



## Surgical dilemmas in the management of colorectal liver metastases: The role of timing

Dimitrios Dimitroulis, Gregory Kouraklis

Dimitrios Dimitroulis, Gregory Kouraklis, Second Department of Surgery, University of Athens Medical School, Athens Greece, Laiko Hospital, 11527 Athens, Greece

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**Correspondence to:** Dimitrios Dimitroulis, MD, PhD, Associate Professor, Second Department of Surgery, University of Athens Medical School, Athens Greece, Laiko Hospital, M. Asias str 75, 11527 Athens, Greece. [dimitroulisdimitrios@yahoo.com](mailto:dimitroulisdimitrios@yahoo.com)  
Telephone: +30-6972-420547  
Fax: +30-210-7456972

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with colorectal liver metastases faces several surgical dilemmas especially in the setting of the timing of operation. Synchronous resectable metastases should be treated prior or after induction chemotherapy? Furthermore in the case of synchronous colorectal liver metastases which organ should we first deal with, the liver or the colon? All these questions are set in the editorial and impulse for further investigation is put focusing on multidisciplinary approach and individualization of treatment modalities.

**Key words:** Colorectal cancer; Chemotherapy; Timing of surgery; Colorectal liver metastases; Liver first procedure; Multidisciplinary approach; Individualized treatment strategies

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**Core tip:** The treatment of colorectal cancer with colorectal liver metastases is a challenge for the multidisciplinary medical team dealing with this problem. The timing of surgery both for synchronous as well as for metachronous metastases is always a matter of debate. Multidisciplinary approach and individualization of treatment strategies is suggested.

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### Abstract

Colorectal cancer (CRC) is an emerging health problem in the Western World both for its raising tendency as well as for its metastatic potential. Almost half of the patients with CRC will develop liver metastases during the course of their disease. The liver surgeon dealing

Colorectal cancer (CRC) remains an important public health issue as it is the third leading cause of death for both men and women in the United States and the most frequent cause of cancer among patients aged 75 years and older<sup>[1]</sup>. Furthermore approximately 10%-25% of patients with CRC present at the time

of diagnosis with liver metastases (CRLM) while 25% will develop liver metastases in the future, a fact that means almost half of the patients with CRC will develop liver metastatic disease. While in the past the presence of multiple or enlarged CRLM was a sign towards palliative treatment the progress in liver surgery, medical oncology and interventional radiology has allowed us to perform liver resections for colorectal liver metastases with intention to treat<sup>[1]</sup>.

The surgeon who confronts with colorectal liver metastases faces several problems. Should I operate first or is it better for the patient to receive neoadjuvant treatment. And when it comes to the operation should I operate both liver and colon or separately and if separately which organ first. The conventional way of thinking in patients with resectable synchronous colorectal liver metastases is to offer an upfront operation and the reason for this attitude is the fear that CRLM will not respond to chemotherapy and that during the time of chemotherapy the liver tumors will grow and become unresectable so that the patient will lose the possibility of a curative liver operation<sup>[2]</sup>. Though, in this case scenario there is always a possibility to develop post-operative complications that will delay the chemotherapeutical approach and the patient will not benefit from medical oncology. Furthermore if we choose chemotherapy prior to surgical resection the tumor load within the liver is assumed to decrease and therefore we could achieve a higher percentage of complete resection rate (R0 resection) as well as the ability to perform minor hepatectomies, another argument counting for neoadjuvant chemotherapy. In some cases we might as well have a complete response, a phenomenon called "vanishing metastases" in the pertinent literature, "where the dream of the oncologist becomes the nightmare of the surgeon", because even if we have a complete radiological response there are still some active tumor cells that require surgical resection. In order to avoid such a problem there several solutions proposed, like marking the metastatic lesions prior to oncological referral. However, the choice of chemotherapy prior to surgical resection will have favorable results only under the circumstance that the tumor is sensitive to the therapeutical regimen we choose, so a complete examination of the k-ras and b-raf should be performed. Another pitfall of this approach is the development of chemotherapy adverse effects that will delay surgery, especially if we take into consideration that almost all oncological agents develop liver toxicity (*e.g.*, blue liver)<sup>[3]</sup>.

The second problem for the surgeon is whether to proceed to a combined liver and colon operation or a staged one. This problem has created a debate in the pertinent literature. The combined operation can theoretically solve the patient's surgical problem with one shot. This approach has a better impact on the patient's psychology as well as the financial aspect because we have one admission and one surgical procedure and in total decreased time of hospitalization.

On the other hand a combined procedure can lead to an increased risk of adverse effects of both colectomy and hepatectomy and in that case the patient will face a delayed post-operative course and might lose the time window for chemotherapy. Most authors conclude that it would be better to avoid low anterior colectomies with major liver resections. For the rest of the cases there is no consensus and the decision should be individualized taking into consideration the tumor load, the patient's performance status and the experience of the institution<sup>[4]</sup>. Furthermore for the case the surgeon decides to proceed to a combined operation our group has published experimental data demonstrating that if we prefer to start with the liver and perform an intermittent Pringle maneuver the post-operative outcomes are favorable<sup>[5]</sup>.

There is also a great amount of patients who present with unresectable liver metastases or with metastatic disease to other organs apart from the liver (lungs, peritoneal deposits *etc.*) at initial diagnosis. Patients with colorectal liver metastases initially considered as unresectable should be under close follow up by the surgical team during chemotherapy. Classical therapeutical agents in combination with biological agents (monoclonal antibodies) have increased the resectability rate of these patients. Furthermore, the use of special maneuvers such as portal vein ligation or embolization together with the above mentioned chemotherapeutical agents enable the decrease of tumor load with a concomitant increase of remnant liver volume so that the number of patients who are candidates for liver resection raises even more. For patients who develop metastatic disease to other organs beside the liver the site of metastasis affects both the treatment and prognosis. In patients with colorectal metastases to liver and lung and in some cases also the peritoneum the most important factor that affects the prognosis is the resectability of the metastatic lesion or lesions, especially the liver metastases<sup>[6]</sup>.

The management of a patient with synchronous colorectal liver metastases is a difficult, complicated and provocative problem to solve. With the evolution of science and technology the resectability rate has raised and more patients have favorable outcome. Surgeons are always enthusiastic but a lot of factors must be taken into consideration before choosing the best approach for each patient. The decision for the optimal treatment should be individualized, based on the results of a tumor board taking into consideration the opinion of surgeons, radiologists and oncologists. However, the most important predictive factors are the patient's performance status, the tumor load and the biological behavior of the disease.

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