Editorial Commentary

Inflammatory indicators such as systemic immune inflammation index (SIII), systemic inflammatory response index (SIRI), neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as prognostic factors of curative hepatic resections for hepatocellular carcinoma

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As the fifth most common gastrointestinal cancer worldwide, hepatocellular carcinoma (HCC) often presents at advanced stages of disease. For the subset of patients who present with tumor and liver-related features amenable to surgery, hepatic resection—in addition to transplantation—offers the best chance at curative-intent therapy. Resection can be associated, however, with risk of complications and perioperative death especially among individuals with concomitant portal hypertension, liver fibrosis, cirrhosis, and portal vein thrombosis (1-3). Post-resection liver failure is also a major concern and can be a devasting complication following hepatic resection (4,5). Overall survival following hepatic resection of HCC ranges from only 30–50%, and recurrence can be common depending on the stage of disease. In turn, there is considerable interest in identifying markers to help stratify patients relative to risk of recurrence and prognosis to define which groups of patients may benefit the most from hepatic resection of HCC (1-5).

Traditional models to predict recurrence and prognosis following resection of HCC have generally include demographic (e.g., sex, age, race/ethnicity, etc.), tumor (e.g., size, number, presence of vascular invasion, grade, etc.), as well as non-tumor (e.g., cirrhosis, portal hypertension, etc.) factors (6-9). Work from our own group has demonstrated that a simple tumor burden score-based score, which included tumor burden, alpha-fetoprotein (AFP) levels, and albumin-bilirubin (ALBI) score accurately predicted risk of non-transplantable recurrences and could help identify candidates for upfront resection versus transplantation (6-10).

More recently, based on the theory of cancer-related inflammation, there has been increased focus on inflammatory indexes as potential clinical risk factors for poor prognosis and recurrence (11,12). Local and systemic inflammation are two components of the cancer-associated inflammation process. Typically, the local component may be in relation to tumorigenesis as part of the tumour micro-environment. Systemic inflammation can occur as a response to malignant neoplasia and be mediated by immune proteins, cytokines, and immune cells (11-13). Along these lines, inflammatory indicators such as systemic

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immune inflammation index (SIII), systemic inflammatory response index (SIRI), neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been reported to be accurate in predicting HCC recurrence (14). In fact, one previous study recommended combining four inflammatory indicators (i.e., SIII, SIRI, PLR, NLR) with three pathological factors (i.e., tumour diameter, degree of differentiation, vascular invasion) to form a combined inflammation and pathology (CIP) model (15). The CIP model demonstrated a strong ability to predict 2-year recurrence-free survival. In a different study, Yang *et al.* proposed a nomogram based on six independent risk factors [i.e., age, AFP, tumour size, satellite nodules, SIII, prognostic nutritional index (PNI)] to predict the risk of recurrence and stratify HCC patients practically and reliably (5).

Previous studies had demonstrated that low albumin and low body mass index (BMI)/sarcopenia were also associated with worse outcomes (16). The American Joint Committee on Cancer (AJCC) and Barcelona Clinic Liver Cancer (BCLC) staging systems also have predictive value for the recurrences of HCC (17). Of note, Yang *et al.* demonstrated that their nomogram based on the aforementioned six independent risk factors demonstrated better ability to predict risk of recurrence of HCC than the BCLC and AJCC 8th staging systems (5). Therefore, the combination of the BCLC and AJCC staging systems with nomograms may help to assess better the risk of postoperative recurrence and consequently help tailor individualised treatments for high-risk patients.

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References

1. Gavriilidis P, Pawlik TM, Meirson T, et al. Associating liver partition and portal vein ligation or combined transarterial chemo-embolisation and portal vein embolisation for staged hepatectomy for HBV-related hepatocellular carcinoma. Hepatobiliary Surg Nutr 2023;12:272-5.
2. Gavriilidis P, Marangoni G, Ahmad J, et al. Simultaneous portal and hepatic vein embolization is better than portal embolization or ALPPS for hypertrophy of future liver remnant before major hepatectomy: A systematic review and network meta-analysis. Hepatobiliary Pancreat Dis Int 2023;22:221-7.
3. Gavriilidis P, Roberts KJ, de'Angelis N, et al. Recurrence and survival following microwave, radiofrequency ablation, and hepatic resection of colorectal liver metastases: A systematic review and network meta-analysis. Hepatobiliary Pancreat Dis Int 2021;20:307-14.
4. Cescon M, Vetrone G, Grazi GL, et al. Trends in perioperative outcome after hepatic resection: analysis of 1500 consecutive unselected cases over 20 years. Ann Surg 2009;249:995-1002.
5. Yang J, Bao Y, Chen W, et al. Nomogram Based on Systemic Immune Inflammation Index and Prognostic Nutrition Index Predicts Recurrence of Hepatocellular Carcinoma After Surgery. Front Oncol 2020;10:551668.
6. Lima HA, Moazzam Z, Endo Y, et al. TBS-Based Preoperative Score to Predict Non-transplantable Recurrence and Identify Candidates for Upfront Resection Versus Transplantation for Hepatocellular Carcinoma.

Ann Surg Oncol 2023;30:3363-73.
7. Xing H, Sun LY, Yan WT, et al. Repeat hepatectomy for patients with early and late recurrence of hepatocellular carcinoma: A multicenter propensity score matching analysis. Surgery 2021;169:911-20.
8. Wei T, Zhang XF, Bagante F, et al. Early Versus Late Recurrence of Hepatocellular Carcinoma After Surgical Resection Based on Post-recurrence Survival: an International Multi-institutional Analysis. J Gastrointest Surg 2021;25:125-33.
9. Chan AWH, Zhong J, Berhane S, et al. Development of pre and post-operative models to predict early recurrence of hepatocellular carcinoma after surgical resection. J Hepatol 2018;69:1284-93.
10. Li SQ, Su LL, Xu TF, et al. Radiomics model based on contrast-enhanced computed tomography to predict early recurrence in patients with hepatocellular carcinoma after radical resection. World J Gastroenterol 2023;29:4186-99.
11. Balkwill FR, Mantovani A. Cancer-related inflammation: common themes and therapeutic opportunities. Semin Cancer Biol 2012;22:33-40.
12. Sohrab SS, Raj R, Nagar A, et al. Chronic Inflammation's Transformation to Cancer: A Nanotherapeutic Paradigm. Molecules 2023;28:4413.
13. Diakos CI, Charles KA, McMillan DC, et al. Cancer-related inflammation and treatment effectiveness. Lancet Oncol 2014;15:e493-503.
14. Wenpei G, Yuan L, Liangbo L, et al. Predictive value of preoperative inflammatory indexes for postoperative early recurrence of hepatitis B-related hepatocellular carcinoma. Front Oncol 2023;13:1142168.
15. Endo Y, Sasaki K, Moazzam Z, et al. Liver transplantation for elderly patients with early-stage hepatocellular carcinoma. Br J Surg 2023;110:1527-34.
16. Valero V 3rd, Amini N, Spolverato G, et al. Sarcopenia adversely impacts postoperative complications following resection or transplantation in patients with primary liver tumors. J Gastrointest Surg 2015;19:272-81.
17. Kee KM, Wang JH, Lee CM, et al. Validation of clinical AJCC/UICC TNM staging system for hepatocellular carcinoma: analysis of 5,613 cases from a medical center in southern Taiwan. Int J Cancer 2007;120:2650-5.

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