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SURGICAL APPROACH TO COLORECTAL CANCER PULMONARY METASTASIS – ONE-YEAR EXPERIENCE OF A REFERENCE CENTER

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Abstract

Introduction: Colorectal cancer is the third most common malignancy, being associated with metastatic disease in 50% of cases. The lung is the second organ most affected by metastasis in colorectal cancer. In this study, we aim to review the cases submitted to resection of pulmonary colorectal metastasis at Hospital Pulido Valente, comprised in the period from the 1st of January to the 31st of December 2017.

Methods: Retrospective analysis. Data were collected from clinical records.

Results: There were 21 patients operated during this period, with a total of 22 surgeries performed, all with curative intent. Data were collected regarding age, gender, site of primary tumour, number of resected lesions, surgical approach, performed procedure, disease-free interval, presence of bilateral disease and existence of extra-pulmonary metastasis.

Conclusion: Lung metastases are frequent in colorectal cancer. Pulmonary metastasectomy is currently accepted as a potentially curative therapy as part of a multimodal approach to metastatic colorectal cancer.

INTRODUCTION

Colorectal cancer is the third most common malignancy, being associated with metastatic disease in 50% of cases.[1] Around 10 to 25% of patients with colorectal tumours will present with metastatic disease at the time of diagnosis, and 15 to 26% of the patients submitted to curative surgery of the primary tumor, will develop distant metastasis.[1]

The lung is the second most affected organ by metastasis in colorectal cancer.

Isolated pulmonary metastasis of colon cancer occurs in less than 10% of patients[2], with twice the incidence in rectal cancer.

In this study, we aim to review the cases of patients referred for lung metastasectomy at the Thoracic Surgery Service, due to colorectal cancer, during the year of 2017. All surgeries were performed with curative intent.

METHODS

Retrospective analysis of clinical records.

All patients were operated as inpatients, in the Thoracic Surgery Service of Hospital Pulido Valente. Data were collected regarding age, gender, site of primary tumour, number of resected lesions, surgical approach, performed procedure, disease-free interval, and existence of bilateral disease or extra-pulmonary metastasis.

RESULTS

There were 21 patients operated for suspected pulmonary metastasis of colorectal cancer during this period. 5 patients did not attain confirmation as colorectal metastasis in the histologic analysis: four had primary pulmonary adenocarcinoma (two synchronous, two metachronous) and one had a pulmonary hamartoma.

There were 16 patients operated with confirmed colorectal adenocarcinoma metastasis during this period, with a total of 17 surgeries performed, all with curative intent.

Regarding the gender, there were 7 female and 9 male patients. The mean age at diagnosis of the primary tumour (colorectal cancer) was 60,5 years, with a standard deviantion of 7,4, minimum of 49 and maximum 74 years. Table 1 lists these demographic data.

The primary tumour was in the colon in 11 patients, and rectal in 5 patients. The number of resected lesions

Table 1 **Demographic data**

Variable	N
Operated patients	16
Age Mean (SD)	60.5(7,4)
Gender	
Female	7
Male	9

ranged from 1 to 5 in each surgery (Table 2). The performed procedures were: single or multiple wedge resections, lobectomy with or without accompanying wedge resection and double segmentectomy. Lymph node sampling was performed in 5 cases, whereas only 2 patients underwent full nodal dissection, due to suspicion of lung primary tumour.

A minimally invasive surgical approach, VATS was used in 5 patients: 3 patients were submitted to wedge resection (2 for a single lesion and 1 for two lesions); 2 patients underwent lobectomy for a single central lesion by this approach.

Thoracotomy was used in the remaining 11 patients: 7 patients underwent lobectomy, 2 of them with associated wedge resection of other lesions; 1 patient underwent single wedge resection; 2 patients underwent multiple wedge resection (2 to 5 lesions); and finally, 1 patient underwent bissegmentectomy and lymph node dissection.

Table 2 **Clinical data**

Variable	N
Site of primary tumour	
Colon	11
Rectum	5
Number of lesions resected	
1	9
2	3
3	1
5	3
Surgical approach	
VATS	5
Thoracotomy	11
Performed procedure	
Single wedge resection	3
Multiple wedge resection	3
Bissegmentectomy	1
Lobectomy	9
Lymph node approach	
Lymphatic node sampling	5
Full nodal dissection	2

VATS – video assisted thoracic surgery

The disease free interval (DFI), is defined as the time occurred between the resection of the primary tumour and the first day of recurrence, whether systemic or loco-regional (3). We will consider the disease free interval as the time occurred between the surgery for colorectal cancer and the time of diagnosis of lung metastasis. In this study, that time interval varied between 0 and 15 years (Table 3).

Table 3 **DFI**

Disease free interval	N
0	5
1	3
2	2
3	1
4	1
5	1
9	1
10	1
15	1

DFI – disease free interval in years

There were 5 patients with synchronous pulmonary metastasis at the time of colorectal cancer diagnosis (DFI of 0 years); 3 patients had a DFI of 1 year;

2 patients a DFI of 2 years and 6 patients with a DFI of 3, 4, 5, 9, 10 and 15 years, respectively.

