

# Endobronchial Metastases from Colorectal Cancers: Natural History and Role of Interventional Bronchoscopy

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## Key Words

Endobronchial metastases · Bronchoscopy · Gastroenterology · Oncology

## Abstract

**Background:** Endobronchial metastases are rare. The most frequent primary tumors associated with endobronchial involvement are breast, colon and renal cell carcinomas. Metastases from colorectal cancers can be treated either surgically or with chemotherapy in order to improve survival. **Objectives:** This paper aims to report the potential role of interventional bronchoscopy in patients with endobronchial metastases from colorectal cancer. **Methods:** This retrospective study included 24 patients who underwent an interventional bronchoscopy procedure between 1988 and 2006. All patients had verified tracheobronchial metastases and were treated to relieve their obstruction. Assessment of the natural history of metastatic colorectal carcinoma, therapeutic options and survival associated with endobronchial metastases are reported. **Results:** Endobronchial metastases occurred at a median of 53 months (range 18–144) following the diagnosis of the primary tumor. Fifty-seven percent of patients had other proven metastases when the endobronchial involvement was diagnosed. All patients had known synchronous pulmonary metastases upon the discovery of tracheobronchial secondary lesions. The most frequently observed symptoms were dyspnea, cough and hemoptysis. Atelectasis was a common radiological finding. In

67% of patients, an interventional bronchoscopy was possible with the primary intent of relieving the obstruction. An endoscopic intervention provided symptomatic relief and an improvement in forced expiratory volume in 1 s. The median overall survival was 70 months (range 23–245) and 14 months once the endobronchial metastase(s) had been diagnosed. **Conclusion:** Endobronchial metastases occur relatively late in patients with a metastatic colorectal neoplasm. Palliative treatment with interventional bronchoscopy to prevent asphyxia is a safe and effective method that may improve the quality of life in these patients.

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## Introduction

Pulmonary and pleural metastases are frequently observed in patients with non-primary pulmonary neoplasms while an endobronchial involvement is rare. An endobronchial metastasis (EM) is defined as a lesion in the tracheobronchial tree with the same histological aspect as the primary tumor from which it derives. According to postmortem studies, the prevalence of EM is 2% [1]. Patients with pulmonary metastases develop endobronchial lesions in 18–42% of cases [2]. EMs are most frequently observed in patients with breast cancer and colorectal and renal cell carcinoma [3]. Colorectal cancers are responsible for 12–26% of EMs [4].

Colorectal cancer accounts for 15% of all cancers. A 50% increase in the number of cases has been observed between 1980 and 2000. More than half of the new cases are diagnosed at either a locally advanced or metastatic stage when curative surgery is no longer possible. Recurrence is reported to occur in 30–40% of patients and is higher than 50% when lymph nodes are involved [5].

This retrospective study includes 24 patients presenting with endobronchial metastases that have been considered or treated with interventional bronchoscopy. The main goal of the intervention was to relieve the obstruction. Furthermore, the aim of our study is also to report the natural history of metastases originating from colorectal carcinomas, the treatment options for EM and survival once the EMs have been diagnosed and treated.

### Materials and Methods

This study was conducted with the interventional bronchoscopy database from the Pulmonary and Thoracic Oncology Department of the Centre Hospitalier Universitaire (CHU) de Saint-Etienne.

Subjects were either referred to our institution after an EM diagnosis was confirmed by a bronchoscopic biopsy in a plausible context of EM or because their imagery suggested an endobronchial involvement. The referring institutions were the following: CHU de Saint-Etienne and 8 hospitals from the Rhône-Alpes region. According to the French ethics regulations, all cases were discussed in a multidisciplinary team conference and the protocol was approved by the local committee. The patients were then treated after the informed consent was obtained.

All interventions were performed by the same bronchoscopist (J.-M.V.).

Subjects were admitted the day before endoscopic intervention. A chest radiograph was performed before and after the bronchoscopy. For the majority of patients, pulmonary function tests were performed before and after intervention. They were discharged the day after the resection or, in the case of a stent insertion, 2 days after.

The endobronchial resection was performed under general anesthesia in an operating room using a rigid bronchoscope. Adequate ventilation for the patient was provided.

