Letter to the Editor

Is liver transplantation superior to liver resection for hepatocellular carcinoma within Milan criteria?

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We read with great interest the recent meta-analysis written by Koh and colleagues entitled "*Liver resection versus liver transplantation for hepatocellular carcinoma within Milan criteria: a meta-analysis of 18,421 patients*" (1), which was published in the latest issue of *Hepatobiliary Surgery Nutrition*.

The authors have reached an important conclusion that liver resection (LR) was associated with poorer overall survival (OS) and disease-free survival (DFS) compared to liver transplantation (LT) and found similar results among intention-to-treat (ITT) studies. In uninodular hepatocellular carcinoma (HCC), DFS is poorer in LR, but OS was comparable to LT. In addition, subgroup analysis revealed that in Europe and North America, LR had poorer OS versus LT, but OS was comparable in Asia. Before 2010, LR had inferior survival versus LT, but not after 2010. Cohorts that undergoing usual surveillance had worse OS after LR, but cohorts underwent enhanced surveillance had comparable OS after LT and LR. These findings emphasize that LT remains the ideal treatment option for HCC by removing both the tumor and the surrounding diseased liver, thus addressing the field change effect and lowering the risk of recurrence. Nevertheless, although the authors discussed some limitations, some deficiencies related to this meta-analysis still existed that we would like to raise.

Firstly, there are some flaws in the literature search. To begin with, only two electronic databases (MEDLINE and Embase) were systematically searched for eligible literature. Second, only studies published in English were eligible for inclusion, which could inevitably introduce some language bias. Thus, to make this meta-analysis invulnerable, the authors are suggested to choose more electronic databases like Scopus, Web of Science, and Cochrane Library to search for eligible studies without language restriction.

Secondly, regarding inclusion criteria, the eligible patients were diagnosed with HCC within Milan criteria. Nevertheless, after a careful review, we noticed that the authors appeared to have made an apparent mistake in this meta-analysis. The reference 27 is not about LR versus LT for HCC within Milan criteria (2).

Third, in consideration of the heterogeneity is significantly high in the results section. It is critical to perform meta-regression and subgroup analyses to explore potential sources of heterogeneity. The covariates such as country (China versus the United States), year of publication (before 2010 versus 2010–2021), and sample size (>50 versus <50) might be taken into account when meta-regression and subgroup analyses are carried out. What's more, results were stratified by date of study, unimodular HCC, region and income were performed by the investigators. However, these forest plots weren't presented. We suggest that the investigators to provide these forest plots in supplementary materials.

Finally, there is an ambiguity in this meta-analysis. In the results section, the authors claimed that LR was associated with poor OS outcome in HCC within Milan criteria. However, we are wondering what does the OS mean, 1-year survival or 3-year survival? The same as DFS.

Much appreciation to the authors for their contribution in supplying us a meta-analysis to assess the efficiency of LT for HCC within Milan criteria. However, the limited number of high-quality clinical trials could unavoidably lead to notable risk of bias. In our opinion, further studies with large samples are still needed to further validate these findings.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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