

Current Approach to Synchronous Liver Metastases of Colorectal Origin: Sequential, Simultaneous or Reverse?

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According to the registry of the National Cancer Institute, in Argentina colorectal cancer (CRC) is the third in incidence and the second with the highest mortality.¹ More than 50% of patients with CRC will develop metastases during the course of their disease.² By definition, in whatever organ they settle, all metastases (detectable or not) are synchronous, because they arise as a consequence of lymphatic, vascular, or traumatic dissemination (spontaneous instrumentation or rupture) of the primary tumor. By consensus and for a better categorization, synchronous liver metastases (SLM) have been defined as those diagnosed before or at the time of diagnosis of the primary tumor. Metachronous liver metastases (MLM) are those not detected during the initial staging of CRC and are classified as early or late depending on whether they are detected before or after 12 months from the diagnosis of the primary tumor, respectively.²

Each of the patients with liver metastases (LM) of CRC should be discussed in an interdisciplinary way, taking into account the systemic aspect of the disease and considering the variables of the patient (performance status, comorbidities, psychosocial environment), the primary tumor (local resectability and symptoms) and the tumor liver involvement. In this last aspect, patients must meet criteria for liver resectability, not only technically (tumor resection with negative margins and future remnant liver with adequate volume and functionality), but also oncologically (absent or resectable extrahepatic disease, controlled or resected primary tumor, absence of tumor progression under systemic chemotherapy).³ From the surgical point of view, regardless of the laparoscopic or conventional approach to LM, modern concepts of parenchyma-sparing surgery should be applied to reduce the unnecessary extent of liver surgery. In this way, a sparing surgery of functioning hepatocytes is carried out, that is, one that preserves the maximum of non-tumor liver parenchyma. Recent publications show that compa-

red to larger resections, this strategy has lower rates of major complications and postoperative liver failure, similar oncological results, and finally increases the possibility of a new future resection in the case of liver recurrence (which occurs in 50-60% of cases).⁴

The surgical strategy for resectable MLMs is always “sequential” (first stage: CRC surgery; second stage: hepatectomy). In this population, colorectal surgery has already been performed at the time of diagnosis and liver surgery is performed in a second stage of the disease progression. Unfortunately, the resectability of CRC LMs using a modern and aggressive hepatic approach is limited to 30-50% of cases.

In those patients with unresectable LM, the appropriate treatment is systemic therapy with the intention of prolonging survival and improving quality of life.

In cases of potentially resectable SLM, unlike of metachronous disease, the decision is usually more complex because there are 3 potential surgical treatment options with curative intent: the sequential, the simultaneous or the reverse approach. There are two important variables that determine the strategy to be used: the symptoms related to the primary tumor and the extent of liver resection. On the other hand, there are two rules that should be followed in every patient with SLM. First rule: all symptomatic CRC should be treated urgently. Second rule: in centers with availability of trained teams in liver and colorectal surgery, the “simultaneous” approach (resection of the CRC and the SLM in a single surgical time) should be prioritized to avoid the summative morbidity effect of two major procedures with general anesthesia. It is important to note that simultaneous surgery should not be recommended in some situations; patients with multiple comorbidities with high surgical risk, need for complex colonic resection, presentation with colonic obstruction or perforation, need for major liver resection (≥ 3 segments), or patients with tumors of the middle or lower rectum requiring neoadjuvant treatment with radiotherapy.

Approximately 20-40% of patients with unresectable SLM at diagnosis are rescued and made resectable

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by the administration of new conversion chemotherapy regimens based on FOLFIRI or FOLFOXIRI, with or without the association of a monoclonal antibody. In this subgroup of converted patients or in those who debut with a high hepatic tumor burden needing a complex hepatectomy with technical resectability “to the limit”, the recommendation would be to innovate with the “reverse” approach (first stage: liver surgery; second time: CRC surgery). This strategy would make it possible to avoid eventual liver progression that could result from a sequential approach requiring a prolonged interval between both surgeries. The concept of the reverse approach would be to resolve first the focus of greatest tumor involvement and then surgery for the asymptomatic CRC. Once the liver disease has been successfully resolved, it is possible to choose whether or not to perform systemic chemotherapy during the interval until definitive primary surgery. Finally, in patients with lower or middle rectal cancer with SLM requiring major liver surgery, systemic treatment and radiation therapy to the rectum could be started and hepatectomy performed in the time period usually required between radiation therapy and rectal surgery.²

The classic “sequential” approach (first stage: CRC surgery; second stage: liver surgery) continues to be valid particularly for patients with CRC and SLM who do not meet the criteria for the simultaneous approach. This strategy should also be applied to patients with SLM and

a symptomatic CRC (clinically relevant bleeding, perforation, or colonic obstruction). In colonic perforations, resection of the primary tumor should be performed whenever possible. In the case of colonic obstruction, resective surgery will be the choice, although the use of colonic stents in lesions located mainly in the sigmoid colon or the left colon is currently a matter of debate.⁵ Once the CRC resective surgery has been performed, liver surgery would be carried out after a variable interval of 1-3 months, with/without the reconstruction of the colonic transit and with/without the administration of prior systemic chemotherapy, depending on the clinical situation of the patient and the interdisciplinary decision. The sequential approach has the additional advantage of a better selection of patients with SLM through the empirical evaluation of the tumor “biology”, avoiding liver surgery in patients with a disease that progresses in the short term of the observation interval.

In conclusion, the selection of the sequential, simultaneous, or reverse strategy in patients with CRC SLM is a complex decision that requires the collective intelligence of an interdisciplinary team that includes hepatic and colorectal surgeons, clinical oncologists, endoscopists, pathologists, and imaging specialists. Each decision must be discussed and agreed upon and then adapted to each patient in particular, with the aim of obtaining the best clinical, surgical and oncological results in the short and long term.

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