A mechanical resection of the tumor was completed using the tip of the bronchoscope. Bleeding was controlled by a tamponade of the tumor with the bronchoscope. An Nd-YAG laser was available for hemostatic purposes if needed. Once the endoscopic debulking was completed, a cryotherapy or stent insertion was considered to supplement the therapeutic session.

Relevant clinical information regarding the subject's outcome was obtained from the various referring institutions. The TNM classification from the International Union Against Cancer, 6th edition, was used in this study [6]. The time interval between EM and the diagnosis of colon cancer, the overall survival and survival after EM diagnosis were assessed.

### Results

From 1988 to 2006, 82 patients were treated for EM of non-pulmonary neoplasms.

Of these, 24 were included provided they had undergone an endobronchial resection of the metastase(s) stemming from the colorectal cancer.

The patients' baseline characteristics, symptoms and radiologic findings upon their initial admission to our center and after the intervention are shown in table 1.

All patients had adenocarcinoma with various differentiation stages. The median time to progression to metastases was 36 months (range 0–144). The median time associated with the diagnosis of EMs was 53 months (range 18–144) following the diagnosis of the primary tumor. At diagnosis, 15 subjects (62%) already had a metastatic disease: 12 with metastases to the lung (including 10 that had undergone a resection), 7 with metastases to the liver (including 5 that had undergone a resection) and 4 with metastatic mediastinal lymph nodes. Upon the EM diagnosis, all subjects had known or synchronous lung metastases.

Four patients did not receive any adjuvant chemotherapy or metastatic disease treatment. They were all diagnosed with EM at the same time as their primary malignancy, and the median age was 78 years (range 70–93).

The number of chemotherapy lines received for the 20 remaining patients varied between 1 and 5. Sixty percent received more than 3 lines of chemotherapy during the colorectal carcinoma treatment.

Bronchial stenosis caused by EM was initially treated in 17 patients (71%) by interventional bronchoscopy within 4 weeks of the diagnosis. Chemotherapy or chemotherapy/radiotherapy or chemotherapy/brachytherapy had been initially given to 7 patients. One patient had undergone surgery, but without any improvement in his condition due to a pleural involvement.

Forty-two sessions of endobronchial treatment were performed in this series. Details pertaining to endoscopic treatments are summarized in table 2. Mechanical resection was performed during every session (fig. 1). When a lesion was considered limited, cryotherapy was used at its base in order to obtain a local cytotoxic effect. Silicone stents were inserted when bulging extrinsic compression from subcarinal lymph nodes was present (fig. 2). If bleeding occurred before or after mechanical resection, Nd-YAG was used for photocoagulation purposes. A complete resection was accomplished in 29 interventions (69%). A partial reopening with more than 80% of the normal lumen diameter was only possible in

**Table 1.** Baseline characteristics of patients, symptoms and radiologic findings in patients upon their first admission to our center and after intervention

a Baseline characteristics		
	n = 24	%
Sex		
Males	12	50
Females	12	50
Age at colorectal cancer diagnosis, years		
Mean	59	
Range	36–86	
Primary tumor location		
Right colon	5	21
Left colon	12	50
Rectum	7	29
Initial stage		
Stage II	11	46
Stage III	10	42
Stage IV	3	12
b Symptoms and radiologic findings		
	Prior to endoscopic treatment (n = 24)	24 h after treatment (n = 24)
Performance status		
0–1	15	18
2–3	9	6
Symptoms		
Dyspnea	16	7
Cough	9	6
Hemoptysis	5	1
Hypoxia	4	1
None	2	10
Chest radiograph findings		
Atelectasis	14	4
Parenchymal nodules	6	6
Lung infiltrates	2	2
Pleural effusion	1	1
Hilar mass	3	3
Mediastinal adenopathy	2	2
None	0	0
FEV <sub>1</sub> , l/s	1.4 ± 0.6	1.8 ± 0.7
FEV <sub>1</sub> , % predicted	63 ± 19	78 ± 26

13 interventions (31%). This was due to one of the following conditions: the distal part of the lesion could not be reached by the bronchoscope, the bleeding was too extensive, or the risk of a bronchial perforation was deemed too high by the endoscopist. Mortality in this series is null.

