



What clinicopathological factors affect the recurrence of hepatocellular carcinoma after surgery?

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We read with great interest the recent research by Dai *et al.* (1) entitled “*Nomograms based on clinicopathological factors and inflammatory indicators for prediction of early and late recurrence of hepatocellular carcinoma after surgical resection for patients with chronic hepatitis B*”.

This study generated nomograms that integrated clinicopathological features and inflammation-related factors to predict recurrence in hepatocellular carcinoma (HCC) patients with hepatitis-B virus infection background after liver resection. HCC is the fourth most common malignancy and the most common primary liver cancer, with high mortality (2). Radical hepatectomy is regarded as the most effective treatment to receive long-term survival for HCC patients. However, a high rate of postoperative tumor recurrence is a major challenge to the survival of patients (3). Therefore, the detection of patients with a high-risk probability of recurrence and the development of postoperative treatment plans after surgery are of great significance. Nomogram, which is easy to use, can provide personal and highly accurate risk assessment of predictive models and guide clinical treatment decisions.

We would like to raise a few questions to the authors of this study. Firstly, the enrolled participants included Barcelona Clinic Liver Cancer (BCLC) stage 0, A, B, and C HCC patients, with stage B and stage C patients exceeding 50% of the whole cohort. According to the BCLC treatment strategy, interventional therapy is recommended for patients with BCLC stage B, whereas systemic treatment is recommended for patients with BCLC stage C (4). The prognosis of patients undergoing hepatectomy at

different tumor stages may be significantly varied, especially in patients with advanced HCC, which may also affect the results of the study.

Secondly, the nomograms developed in this study include some inflammation-related factors and clinicopathological features. However, several indicators that are generally considered to be associated with high recurrence rate, such as macrovascular invasion, microvascular invasion (MVI), etc., were not included in the models. Although macrovascular invasion affects the prognosis of patients, it is still controversial whether surgical resection should be performed (5,6). The appearance of MVI is also closely related to prognosis and recurrence (7). One study has confirmed that if the postoperative pathology indicates the existence of MVI, early postoperative intervention therapy can significantly improve the patients' outcomes (8).

Thirdly, studies have revealed that inflammation-related factors are closely related to patients' prognoses (9). The cut-off values of inflammation-related indicators in this study differed from those in published literature (10). For example, neutrophil-to-lymphocyte ratio (NLR) greater than or equal to 5 is often used as a cut-off value, whereas NLR greater 1.92 is regarded as a cut-off value in this research.

Finally, the concordance index (C-index) is a tool to evaluate the predictive ability of the model. The low C-index of this study reflected the poor performance of the model. In addition, this study was based on a single-center retrospective analysis, and the bias may be inevitable. It would be more convincing if there were multiple centers of

external validation.

Therefore, the accurate prediction of the recurrence in HCC patients is significant, and further studies with large-scale and multiple centers of external validation are needed.

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