

Answering Reviewers

In this manuscript, the authors explored the predictive value of Gd-EOB-DTPA-enhanced MRI combined with clinical features in predicting early recurrence of hepatocellular carcinoma after liver resection. They collected clinical features and MRI imaging features from 161 HCC patients confirmed by pathology, and grouped and analyzed the patients based on early recurrence and non-early recurrence after resection. The results showed significant differences between the early recurrence and non-early recurrence groups in factors such as patient age, serum AFP levels, pathological satellite lesions, microvascular invasion, BCLC staging, and CNLC staging. Additionally, MRI imaging features such as tumor size, number, margins, and portal vein tumor thrombus were also associated with the early recurrence group. It is meaningful to achieve early prediction of recurrence in clinical practice and improving patient prognosis, but there are several questions that need to be addressed.

Major concerns:

1. The authors has provided independent predictive factors for early recurrence, but it appears they have not been validated, and the specificity, sensitivity, and accuracy of each predictive factor have not been provided in the table.

Response: Thank you very much for your professional advice. Up on your suggestion, we collected an external data set including 14 early and 17 non-early recurrence patients for external validation with the same inclusion and exclusion criteria. The specificity, sensitivity, and accuracy of each predictive factor were validated, and the predictive efficiency of each predictive factor was tested by ROC analysis. Relevant changes were made in the Materials/methods, Results and Discussion sections.

2. And the manuscript mentions that age, AFP level, CNLC staging, tumor margins, as well as major vessel invasion and hypo-intense tumor periphery in hepatobiliary phase on MRI are independent risk factors for early recurrence after HCC surgery. It seems that relying solely on these factors may not achieve the prediction objective stated in the title of manuscript. It would be better to construct a comprehensive prediction model by integrating these factors to achieve the goal of early recurrence prediction.

Response: Thanks for your suggestion. After deep discussion with statistic experts referring to the statistics methods used in this study, statistic experts suggest us better to build a logistic regression model rather than Cox proportional hazard analysis for this study. So we performed the statistics analysis again upon expert suggestions. The results from multivariate logistic regression analysis showed that patient age, MVI, CNLC stage, tumor boundary and large vessel invasion are the independent predictive factors for early recurrence of HCC. As a matter of fact, based on the results of multivariate logistic regression, these factors have constructed a predicting model. By adopting external data, the predicting specificity, sensitivity and accuracy of each predictive factor were validated, and the predictive efficiency of each factor and the model were further tested by ROC analysis. Results showed that

the AUC of the combined factors was 0.861, suggesting the multivariate logistic regression was a reasonable predictive model for HCC early recurrence.

3. Additionally, it is important to compare the advantages of the constructed predictive model with existing models to determine if there is higher accuracy.

Response: Thanks for your suggestion. We added a paragraph in the discussion discussing the advantages and predictive efficiency compared with existing models. Compared with previous studies, this study obtained similar research results and diagnostic accuracy. While different from most previous studies, we introduced an external data set to validate the constructed model, further evaluating the sensitivity, specificity and accuracy of various predictive factors, and that is an advantages of the present study.

4. Based on the study results, how can these predictive factors be utilized to guide the treatment and prognosis management of HCC patients? What is the effect to survival outcomes of patients?

Response: Upon your suggestion, we made improvement in the discussion. As in clinical setting, it is very important to know the risk factors for early recurrence of liver cancer, especially at the time of they are fist in hospital. By analyzing the clinical and MRI features, we would find out patients with high-risk of early recurrence. And for those patients, special attentions like closely followed-up, post-operative adjuvant treatment using TACE or molecular targeted agents should be discussed with these patients. All efforts made were for the aim of reducing the chance of recurrence and get better survival outcomes.

Minor concerns:

1. In the description of the results for 2.2 MRI Imaging Features, please confirm if it is “non-recurrence” or “non-early recurrence”.

Response: All confirmed and corrected: “non-early recurrence”.

2. In the part of Materials and methods, examples of feature definitions and representative MRI images should be provided to enable the authors to gain a better understanding of your analysis.

Response: Thanks for your suggestion. We added typical examples of feature definitions and representative MRI images to enable the authors to gain a better understanding.