**Table 2.** Endoscopic treatments: number of sessions, modalities and results

Number of endoscopic sessions (n = 42)	
1	14 patients
2	7 patients
3	0 patients
4	2 patients
5	0 patients
6	1 patient
Modality used	
Mechanical resection	42
Cryotherapy	7
Silicone stent insertion	4
Nd-YAG	5
Resection	
Complete	29
Partial	13

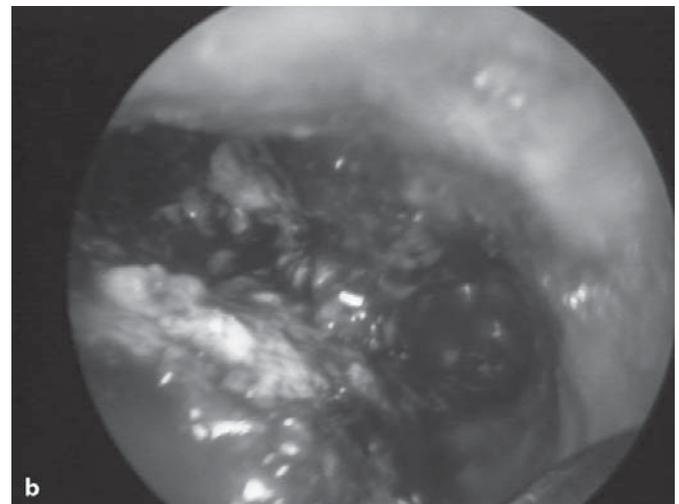
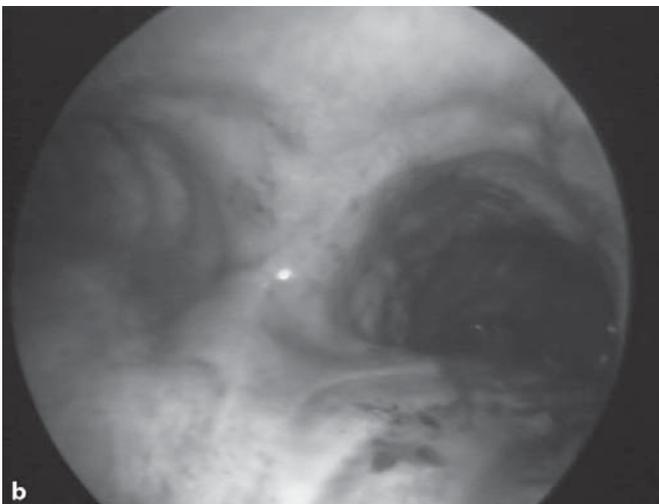
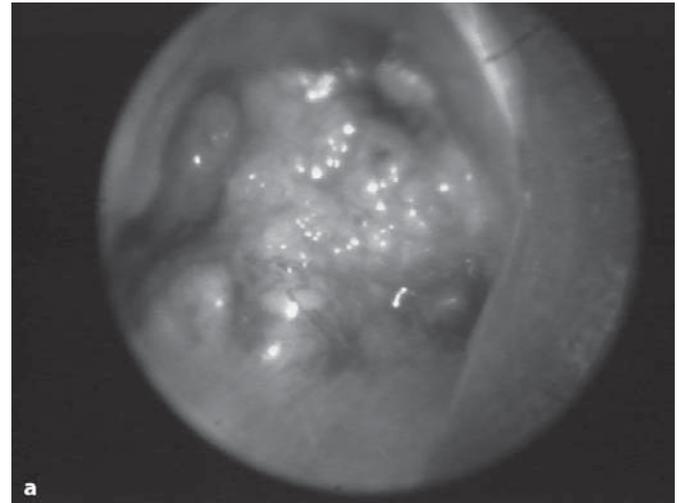
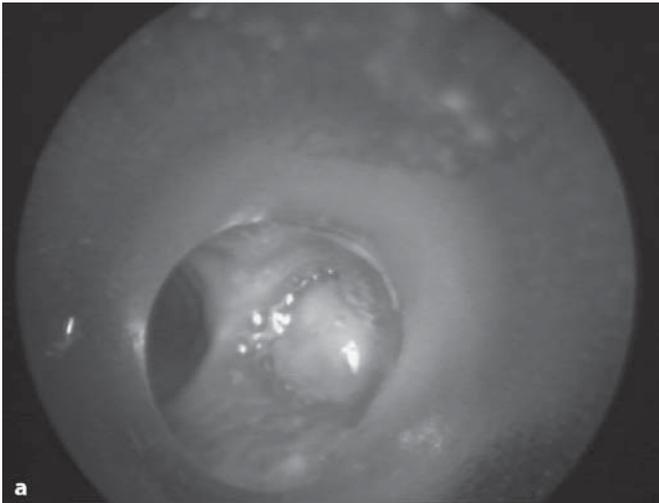
During the endobronchial examination, 1–4 bronchial lesions were found. We did not find any predilection site for EM. In 4 subjects, an EM was found at the anastomotic site of lobectomy or pneumonectomy. The typical macroscopic aspect of the EM from colorectal neoplasms is a large bulky polypoid-shaped lesion with necrosis.

