Down-staging of Hepatocellular Carcinoma Prior to Liver Transplantation: The Power of Selection

To the Editor:

We enjoyed the article by Yao et al. in the recent issue of HEPATOLOGY[1] in which they report an excellent outcome of liver transplantation (LT) following preoperative down-staging of hepatocellular carcinoma (HCC).

Yao et al. selected HCCs without vascular invasion by imaging studies and out of the Milan criteria[2] but meeting the following criteria: single nodule measuring 5-8 cm, 2-3 nodules measuring 3-5 cm (total ≤8 cm), 4-5 nodules measuring ≤3 cm (total ≤8 cm). They needed to meet the Milan criteria after chemoembolization (TACE), percutaneous ablation techniques, or liver resections. Thirty-five patients received LT without tumor recurrence after a median follow-up of 25 months. Two cases died due to nontumoral causes.

The efficacy of patient selection based on clinical response to preoperative treatments is confirmed by our recent down-staging study, which is similar in terms of inclusion criteria and follow-up.[3] In an intention-to-treat analysis, our recurrence rate and patient survival were not as excellent as those reported by Yao et al., but they were comparable to our control group meeting the Milan criteria. We think it remarkable that LT can achieve good results even in a population with many multinodular (>3) HCCs (58.3%), in contrast with the 5 out of 61 cases (8.2%) of the University of California, San Francisco (UCSF) series. Furthermore, many of our cases showed microvascular invasion and poorly differentiated tumor, whereas none of the UCSF cases revealed these unfavorable features, providing a fairly surprising picture in contrast with several previous series.[4-8] As discussed by the authors, these results may have been generated by the selection of tumors with more favorable biology during the down-staging process. Nonetheless, we had quite different results following a very similar selection process. We wonder if they applied other specific selection criteria that we failed to understand.

As described by the authors, most patients received a biopsy before LT, and in the same period two different studies were performed: the present one, where patients must meet the Milan criteria after down-staging procedure, and another in which patients were listed with slightly extended Milan criteria (UCSF criteria) without any restrictions concerning treatments during the waiting time.[4] We would like to know how the authors decided whether to include a case in one study or the other, if the pre-liver biopsy played any role, if all cases were first HCC diagnosis, and if patients progressed during follow-up could be still eligible for down-staging procedures. Finally, because the authors showed the efficacy of the UCSF criteria, it would be interesting to know how many patients met these criteria in the down-staging group before any treatments.

In conclusion, both the UCSF and Bologna studies confirm the power of selection to improve LT results for HCC and suggest how it should be properly applied. We have learned how to minimize the graft/patient loss for tumor recurrence; now we are learning how to offer to patients with HCC—even those outside the Milan criteria—the same chance of survival of those listed for LT with other indications.

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The Quest for Liver Fibrosis Biomarkers: Promises from the Enhanced Liver Fibrosis Panel and Beyond

To the Editor:

Guha and coworkers[1] reported the results of their study aiming to validate a surrogate diagnostic biomarker-based panel for the diagnosis of liver fibrosis. The authors investigated a total of 192 patients who had liver biopsies because of elevated aminotransferases and demonstrated that the Enhanced Liver Fibrosis (ELF) Panel yielded an area under the curve (AUC) of 0.90 for distinguishing severe fibrosis, 0.82 for moderate fibrosis, and 0.76 for no fibrosis.[1] The ELF panel includes a series of enzyme-