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Reply

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Reply

We thank Jiang et al. for their letter and keen interest in our study.[1] In accordance with interpreting results from application of any statistical technique, we acknowledge the value of contextualizing our findings with inherent limitations in mind.

As pointed out by the authors, we recognize the importance for identifying and adjusting for unmeasured confounders. These include the receipt of antiviral therapy for patients with Hepatitis B and the use of the Pringle maneuver. Regarding surgical margins, a recent meta-analysis found that margin width was associated with prognosis in Eastern but not Western countries.[2] Notwithstanding the relevance of specific risk factors not included in the analysis, we recognize that the sample size of our study limits accommodation of an increasingly large number of variables in the models without compromising stability. In order to address this, we encourage well-designed multicenter studies with clearly defined variables and endpoints.

To clarify methodological concerns, death in the study was the exact death date of the patient if the patient had died. Further, as noted in the methods section, transitions between states were only allowed in the forward direction. Lastly, the proportional hazard assumption was fulfilled in our study cohort for all covariates using the Schoenfeld residuals against the transformed time (preoperative model: age, sex, preoperative alpha-fetoprotein, tumor number [preoperative], tumor size [preoperative], satellite lesions [preoperative], and the postoperative model: age, sex, microvascular invasion, tumor number [pathology], tumor size [pathology], satellite lesions [pathology], cirrhosis).

It is important to highlight that our study cohort was patients who were treatment-naïve and underwent resection operations with curative intent. We agree that recurrence treatment remains widely heterogeneous, largely due to a lack of standardization—something urgently needed in the field. Appropriate adoption and implementation of clinical algorithms from the most recent Barcelona Clinic Liver Cancer update offers an opportunity for realignment of treatment paradigms and generalizability of data from follow-up studies.[3]

In conclusion, we firmly believe that multistate modeling represents an innovative technique for clinical research and offers a more meaningful approach to prognostication than can be achieved by standard single time-to-event models for patients with HCC. We hope that continued exploration in illnesses where patients can exist in various distinct disease states may yield additional insight into disease biology and help inform clinical decision-making.

CONFLICT OF INTEREST

Nothing to report.

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