A clinical improvement following the intervention was achieved in 30/42 cases (72%).

A mean increase of 34% (±27%) in the forced expiratory volume in 1 s was observed following an endoscopic intervention.

Eight patients did not receive further treatments. A complementary treatment with chemotherapy was initiated in 13 patients (54%), and radiochemotherapy was given in 3 patients (18%) – irradiation of the mediastinal lymph nodes. In 10 patients, the median delay before a second endoscopic intervention was 6 months (range 3–29). When more than 2 sessions were performed, the observed median delay was 15 weeks. In 7 patients treated with cryotherapy, 5 also developed new EM within weeks.

All the patients died. Survival following diagnosis of the primary tumor was 70 months in our study (range 23–245). A survival beyond 5 years was observed in 13 patients (54%). The median survival after EM was 14 months (range 3–40). During this period, 6 patients were diagnosed with other metastases (brain, bone and liver). No patient died of asphyxia.

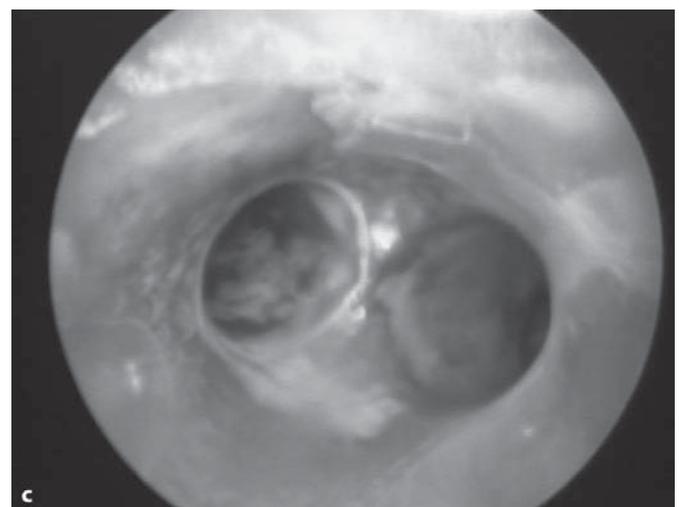


**Fig. 1.** An endobronchial metastasis of colorectal cancer in the right main bronchus, before (a) and after an interventional bronchoscopy (b).

### Discussion

EMs are rare. All studies found in the literature are thus retrospective. Some studies report a prevalence of 1.5–25% of patients with solid tumors, whereas the prevalence of this entity is only 2% at autopsy [1, 7, 8]. Prevalence is higher if the definition of EM includes an invasion of the bronchial wall by a parenchymal mass or lymph nodes.

In 2004, a review of EM included 204 cases [3]. Thirty of those were metastatic lesions from colorectal neoplasms. Carlin et al. [9] included 9 cases in their report. Our study of 24 patients with EM from colorectal cancer



**Fig. 2.** Main carinal obstruction following subcarinal nodal invasion by metastatic colorectal cancer. Before resection (a), after mechanical resection (b), and after Y stent placement (c).

treated by endobronchial intervention and by the same operator is the largest that we are aware of. However, the results from this study are still limited due to the small number of patients.