Regarding the patients with synchronous presentation of pulmonary metastasis, 4 underwent chemotherapy before the pulmonary resection, achieving 30% of reduction of the lesion size in only 1 case.

Of all patients, 5 had already a history of previous pulmonary metastasectomy. Two patients had two previous surgeries and one patient had one previous surgery. Of these 5 patients, 4 had bilateral pulmonary disease.

As for the 11 patients whose first pulmonary resection occurred in 2017, 3 presented with bilateral disease. The contralateral pulmonary metastases were treated with radiotherapy in two cases and with contralateral resection in one patient. In this patient, the interval between the two surgical resections was 48 days. This case explains why we have a total of 16 patients operated, with a total of 17 surgeries performed.

As for post-surgical complications we report two cases of empyema and one bilateral pulmonary embolism.

Concerning extra-pulmonary dissemination, 8 patients had a history of hepatic metastasectomy previous to the pulmonary resections, with 3 hepatic lesions in one case. We report only one patient with extra-pulmonary and extra-hepatic metastasis: a cerebellum metastasis resected 2 years before pulmonary resection.

The analysis of the majority of the specimens of the lesions resected (14 out of 16) was made with immunohistochemistry. The lesions were positive to cytokeratin 20 and CDX-2 and negative to cytokeratin 7 and thyroid

transcription factor 1 (TTF1), which is compatible with colorectal origin of the metastasis.

DISCUSSION

Pulmonary metastasectomy in colorectal cancer is a potentially curative therapy[4] and may be associated with an increase of the 5 year survival (30-71%).[4,5,6] This survival is superior to the natural history of stage IV colorectal cancer, which has a 5 year survival of only 10%.[6]

The decision to perform metastasectomy should be made by a multidisciplinary team, regarding the following resectability criteria[1,5]: control of the primary tumour; resectability of all the metastatic disease; pulmonary function allowing resection of all lesions; and absence of extra-pulmonary unresectable metastasis. In patients in whom these criteria are not met, resection might be indicated in symptomatic cases or primary lung tumour suspicion.

The characteristics of the metastatic lesions will dictate their surgical approach. These characteristics are: number of lesions, size, over-time stability[1] and anatomical distribution.[7]

The surgical approach preferred in the Thoracic Surgery Service in Hospital Pulido Valente is the minimally invasive. Before surgical proposal, the lesions are evaluated for their stability over time with serial exams, and the assessment of feasibility of complete excision is also performed.

The open approach is chosen in cases of deep, non-palpable lesions by VATS approach, multiple lesions, or if there are technical difficulties to obtain a clear margin.

The wedge resection by VATS is appropriate for preferably single to two[7] lesions, stable, peripheral lesions and nodules smaller than 3 cm.[6]

Some authors consider that the VATS approach has the disadvantage of the inability to palpate the remaining pulmonary parenchyma. This is defended by some thoracic surgeons[9], in order to permit identification of small metastatic foci.[6]

Patients approached by VATS do as well as thoracotomy approached patients, and have similar disease free survival and overall survival.[6]

The pulmonary resection should be performed in the manner that will allow the best preservation of parenchyma, in order to allow eventual future resections.[6]

The presence of bilateral pulmonary metastatic disease is no longer considered a contra indication for resection.[1] The interval between resections for bilateral disease can by 4 to 6 weeks.[8] Multiple metastasectomy might improve overall survival.[9]

Similarly, the existence of extra-pulmonary metastatic disease is not a formal contra-indication for pulmonary metastasectomy, as long as the lesions are ressectable.

About 5% of patients with colorectal cancer will develop pulmonary and hepatic metastasis, whether synchronous or metachronous.[1] In cases of synchronous lesions, an initial hepatic approach is preferred for several reasons: it might be more laborious; there is a greater probability of progression of the hepatic lesions over time[7] and it will allow excluding abdominal disease that had not been previously identified. On the other hand, the initial abdominal approach will allow to maintain a better pulmonary reserve in the post-operative period.[9] The pulmonary resection may be performed 6 weeks after the hepatic resection.[9]

Several studies have identified prognostic factors associated with a decreased survival: stage III/IV at presentation of the colorectal cancer, multiple metastatic lesions[6], presence of both lung and liver metastasis[5], elevated CEA[9] and a disease free interval inferior to 12 months (7). In these patients who present with poor prognostic factors, it is accepted to adopt a *watchful waiting* of 6 to 12 weeks. If there is no disease progression in this interval, surgery may be performed.[9]

For the patients who do not meet criteria for surgical resection, there are alternatives such as stereotaxic radiotherapy, radiofrequency ablation[6,10], microwave energy, cryotherapy[6] or systemic chemotherapy.

CONCLUSION

Pulmonary metastases are frequent in colorectal cancer. Pulmonary metastasectomy is currently accepted as a potentially curative therapy in the multimodal approach of metastatic colorectal cancer.[4]

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