JBUON 2021; 26(4): 1208-1209
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
Email: editorial_office@jbuon.com

COMMENTARIES

Commentary no.1

Oncologic outcomes after laparoscopic versus open resection for colorectal liver metastases

I read with great interest the recent trial by Aghayan et al showing that laparoscopic resection of colorectal liver metastases (CRLM) is non-inferior to open approach in terms of longterm outcomes [1], that generated some questions regarding the study design and some of its conclusions.

First of all, the authors did not provide any data on the tumor biology and especially on genetic mutations such as KRAS and BRAF. It is well described in the literature that mutant KRAS and BRAF tumors are related with poor longterm outcomes [2], so it is unclear whether patients were also randomized according to tumor biology. Moreover, KRAS status dictates resection margin, so some patients undergoing parenchymal-sparing resection might eventually need anatomic resection [3]. The latter is of paramount importance since it can be potentially a source of bias in the study and also partially explain the finding of no difference in recurrence-free survival despite the fact that more patients in the open group received neoadjuvant chemotherapy. Also, it would be interesting to know whether patients were randomized according to the site of primary tumor. It is known that CRLM of right colon origin have worse overall survival, mostly attributed to different KRAS status and more indolent tumor biology [4]. Finally, the median tumor size in the trial was 1.8 cm and no detailed data are provided regarding the number of lesions. I guess that the total tumor burden score in the trial is low that could potentially be a source of bias since it is a surrogate of less aggressive disease. This is also reflected by the fact that all patients in the trial were eligible for non-anatomic resections. It would be of interest if the authors provided data on the longterm outcomes of patients with large tumors when comparing different surgical approaches.

In the era of precision medicine in patients with CRLM, disease-related factors such as tumor biology, sidedness of primary tumor, and magnitude of resection are more important than the surgical modality used for treatment [5]. I hope that my comments will generate further discussions in the field.

References

1. Aghayan DL, Kazaryan AM, Dagenborg VJ et al. Long-Term Oncologic Outcomes After Laparoscopic Versus Open Resection for Colorectal Liver Metastases : A Randomized Trial. Ann Intern Med 2020, PMID 33497211, DOI 10.7326/M20-4011.
2. Tsilimigras DI, Ntanasis-Stathopoulos I, Bagante F et al. Clinical significance and prognostic relevance of KRAS, BRAF, PI3K and TP53 genetic mutation analysis for resectable and unresectable colorectal liver metastases: A systematic review of the current evidence. Surg Oncol 2018;27:280-8.
3. Margonis GA, Sasaki K, Andreatos N et al. KRAS Mutation Status Dictates Optimal Surgical Margin Width in Patients Undergoing Resection of Colorectal Liver Metastases. Ann Surg Oncol 2017;24:264-71.
4. Creasy JM, Sadot E, Koerkamp BG et al. The Impact of Primary Tumor Location on Long-Term Survival in Patients Undergoing Hepatic Resection for Metastatic Colon Cancer. Ann Surg Oncol 2018;25:431-8.
5. Moris D, Pawlik TM. Personalized treatment in patients with colorectal liver metastases. J Surg Res 2017;216:26-9.

Dimitrios Moris

Dept.of Surgery, Duke University School of Medicine, Durham, NC, USA.

Corresponding author: Dimitrios Moris, MD, MSc, PhD
Email: dimmoris@yahoo.com

Commentary no.2

Liver transplantation for unresectable colorectal liver metastases

I read with great interest the recent study by Dueland et al [1] demonstrating better overall survival (OS) in selected patients with unresectable colorectal liver metastases (CRLM) and high tumor load after liver transplantation (LT) compared to portal vein ligation and liver resection. These data further support the role of LT in highly selected patients with CRLM and the authors should be commented on their pioneer work in this field.

It is well shown in the literature that outcomes of patients with CRLM are mainly driven by tumor biology

[2]. However, in this study the authors did not present any data regarding the mutational status of the patients in each group that could provide deeper understanding of the results of the study. The authors provided data on the laterality of the primary disease, where right colon tumors have been shown to be related with worse outcomes [3]. However, one of the explanations of this finding has been shown to be the high incidence of mutant KRAS in right colon tumors [3]. This is of paramount importance since mutations in the SMAD and RAS-RAF pathway have been showed to be related with poor outcomes in patients with CRLM [4]. Especially KRAS mutant status has been shown to be related to worse outcomes (overall and recurrence-free survival) as well as poor response to cetuximab and 5FU-based regimens [2].

Also, the authors used tumor burden score (TBS) as prognostic factor of survival in both groups. However, TBS should be evaluated in concordance with the KRAS status since a recent study showed that in wild-type KRAS tumors, lower TBS was related to better outcomes (5-year OS, low TBS: 59.1% vs high TBS: 38.4%, p=0.002); however, TBS failed to discriminate long-term prognosis among patients with mutant KRAS tumors (5-year OS, low TBS: 37.4% vs high TBS: 26.7%, p=0.19) [5].

In conclusion, the results of LT for CLM are appealing but they should be interpreted cautiously, especially in the era of organ shortage where there is a significant ethical dilemma in using organs for the CRLM indication. With the recent technical advances and the increasingly better systemic treatment options, LT will need to be compared with current systemic and locoregional options at institutions with experience in disease management.

References

1. Dueland S, Yaqub S, Syversveen T et al. Survival Outcomes After Portal Vein Embolization and Liver Resection Compared With Liver Transplant for Patients With Extensive Colorectal Cancer Liver Metastases. JAMA Surg 2021.
2. Tsilimigras DI, Ntanasis-Stathopoulos I, Bagante F et al. Clinical significance and prognostic relevance of KRAS, BRAF, PI3K and TP53 genetic mutation analysis for resectable and unresectable colorectal liver metastases: A systematic review of the current evidence. Surg Oncol 2018;27:280-8.
3. Creasy JM, Sadot E, Koerkamp BG, et al. The Impact of Primary Tumor Location on Long-Term Survival in Patients Undergoing Hepatic Resection for Metastatic Colon Cancer. Ann Surg Oncol 2018;25:431-8.
4. Lang H, Baumgart J, Heinrich S et al. Extended Molecular Profiling Improves Stratification and Prediction of Survival After Resection of Colorectal Liver Metastases. Ann Surg 2019;270:799-805.
5. Tsilimigras DI, Hyer JM, Bagante F et al. Resection of Colorectal Liver Metastasis: Prognostic Impact of Tumor Burden vs KRAS Mutational Status. J Am Coll Surg 2021;232:590-8.

Dimitrios Moris

Dept.of Surgery, Duke University School of Medicine, Durham, NC, USA.

Corresponding author: Dimitrios Moris, MD, MSc, PhD
Email: dimmoris@yahoo.com