



ASO Author Reflections: The Liver-First Approach: A New Standard for Patients with Multiple Bilobar Colorectal Metastases?

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PAST

The best surgical strategy for patients with colorectal cancer and synchronous liver metastases is a matter of endless debate. Technical and oncological issues must be considered but have often been confounded. In 2006, Mentha et al.¹ proposed an innovative and convincing oncosurgical approach, whereby they reversed the strategy, focusing attention on the prognostically most relevant target, i.e. the liver. Even if appealing, the liver-first approach struggled to find its role and failed to demonstrate a benefit, except for the inclusion of chemoradiotherapy in the treatment schedule of patients with locally advanced rectal tumors. The proposers themselves reported non-inferiority (and not superiority) of the reverse strategy in comparison with the standard primary-first approach.² A recent network meta-analysis ranked the liver-first approach as the best treatment option for its relative efficacy based on 5-year overall survival outcomes,³ but the evidence is too weak to impact current clinical practice.

PRESENT

The present study represents a potential breakthrough toward precision medicine.⁴ We unveiled the fact that the oncological impact of the treatment strategy increases with hepatic tumor burden, i.e. nil in patients with solitary metastasis, marginal in those with multiple unilobar metastases, and clinically relevant in those with multiple bilobar metastases. In patients with multiple bilobar lesions, the liver-first approach was associated with a prognostic advantage over the alternative strategies, considering survival from both diagnosis and surgery. The study is retrospective and non-intention-to-treat, but our conclusions rely on robust backgrounds: more than 7000 patients treated worldwide; a large series of patients undergoing a liver-first approach ($n = 552$); and a strict propensity score matching among groups. Waiting for a randomized trial, we believe that according to the present evidence, the reverse strategy could be proposed as standard for patients with multiple bilobar synchronous disease.

FUTURE

Major clinical implications of the present data can be anticipated. First, surgeons must change their mindset; the liver-first approach, which is currently the less common strategy (<10% of patients in the LiverMetSurvey database), should become the preferred option in patients with more advanced liver disease. Second, the reverse strategy makes mandatory the upfront evaluation, at diagnosis, of patients with multiple bilobar metastases by dedicated

multidisciplinary teams with liver surgery expertise. Third, assuming that the liver-first approach is effective in patients with aggressive tumors, additional indications could be explored, e.g. patients with numerous unilobar metastases, high tumor markers, or unfavorable mutational status.

Finally, patients with multiple bilobar metastases could be treated, according to the surgeon's policy, with a liver-first approach, performing multiple one-stage resections, or with a two-stage hepatectomy, resecting the primary tumor during the first stage.⁵ At present, we prefer a liver-first approach whenever a complete removal of the metastases is possible, even with complex multiple one-stage resections, whereas a two-stage hepatectomy is scheduled for otherwise unresectable patients. Further studies are needed to clarify the role of the two approaches in this setting of patients.

DISCLOSURE Felice Giuliani, Luca Viganò, Agostino M. De Rose, and René Adam declare no conflicts of interest.

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