (9)	4 (10)	
Unknown	32 (36)	16 (41)	

*Include pneumonectomy, (bi)lobectomy, and segmentectomy.

2 years after the first radiologic evidence of complete response, and no hepatic surgery was performed. In the other 2 cases, a partial clinical response was obtained but no viable tumor cells were found after hepatic resection for the residual.

Clinical characteristics of patients in both groups are listed in Table 3. The 2 groups were well balanced. No statistically significant differences ($P < .05$) were observed for the variables sex, age, number, site and size of pulmonary

lesions, pathologic nodal involvement, surgical techniques, and hospital stay after pulmonary resection. Patients in group B more often had metastatic disease at the time of initial diagnosis (43% vs 20%), had had an earlier relapse after colorectal surgery (69% vs 37% by 12 months), and had received a greater number of lines of chemotherapy before the time of pulmonary resection (87% vs 25%).

Characteristics of patients in group B are described in detail in Table 4. A repeat hepatic resection was necessary to control hepatic metastases in only 4 patients (2 successive resections in 3 patients and 3 in 1 patient). Two sequential surgical procedures (hepatic first and pulmonary later) were carried out in 31 (79%) patients. In the remaining 8 (21%) patients, hepatic surgery and pulmonary resection were performed synchronously. In 7 patients a 2-stage surgical procedure was carried out, with pulmonary resection following hepatic resection in 5 patients. In only 1 patient was a 1-stage procedure performed.

Median follow-up was 63.2 months (2.0-159.1 months) for patients in group A and 68.8 months (0.4-98.7 months) for patients in group B. Postoperative morbidity rate was 16% in group A and 3% in group B, and 1 postoperative death was recorded in each group. At the time of data collection, 49 (56%) patients in group A and 25 (64%) patients in group B had died. Twenty-four (27%) patients in group A and 9 (23%) in group B were alive 5 years after pulmonary resection. The median overall survival was 59.4 months for patients in group A and 30.1 months for patients in group B. Overall survival at 5 years was 51.4% for patients in group A and 31.9% for patients in group B. The difference in outcome between the 2 groups did not reach statistical significance (HR, 1.38; 95% CI, 0.85-2.25; $P = .19$).

DISCUSSION

Although no results of randomized trials are available, surgery is currently considered, when feasible, the best option for resectable pulmonary metastases from CRC.

TABLE 4. Details of patients with a history of hepatic disease

	n (%)
No. of hepatic resections	
1	34 (89)
>1	4 (11)
Timing of hepatic and pulmonary resection	
Synchronous resection	8 (21)
Metachronous resection	31 (79)
Time from primary resection to pulmonary relapse (mo)	
0-12	13 (33)
>12	26 (77)
Median (range)	27 (0-142.4)
Time from hepatic relapse to pulmonary relapse (mo)	
0-12	16 (41)
>12	23 (59)
Median (range)	19 (0-107)

Five-year survivals ranging from 37% to 67% have been reported in retrospective series.^{12,14} However, pulmonary resection is not yet as widely established and frequently practiced as hepatic resection, and controversy still exists about its role in the management of metastatic CRC.

Several attempts to identify patients most likely to benefit from such strategy have been made, but the small number of patients in most series has limited the identification of prognostic factors influencing the outcome after resection.⁶ As a result, the decision for a surgical approach is still dependent mainly on the conviction and expertise of the surgeon rather than on the adherence to established prognostic criteria.

In this study, we investigated the prognostic role of a number of clinicopathologic variables previously reported as potentially predictive of outcome. Consistent with the results of some studies^{8,11,12} but in disagreement with the results of some others,¹⁴⁻¹⁶ the number of pulmonary metastases was the only factor found to independently predict prognosis, with a significantly better outcome for patients with a solitary lesion than for patients with multiple pulmonary lesions. If further confirmed in larger series, the prognostic significance of pulmonary tumor burden would influence the diagnostic and therapeutic algorithm for pulmonary metastasectomy. An accurate preoperative radiologic assessment of the pulmonary parenchyma would in fact be necessary to identify the extent of metastatic pulmonary involvement, the presence of multiple pulmonary lesions, as well as the presence of active disease in extrathoracic sites, potentially affecting the survival benefit deriving from the use of an aggressive surgical approach. Moreover, in the presence of multiple, small pulmonary nodules of indeterminate nature and not amenable to a definitive characterization by imaging, it would be worth using preoperative medical treatments (ie, preoperative chemotherapy) aiming at reducing disease burden and clarifying empirically the extent of pulmonary disease. Unfortunately, the limited number of patients who were enrolled in our study and had received a complementary systemic treatment precluded any proper investigation of the role of preoperative, postoperative, or perioperative strategies.

