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## Original research

# Analysis of long-term results after liver surgery for metastases from colorectal and non-colorectal tumors: A retrospective cohort study



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#### HIGHLIGHTS

- Liver resections for metastases has been developed in last years.
- Selected patients with non-colorectal metastases can benefit from surgery.
- A multidisciplinary therapy is required and new guidelines are awaited.

#### ARTICLE INFO

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#### ABSTRACT

*Background:* During the last decade, criteria for liver resection were extended thanks to surgical and oncological developments, thus increasing the number of surgeries for non-colorectal liver metastases. However, the real advantages of surgery in this category of patients remain debated, due to the few studies available in the literature.

The present study aims to analyze liver surgery performed for metastatic disease at a single referral center, comparing outcomes of patients that underwent resections for colorectal and non-colorectal metastases

*Methods:* The overall study period was January 2005—May 2015. A total of 170 patients were selected from the institutional database and then included in the analysis. Patients and tumors characteristics were reported. Overall survival and subgroup analyses based on different primary malignancies were performed. The Kaplan-Meier method was used.

*Results*: The mean age of the patients was  $67.68 \pm 10.98$  years. Primary malignancies distribution resulted as follows: colorectal (77.1%), genitourinary (7.6%), neuroendocrine (5.3%), breast (4.7%), foregut (2.9%), melanoma (2.4%).

The overall survival rates at 1, 3, 5 years, were 96.2%, 42.8% and 14.7%, respectively.

The survival analysis showed a mean overall survival of 54 months in the colorectal metastases group vs 32 months in the non-colorectal liver metastases group (HR = 5.92, P = 0.015).

Conclusion: Surgery for patients with non-colorectal liver metastases must be considered in the context of a multidisciplinary treatment where chemotherapy plays the main role. International guidelines and a specific consensus on this field are desirable to offer the best available therapy for the metastatic liver disease.

Ethics and dissemination: This study is conducted in compliance with ethical principles originating from the Helsinki Declaration, within the guidelines of Good Clinical Practice and relevant laws/regulations.

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#### 1. Background

In contrast to the well-defined guidelines for liver metastases from colorectal cancer (CLM), surgical policy for non-colorectal liver metastases (NCLM) is mainly based on institution-related criteria.

Up to this day, evidence on NCLM is lacking because few studies have been undertaken in this field and the clinical benefits of surgical resection for NCLM are still not widely accepted [1]. On the other hand, nonsurgical therapies have not achieved satisfactory results, with a survival time of only a few months.

The mechanism for the development of liver metastases differs based on the location of the primary tumor site. In colorectal adenocarcinoma and gut-associated neuroendocrine tumors, it depends on the portal venous drainage and the direct intra-abdominal lymphatic channels. In non-colorectal non-neuroendocrine liver metastases, it derives from the systemic circulation. This is an important consideration to keep in mind before tackling this field.

The last decade has witnessed a progressive increase in interest in NCLM [2].

Advancements in surgical technique and in intraoperative ultrasound anatomy studies and new devices have significantly improved the safety of liver resections. Consequently, the most complex liver surgeries can now be performed in referral centers, with an operative mortality of less than 5% [3]. For this reason, liver resection for NCLM has gained acceptance during the last years and eligibility criteria have been extended [1].

However, the effectiveness of these resections and survival outcomes after surgery remain unclear.

Optimal results were seen in several studies of selected patient groups [2], and it seems that the main factor in success is the selection of patients with a favorable tumor biology.

When considering NCLM as an overall group, it is difficult to determine factors that can improve survival because of the different primary tumors included; thus the correct selection of patients eligible for surgery is the most critical issue that needs to be clarified and to reach an international consensus.

This study aimed to analyze long-term outcomes after colorectal and non-colorectal liver resections in a single referral center for hepatic disease.

#### 2. Methods

Patients who underwent liver resections between January 2005 and May 2015 were considered for enrollment in this study. After screening the institutional database, we conducted a chart review on 170 patients on the basis of their eligibility criteria.

The inclusion criteria for patient enrollment were histologically proven liver metastasis; preoperative staging work-up performed by ultrasound, CT scan, MRI; and treatment with curative intent. The exclusion criteria were advanced tumor infiltrating neighboring organs; metastases in other sites; patients with high operative risk, defined as having an American Society of Anesthesiologists (ASA) score of >4; synchronous malignancy in other organs; and palliative surgery cases.

The analyzed data and outcomes included patient and tumor

characteristics; site of primary malignancies; histopathological features; and a 1-, 3-, or 5-year survival rate.

After evaluating the characteristics of the patients, we identified three groups based on different primary tumor sites: a colorectal liver metastases group (CLM), a non-colorectal liver metastases group (NCLM), and a non-colorectal non-neuroendocrine liver metastases group (NCNNLM). We performed a comparison of long-term survival (over a period of ten years) among these groups, as well as an evaluation of the impact of the different tumors' biology on NCLM.

#### 2.1. Statistical analysis

We used SPSS Statistics 20 to carry out this statistical analysis. The dichotomous variables will be expressed as numbers and percentages, while continuous variables will be expressed as mean and standard deviation (SD) or median and interquartile range (minimum and maximum values).

We used a paired *t*-test for testing the mean difference between paired observations.

We considered  $\alpha=0.05$  for the level of significance and regarded *p*-values <0.05 as statistically significant.

We calculated overall survival (OS) from the day of surgery to the date of death.

We considered disease-free survival (DFS) to last from the day of surgery to the first follow-up visit when the recurrence of the tumor was proved. Particularly, the latter was considered to evaluate the months after the surgery for the primary tumor to the evidence of hepatic metastases.

We obtained the analyses of OS and DFS using the Kaplan-Meier

For the comparison between groups, we used the Log-Rank test. In addition, we determined the hazard ratio (HR) with a confidence interval (CI) of 95%.

#### 2.2. Ethical aspects

All the investigators conducted the study in compliance with ethical principles originating from the Helsinki Declaration, within the guidelines of good clinical practice and applicable laws.

The investigators acted according to the rules of the Institutional Review Board (IRB) regarding the collection of data.

#### 2.3. Study registration

This study was registered on January 26, 2016 at www. researchregistry.com and obtained the following identification number: researchregistry898.

### 3. Results

The study examined 170 patients (male/female: 107/63), with a mean age of  $67.68 \pm 10.98$ , all diagnosed with liver metastases. Fig. 1 shows the rate of involvement of the different hepatic segments. Overall, 58.24% of metastases were located in the right hepatic lobe, while 55.3% in the left lobe. Ninety-four patients with one or more comorbidities and patients with chronic liver disease

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