#### *EMs in the Natural History of Colorectal Cancer*

In this series, the median age associated with the diagnosis of colorectal cancer is 60 years (range 36–86), which is younger than the commonly reported age of 70. The primary involvement site does not appear to exert any influence on the emergence of EM [4].

EMs occur in patients with longer survival from metastatic colorectal cancer. In this study, overall survival is 70 months (range 23–245) and is more than 5 years in 54% of patients. Compared with the overall 5-year survival of metastatic colorectal cancer of 7 and 0–2% in non-surgical patients [5], the subjects in our study survived longer.

Other metastatic sites before EM were found in 62% of our patients. They are reported in 54–87% of cases regardless of the primary tumor [2, 10, 11].

In 75% of these patients, a metastasectomy from either the liver or lung was possible. This rate is significantly higher than the reported 10–15%. When solitary, a metastasectomy is performed and a survival gain is possible: the 5-year survival can reach 35–58% [12].

When the metastasis is deemed unresectable, but the patient is in good condition, palliative chemotherapy can be given to improve survival [5, 13].

In our study, the median free interval to EM diagnosis was 53 months (range 18–144). Carlin et al. [9], Kiryu et al. [2] and Ormerod et al. [7] reported comparable intervals of 63, 59 and 44 months, respectively, for colorectal cancers.

The median survival following EM diagnosis is 14 months (range 3–40). All primary tumors included, the median survival reported in other studies ranges from 9 to 18 months [9, 11, 14]. This seems rather short compared with the overall survival numbers. However, it is important to remember that patients presenting with EM are already at an advanced stage of their disease and have already received multiple treatments for their malignancy. Exceptionally long survivors of up to 150 months have been reported [3].

An increase in the incidence of EM was observed in our study over the period from 1988 to 2006. In fact, 66% of patients were referred for an interventional bronchoscopy after 2001. This could reflect the improvements in treatments offered for colorectal cancer in recent years with newer chemotherapy regimens and surgical techniques.

#### *Diagnosing EM*

Some studies suggest that EM frequency is underestimated [7, 15, 16]. Bronchoscopy with biopsies is needed for the diagnosis of this entity. The endoscopic aspect of this lesion is a bulging or polypoid mass with a necrotic component that bleeds, although less than renal cell carcinoma metastases.

The symptoms of EM are indistinguishable from those of primary bronchial neoplasms: cough, shortness of breath, hemoptysis. Radiologic findings include nodules, atelectasis or lymph node enlargement [2–4, 7–10]. It might be possible to distinguish primary from second primary tumors using immunohistochemical studies.

In 52–62.5% of cases, patients are asymptomatic upon EM diagnosis [4, 11]. While 95% of lung metastases are seen on CT scans, only 55% of endobronchial lesions are detected by this technique. A good correlation with bronchoscopic findings is found when the endobronchial lesion is visible on CT [17].

It is not recommended that a bronchoscopy be performed in every patient presenting with parenchymal lung metastases from colorectal cancer. However, bronchoscopy can be considered in patients experiencing new symptoms or presenting with radiological findings compatible with an endobronchial involvement.

