Letter to Editor

Repeated Hepatectomy and the Role of Alpha-Fetoprotein Kinetics in Recurrent Hepatocellular Carcinoma

Haider Imran[1] iD , Zahra Ali Haque [2]✉ iD , Amal Khan[1] iD

[1] Department of Medicine, Foundation University Medical College, Islamabad, Pakistan

[2] Department of Medicine, Islamic International Medical College, Rawalpindi, Pakistan

✉**Corresponding Author:** Tel: +923249895985; Email: zahraalihaque5@gmail.com

Dear Editor,

Hepatocellular carcinoma (HCC), the sixth most common cancer and the third leading cause of cancer deaths worldwide, remains a major health concern. Recurrence occurs in up to 70% of cases within five years post-surgery, underscoring the need for better management strategies (1). Despite advancements in surveillance, detection, and treatment, such as surgical resection, liver transplant, and local ablative therapy, the prognosis remains poor. This persistent risk underscores the need for improved strategies in surgical patient selection, prognostic stratification, and postoperative management.

Alpha-fetoprotein (AFP), long regarded as a diagnostic and surveillance biomarker, has gained renewed attention for its dynamic role in predicting outcomes after surgical intervention. Recent studies, including one performed by Song et al., highlight the importance of recurrent AFP (r-AFP) kinetics in patients undergoing repeat hepatectomy. Their results show a substantial correlation between r-AFP positivity and a worse recurrence-death survival rate, indicating that AFP dynamics offer useful information beyond static baseline measures (2).

From a surgical perspective, this insight is vital in the management of recurrent HCC, where decisions regarding repeat hepatectomy versus alternative strategies (such as transplantation, ablation, or adjuvant therapy) are complex. The AFP kinetics not only reflect tumor biology, including vascular invasion and heterogeneity (3), but also serve as a practical tool to guide intensity of surveillance, timing of reoperation, and selection of patients most likely to benefit from aggressive surgical management.

Furthermore, recurrent HCC exhibits notable tumor heterogeneity, with AFP positivity closely linked to microvascular invasion (MVI), a key factor driving recurrence post-treatment (5). It is clinically important to differentiate between intrahepatic metastasis and multicentric recurrence, as advanced tumors most often recur through intrahepatic spread, whereas early-stage, cirrhosis-related HCCs are more likely to recur multicentrically. After resection, a decline in r-AFP levels may help predict recurrence risk and inform decisions regarding adjuvant therapy. High-risk patients, especially those with MVI and elevated preoperative AFP, appear to benefit from adjuvant transarterial chemoembolization, which has been shown to improve both overall and disease-free survival (6).

While promising, these findings must be interpreted with caution, given the predominance of HBV-related disease in existing studies and their single-center design. Multicenter, prospective investigations are needed to validate the integration of AFP-guided approaches into standard surgical decision-making and postoperative pathways across diverse patient populations.

In conclusion, AFP kinetics are potent prognostic indicators that directly affect trauma-hepatobiliary care and surgical oncology. Surgeons may optimize patient selection for repeat resection, increase recurrence risk classification, and eventually improve long-term outcomes in HCC by integrating dynamic AFP assessment into perioperative evaluation.

Conflict of Interest

The authors declare that they have no conflict of interest.

Declaration of Generative Artificial Intelligence (AI) in Scientific Writing

The authors declare that generative AI tools (specifically QuillBot) were used solely for language editing and grammar improvement, and they take full responsibility for the content, originality, and accuracy of the manuscript.

References

1. Abdelhamed W, & El-Kassas M. Hepatocellular carcinoma recurrence: Predictors and management. Liver res. 2023;7(4): 321-32.
[DOI: 10.1016/j.livres.2023.11.004]
2. Song Z, Chen B, Wen H, Zhou Q, Lin S, Qian B, et al. Negative serum alpha-fetoprotein at recurrence predicts good prognosis in recurrent hepatocellular carcinoma patients receiving repeated hepatectomy: a single-center retrospective cohort study. Eur J Surg Oncol. 2025;51(9):110145.
[DOI: 10.1016/j.ejso.2025.110145]
3. Akabane M, Kawashima J, Altaf A, Woldesenbet S, Cauchy F, Aucejo F, et al. Enhancing recurrence-free survival prediction in hepatocellular carcinoma: a time-updated model incorporating tumor burden and AFP dynamics. Ann Surg Oncol. 2025; 32(8), 5648-5656.
[DOI: 10.1245/s10434-025-17303-y]
4. Nakashima O, Kojiro M. Recurrence of hepatocellular carcinoma: multicentric occurrence or intrahepatic metastasis? A viewpoint in terms of pathology. J Hepatobiliary Pancreat Sci.2001;8(5):404-9.
[DOI: 10.1007/s005340100001]
5. Du M, Chen L, Zhao J, Tian F, Zeng H, Tan Y, Sun H, Zhou J, Ji Y. Microvascular invasion (MVI) is a poorer prognostic predictor for small hepatocellular carcinoma. BMC cancer. 2014;14(1):38.
[DOI: 10.1186/1471-2407-14-38]
6. Chen ZH, Zhang XP, Zhou TF, Wang K, Wang H, Chai ZT, et al. Adjuvant transarterial chemoembolization improves survival outcomes in hepatocellular carcinoma with microvascular invasion: a systematic review and meta-analysis. Eur J Surg Oncol. 2019;45(11):2188-96.
[DOI: 10.1016/j.ejso.2019.06.031]