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Research Article

RISK FACTORS FOR EARLY RECURRENCE AFTER CURATIVE HEPATECTOMY IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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ABSTRACT

Background: Hepatocellular carcinoma (HCC) remains one of the most prevalent primary liver malignancies worldwide and is associated with a high rate of postoperative recurrence despite curative hepatectomy. Early recurrence significantly compromises long-term survival and remains a major challenge in hepatobiliary surgery. Identification of clinicopathological factors associated with early recurrence may facilitate individualized postoperative surveillance and optimize therapeutic decision-making [1–7].

Objective: To investigate the clinicopathological factors associated with early recurrence following curative hepatectomy in patients with hepatocellular carcinoma treated at the First Affiliated Hospital of the University of South China.

Methods: A single-center retrospective cohort study was conducted in the Department of Hepatobiliary Surgery at the First Affiliated Hospital of the University of South China. Medical records of patients who underwent curative (R0) hepatectomy for histopathologically confirmed hepatocellular carcinoma between 14 July 2025 and 17 January 2026 were retrospectively reviewed. Twenty-four consecutive eligible patients were included according to predefined inclusion and exclusion criteria. The study design and reporting followed the recommendations of the STROBE Statement for observational studies [11].

Demographic characteristics, clinical history, laboratory investigations, radiological findings, operative details, pathological characteristics, and follow-up information were extracted from the institutional electronic medical record system. Variables of interest included age, sex, hepatitis B virus infection status, liver cirrhosis, Child–Pugh classification, serum alpha-fetoprotein (AFP) level, liver function parameters, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), tumor size, tumor number, operative duration, intraoperative blood loss, surgical margin status, tumor differentiation, and microvascular invasion [2,3,6–10,12–15]. Early recurrence was defined as tumor recurrence occurring within 24 months after curative hepatectomy, consistent with commonly accepted definitions in the literature [6–8]. Appropriate descriptive and comparative statistical analyses were performed to explore potential associations between clinicopathological variables and early recurrence [11].

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver and represents a major global health burden. It ranks among the leading causes of cancer-related mortality worldwide, with the highest incidence occurring in East Asia and other regions where chronic hepatitis B virus (HBV) infection is endemic [1–5]. In China, HCC continues to pose a significant public health challenge owing to the high prevalence of chronic HBV infection, liver cirrhosis, and other chronic liver diseases [2–5]. Despite substantial advances in diagnostic imaging, perioperative management, and multidisciplinary treatment strategies, the long-term prognosis of patients with HCC remains unsatisfactory, primarily because of the high rate of postoperative tumor recurrence [2–6].

Curative hepatectomy remains one of the most effective treatment options for patients with resectable HCC and preserved liver function [2–5]. Improvements in surgical techniques, anesthetic management, and perioperative care have significantly reduced postoperative morbidity and mortality over the past decade [2,5]. Nevertheless, recurrence following apparently curative liver resection remains common, with previous studies reporting recurrence in a substantial proportion of patients within the first two years after surgery [6–9]. Early recurrence is generally considered to reflect aggressive tumor biology, including microscopic intrahepatic dissemination and occult vascular invasion, and is associated with poorer disease-free and overall survival compared with late recurrence [6–10].

Accurate identification of patients at increased risk of early recurrence is therefore of considerable clinical importance. Reliable risk stratification may facilitate individualized postoperative surveillance, improve the selection of patients for adjuvant therapies or clinical trials, and support timely detection of recurrent disease when further curative treatment may still be feasible [2,3,5,10]. Numerous clinicopathological variables have been investigated as potential predictors of recurrence, including serum alpha-fetoprotein (AFP) concentration, tumor size, tumor multiplicity, histological differentiation, liver cirrhosis, surgical margin status, and microvascular invasion [6–10,14,15]. In addition, systemic inflammatory markers such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio

(PLR) have recently attracted increasing attention because they are inexpensive, routinely available, and may reflect the interaction between tumor progression and the host immune response [12,13].

Although these prognostic factors have been widely studied, considerable variability exists among published reports because of differences in patient characteristics, underlying liver disease, treatment protocols, and institutional practice [2,3,6–10]. Furthermore, relatively few studies have specifically examined the clinicopathological characteristics of patients treated within individual hepatobiliary centers in China. Institutional analyses remain valuable because they provide insight into local patient populations, treatment outcomes, and opportunities for quality improvement while generating hypotheses for future multicenter investigations [2,3,16].

The present pilot retrospective cohort study was conducted in the Department of Hepatobiliary Surgery at the First Affiliated Hospital of the University of South China. Consecutive patients who underwent curative (R0) hepatectomy for histologically confirmed hepatocellular carcinoma between 14 July 2025 and 17 January 2026 were retrospectively reviewed. The study aimed to evaluate the association between routinely collected demographic, clinical, laboratory, operative, and pathological variables and early postoperative recurrence. By identifying potential predictors of recurrence within this institutional cohort, this study seeks to contribute preliminary evidence that may assist clinicians in postoperative risk assessment and provide a foundation for larger prospective and multicenter studies in the future [2,3,16].

