French Editorial from the ACHBPT

Comment on: survival outcomes after portal vein embolization and liver resection compared with liver transplant for patients with extensive colorectal cancer liver metastases

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We read with great interest the work of Dueland *et al*. recently issued in *JAMA Surgery* (1). In this retrospective study gathering data from several prospective cohorts from Norway, the authors compare oncological outcome of patients who underwent liver transplantation (LT) *vs*. portal venous embolization (PVE) followed by liver resection (LR) for colorectal liver metastasis (CRLM). To this end, they gather data from three prospective cohort studies including patients who underwent LT for CRLM, and data from another cohort of patients who underwent PVE and LR for CRLM. In the cohort of PVE patients (n=53), they find a high drop-out rate (28%) of patients who do not undergo LR after PVE. The reported 5-y overall survival (OS) of patients who undergo PVE + LR (n=38) is 44.6% *vs*. 0% in unresected patients (n=15). In the LT group (n=50), just as in the PVE group, the authors analyze patient survival according to their tumor burden, distinguishing a high tumor load (HTL) group (number of lesions ≥9 or maximum diameter ≥55 mm) opposed to the low tumor load (LTL) group. In the LTL-PVE group, authors find a 5-year OS rate of 69.3% in 23 patients receiving PVE + LR, which lowered to 53.1% when considering the whole PVE group in an intention to treat (ITT) analysis (n=30); in the LTL-LT group, the 5-y OS is 72.4% (n=21). In the HTL group, PVE + LR (n=8) led to 10% 5-y OS; PVE in ITT (n=15) led to less than 10% 5-y OS; while LT (n=29) led to a 5-y OS of 40% (not provided, read on the survival curves).

Amongst HTL patients the authors further dichotomize patients with left-sided (n=21) and ascending colon (n=8) primary cancer, finding patients with ascending colon primary having more N+ status and worse 5-y OS after either PVE + LR (12.5%) or LT (0%). The authors conclude to a high survival probability for LT as a treatment of selected patients even with high tumor load, or for patients who do not respond to PVE.

Dueland *et al*. must be commended for their work and their dynamism in initiating such an innovative and disruptive treatment as LT for CRLM (2). LT may indeed be considered as a last resort for young patients with unresectable CRLM with low aggressive biology, and future studies on LT in CRLM must be pursued.

Some additional thoughts on the present work may be interesting to share. Overall, the message of this study tends to favor LT versus PVE strategy for patients with extensive CRLM, although the authors maintain with reason a cautious position in their conclusion. Indeed, 5-y OS in LT patients seems significantly higher compared to PVE, especially in HTL group. However, making the comparison between these two groups of patients may be highly debatable. PVE patients suffer from high drop-out rate (28%) of patients who either do not increase enough their future liver remnant, or progress before resection. The authors do not provide the proportion of patients according to their reason for drop-out, but disease progression is usually the main limiting factor (3). The disease history of these patients who quickly progress mostly due to an aggressive tumor biology is never comparable to the disease history of patients who undergo LT after a long selection

process including many lines of chemotherapy and months of disease stability under systemic treatment. Therefore, concluding that those patients with aggressive tumor behavior who cannot undergo resection may benefit from LT is irrelevant. Most probably, these patients would never have made it through the long and demanding selection process of LT for CRLM. If the authors wanted to make a fair analysis in ITT, it would have been reasonable to compare patients who were selected for LT at the very beginning of the treatment (which is probably not possible since LT comes usually as a salvage option after months of stability under systemic treatment) to patients who had PVE in the objective of LR; here, only one group is in ITT, and the other (LR) is not. So, when one compares what is relevant to compare, meaning patients who effectively had PVE + LT *vs.* LT patients, the OS difference may not be that significant. Moreover, the 5-y OS of patients who underwent LT is not provided here, and the authors only analyze OS in "tumor load" subgroups. A direct comparison of 5-y OS between LT and PVR + LR, which would have been the most relevant analysis, is thus not feasible. However, in the LTL group, 5-y OS in LT and PVE + LR are 72.4% and 69.3%, respectively, which may be considered comparable or at least close. In the HTL group, on the other hand, results are once more subdivided in right or left-sided primary cancer groups and comparisons are not given on the global population. One must also take into consideration that OS as a primary outcome measure includes deaths due to LT complications including those related to the immunosuppressive treatment, which account for a substantial one-year post LT mortality (4).

Moreover, it is surprising that very few data on chemotherapy and disease history between LT and PVE groups are provided. The reader is not provided with patients' disease duration, how many systemic treatment lines they underwent, or what their RAS mutational status is, which makes the comparison between PVE and LT groups uninterpretable. One can at least retrieve the information on nodal primary tumor status which is 78% N+ in PVE + LR groups *vs.* 66% in LT group (no statistical comparison made).

The authors state in the methods "a matched cohort of 53 patients with resectable CRLM lesions and insufficient future liver remnant (FLR) (<30%) received PVE to expand the FLR prior to LR but otherwise displayed similar selection criteria as patients treated with LT". However, we cannot see any matching or even any statistical comparison between the two groups in the results, besides "all patients in the LT and PVE groups had an Eastern Cooperative Oncology Group score of 0 to 1, were younger than 72 years of age, and had the primary tumor resected before LT or PVE" which cannot be assimilated to a matching or a proper comparison of oncological characteristics.

Finally, one additional comment may be made on the PVE group. The authors do not mention any patient who underwent two-stage resections which is a common strategy for bilobar extended CRLM. Such patients may have been excluded from the PVE cohort, although the analysis of this subgroup having bilobar extended disease would have been interesting to study (5).

In conclusion, although LT for CRLM remains an innovative treatment option in CRLM, the results of retrospective analysis should be handled with caution due to the high risk of bias and the difficulty to compare patients with very different tumor natural history.

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Footnote

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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;156:550-7.
2. Dueland S, Syversveen T, Solheim JM, et al. Survival Following Liver Transplantation for Patients With Nonresectable Liver-only Colorectal Metastases. Ann Surg 2020;271:212-8.
3. Passot G, Chun YS, Kopetz SE, et al. Predictors of Safety and Efficacy of 2-Stage Hepatectomy for Bilateral Colorectal Liver Metastases. J Am Coll Surg 2016;223:99-108.
4. Burroughs AK, Sabin CA, Rolles K, et al. 3-month and 12-month mortality after first liver transplant in adults in Europe: predictive models for outcome. Lancet 2006;367:225-32.
5. Brouquet A, Abdalla EK, Kopetz S, et al. High survival rate after two-stage resection of advanced colorectal liver metastases: response-based selection and complete resection define outcome. J Clin Oncol 2011;29:1083-90.

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