Interestingly, in our study a history of hepatic metastases did not significantly affect the survival of patients undergoing curative pulmonary resection. To our knowledge, 18 series including more than 30 patients treated with hepatic and pulmonary resection have been reported so far,⁸⁻²⁴ with 5-year survivals, from the time of the second metastasectomy, ranging from 11% to 43.1%. However, only 6 studies have investigated the prognostic impact of a previous (or synchronous) hepatic operation and the results are not fully consistent.⁸⁻¹³

In a retrospective series of 47 patients, Kobayashi, Kawamura, and Ishihara⁸ reported an actuarial 5-year

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survival of 31% for patients receiving sequential hepatic and pulmonary resection, and no significant survival difference was observed in these patients compared with 304 patients undergoing pulmonary resection only. Less promising results were reported by Regnard and colleagues.⁹ In this study, the 5-year survival for patients undergoing sequential surgery (43 patients) was 11% and, more interestingly, none of the patients in this group was alive at 6 years, compared with 17% of patients alive at 10 years in the group without hepatic disease. Yedibela,¹⁰ Watanabe,¹¹ and their associates reported 2 retrospective monocentric series of 153 and 122 patients, respectively, treated with pulmonary metastasectomy. In neither of these studies was a history of hepatic metastases (reported in 43 and 33 patients, respectively) demonstrated as an unfavorable prognostic factor. More recently, in the largest series ever reported by Onaitis and coworkers¹² (378 patients, 166 treated with repeat surgery), the occurrence of a previous extrathoracic relapse was found to have a trend toward a negative prognostic influence on outcome after pulmonary resection. Finally, in the recent study by Brouquet and associates,¹³ the survival of 112 patients undergoing hepatic and pulmonary resection was greater than that of patients receiving hepatic resection only (5-year overall survival 50% and 40%, respectively), and the presence of resectable lung metastases was not demonstrated to be a poor prognostic factor or a contraindication to resection of hepatic metastases.

All these studies lacked a well-defined control group and were potentially affected by biases derived from the retrospective analysis of highly selected patients, deemed suitable for a repeat resection and possibly yielding a biologically less aggressive tumor with a more favorable prognosis. Moreover, some of the mentioned studies^{8,12} recruited patients from different hospitals, with the study populations likely to be affected by the heterogeneity derived from receiving treatment at different institutions.

As result of the limited available data and the lack of strong evidence, the investigators of the Pulmonary Metastasectomy in Colorectal Cancer (PulMiCC) trial (the first feasibility study to determine whether it is possible to conduct a larger randomized trial on the role of pulmonary metastasectomy) included a history of hepatic metastases into what they called the “zone of uncertainty.”²⁵ That is, a previous (or synchronous) history of hepatic metastases does not represent an absolute contraindication for a metachronous (or concurrent) pulmonary resection. It should, however, be taken into consideration and carefully weighed with other variables when evaluating the individual clinical benefit derived from a surgical approach to metastatic pulmonary disease.

In our study, we included consecutive patients treated at a single institution over a relatively short period. We reported 5-year survivals of 31.9% and 51.4% for the group

with a history of hepatic metastases and the group without a history of hepatic metastases, respectively. The outcome of either group appeared consistent with that reported in previous series.^{10,14,18} More interestingly, the difference in survival between the 2 groups was not statistically significant and only a trend toward a worse outcome was observed for patients with hepatic metastases. Whether this result truly represents the absence of a prognostic difference between the 2 groups or is rather affected by the lack of statistical power of the study is not known. To analyze the prognostic role of hepatic metastases and detect a 38% increase in the hazard of death after pulmonary resection for CRC, we estimated that, with a power of 80% and an alpha value of .05 (2 sides), at least 300 deaths would be necessary. The current study is therefore underpowered (beta > 50%) to detect such a clinically relevant difference.

Indeed, our analysis is limited by several factors such as the relatively small number of patients and the retrospective design. However, the analysis of 2 comparable, homogeneous groups with only few imbalances strengthens the clinical suitability of the results of our study.

In conclusion, the recent increase of the indication for surgical resection of pulmonary metastases from CRC warrants a careful patient selection based on the identification of reliable prognostic factors. Unfortunately, at present no definitive data about predictors of outcome exist. Furthermore, whether the presence of synchronous hepatic and pulmonary metastases or the development of pulmonary metastases after a previous hepatic resection for CRC demonstrate a biologically aggressive tumor and represent a clear sign of the failure of an aggressive surgical approach is still unclear. The results of our study confirm pulmonary resection as an effective strategy for the treatment of metastatic CRC and support the number of pulmonary metastases as the most important predictor of survival after surgery. Larger series are probably needed to clarify the prognostic role of other factors such as a history of hepatic metastases.

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