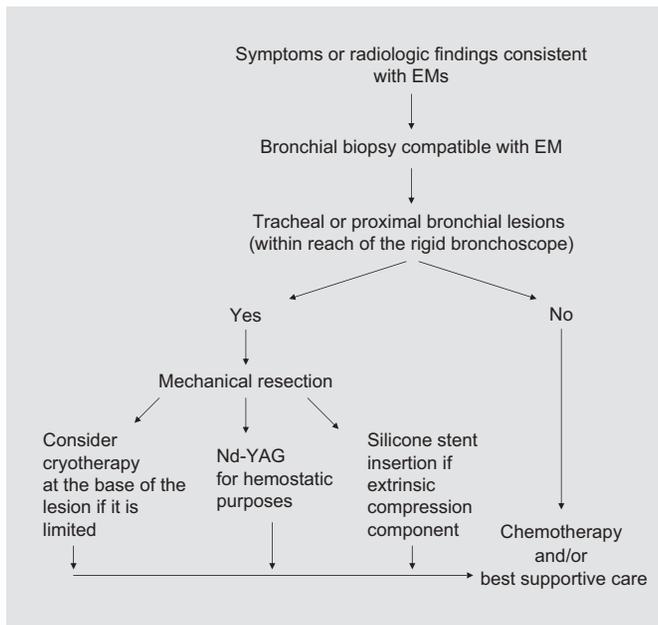
#### *Therapeutic Management*

Bulky lesions of the main and lobar bronchi are amenable to palliative endobronchial treatment [9, 18]. An interventional bronchoscopy can be considered in cases of impending asphyxia due to a tumoral invasion of the carina or trachea. The pulmonary parenchyma distal to the stenotic region should be assessed as well. For instance, atelectasis with visible air bronchogram is a favorable finding [18] (fig. 3).

A subjective improvement in symptoms has been reported by 76% of patients. No death was caused by the procedure.

Even though comparable series are not found in the literature, it has been reported that bronchial neoplasms obstructing the airways can benefit from an interventional endoscopy in 93% of cases, with a low mortality rate (5/1,000 cases). Morbidity associated with the procedure is 2% due to the risk of bleeding, pneumothorax, mediastinal emphysema, and respiratory/cardiac failure [18, 19]. Similarly, other benign endobronchial tumors causing significant symptoms have also been shown to be effectively treated using rigid bronchoscopy [20].

Although a general anesthesia is required, an endobronchial intervention improves the patient's quality of



**Fig. 3.** Indications and contraindications of bronchoscopic treatment.

life and prevents the risk of death due to asphyxia. In this study, there was no benefit in terms of preventing the recurrence after cryotherapy. Nevertheless, a laser-assisted mechanical resection followed by cryotherapy is very efficient on other tumors [21, 22].

Few stents were inserted due to the local aspect showing a high rate of bulky tumors and a low rate of external compression requiring stent insertion. Other techniques such as electrocoagulation and photodynamic therapies have been successfully used in other centers [12, 18, 20, 23].

In our patients, surgery could not be considered as a palliative treatment due to the advanced stage of the disease. External radiation alone does not generally suffice to relieve atelectasis [24]. Brachytherapy can be considered in the treatment of tumors with a lesser volume [21, 24]. However, it can be associated with cartilage damage, and airway obstruction can occur due to pseudomembranes or residual stenosis as in the case of 1 patient in this series [21]. With a success rate of approximately 30%, chemotherapy alone is not very effective in relieving the obstruction [25].

Interventional bronchoscopy done prior to radio- or chemotherapy could be a better option [19]. Doing so will improve the tolerance to radiotherapy and decrease the risk of bronchial stenosis or radiotherapy-induced pneu-

monitis. A better tolerance of chemotherapy treatment might be observed as well as a decreased risk of obstructive pneumonia during the neutropenic phase.

More than one therapeutic session was needed in 41% of subjects due to the recurrent nature of the EM. Interventional bronchoscopy has the great advantage that if necessary, it can be repeated, whereas radiotherapy and brachytherapy are not recommended in regions already treated. In patients with EM, there was a 15-week period between 2 treatments, which is similar to what we observed in primary bronchial tumors [26].

Palliative chemotherapy in order to improve quality of life more than survival seems appropriate in the context of a multimetastatic disease [5]. If not possible, we recommend a bronchoscopic surveillance to detect new lesions. This would allow further therapeutic procedures to be performed electively rather than as an emergency on a patient with impending asphyxia or critical respiratory failure.

In the last 30 years, the median survival in patients with EM has not significantly improved despite advances in chemotherapy and interventional bronchoscopy. However, the latter can be considered as a palliative measure to prevent a distressing event such as asphyxia.

## Conclusion

Advances in chemotherapy after surgery have brought to our practice a new population with increased survival following the diagnosis of colorectal cancer. In this context, endobronchial metastases might arise in the later stages of the disease. Clinical or radiological signs of airway obstruction should enable us to be aware of a possible endobronchial involvement. Initial treatment by interventional endoscopy is safe and can be repeated if needed. This palliative measure requires a concerted effort by oncologists and bronchoscopists because it should be considered where available in the management of these patients.

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