MATERIALS AND METHODS

This study was designed as a single-center retrospective observational cohort study conducted in the Department of Hepatobiliary Surgery at the First Affiliated Hospital of the University of South China, Hengyang, Hunan Province, China. The primary objective was to investigate clinicopathological factors associated with early recurrence following curative hepatectomy in patients with hepatocellular carcinoma (HCC) [2,3,5,11].

Medical records of consecutive patients who underwent curative-intent (R0) hepatectomy for histopathologically confirmed HCC between **14 July 2025 and 17 January 2026** were retrospectively reviewed. Consecutive sampling was adopted to reduce selection bias and ensure that all eligible patients treated during the study period were considered for inclusion [11].

The hospital is a tertiary academic teaching institution with a specialized hepatobiliary surgery service that performs a high volume of liver resections and maintains comprehensive electronic medical records, pathology databases, laboratory information systems, and radiological archives. These institutional resources enabled systematic retrieval of clinical data for retrospective analysis.

A total of **24 eligible patients** satisfied the study criteria and were included in the final analysis. All demographic, clinical, laboratory, imaging, operative, pathological, and follow-up information was collected using a standardized data extraction form prepared before data collection. Data were independently verified by members of the research team to improve completeness and consistency [11].

Survey Methodology (Data Collection):

As this was a retrospective observational study, no direct patient interviews or questionnaires were administered. Clinical information was extracted from the hospital electronic medical record system, operative notes, anesthesia records, pathology reports, laboratory databases, radiological imaging records, and outpatient follow-up documentation [11].

A standardized case report form was developed before data collection to ensure uniform extraction of all study variables. Only routinely documented clinical information generated during standard patient care was included. Missing or inconsistent information was verified by reviewing the original medical records whenever possible [11].

Study Population:

Inclusion Criteria:

Patients were eligible if they:

- were aged 18 years or older;
- had histopathologically confirmed hepatocellular carcinoma [2,3];
- underwent curative (R0) hepatectomy with curative intent [2,3,5];
- had complete clinical, operative, pathological, and follow-up records; and
- were treated within the predefined study period.

Exclusion Criteria:

Patients were excluded if they:

- underwent palliative or non-curative surgery [2,3];
- had recurrent HCC before the index operation;
- had metastatic liver tumors from another primary malignancy;
- underwent liver transplantation;
- had incomplete medical records; or
- lacked sufficient postoperative follow-up information for recurrence assessment.

Demographic and Clinical Information:

Baseline demographic characteristics included:

- Age
- Sex
- Body mass index (BMI)
- Smoking history
- Alcohol consumption
- Diabetes mellitus
- Hypertension
- Chronic hepatitis B virus infection

- Chronic hepatitis C virus infection
- Liver cirrhosis
- Child–Pugh classification
- ECOG performance status (where available)

These variables were selected because they have been reported to influence prognosis and postoperative outcomes in patients with HCC [2–6].

Preoperative Clinical Assessment:

Preoperative laboratory investigations included:

- Alpha-fetoprotein (AFP)
- Alanine aminotransferase (ALT)
- Aspartate aminotransferase (AST)
- Total bilirubin
- Serum albumin
- Platelet count
- International normalized ratio (INR)
- Neutrophil-to-lymphocyte ratio (NLR)
- Platelet-to-lymphocyte ratio (PLR)

Radiological assessment was performed using contrast-enhanced computed tomography (CT) and/or magnetic resonance imaging (MRI). Tumor size, tumor number, anatomical location, and radiological evidence of vascular invasion were documented [2,3,6–10,12–15].

Operative and Histopathological Variables:

Operative variables included:

- Type of hepatectomy (major or minor)
- Surgical approach (open or laparoscopic, if applicable)
- Operative duration
- Estimated intraoperative blood loss
- Blood transfusion requirement
- Surgical margin width
- Length of postoperative hospital stay

Histopathological evaluation included:

- Maximum tumor diameter
- Tumor number
- Edmondson–Steiner differentiation grade
- Microvascular invasion
- Satellite nodules
- Liver cirrhosis

- Pathological TNM stage
- Confirmation of R0 resection

These pathological variables have previously been identified as important prognostic indicators of postoperative recurrence and survival following curative hepatectomy [6–10,14,15].

Follow-up and Outcome Assessment:

Patients underwent routine postoperative surveillance according to institutional clinical practice. Follow-up consisted of outpatient clinical assessment, liver function testing, serum AFP measurement, and contrast-enhanced CT or MRI performed at intervals determined by the treating hepatobiliary team, consistent with international recommendations for surveillance after curative treatment of HCC [2,3,16].

The primary study endpoint was early recurrence, defined as the first radiological and/or pathological evidence of recurrent hepatocellular carcinoma occurring within 24 months after curative hepatectomy [6–8].

Secondary outcomes included:

- Disease-free survival during the observation period
- Postoperative complications
- Readmission during follow-up
- Length of hospital stay
- Identification of clinicopathological variables associated with recurrence

Outcome Measures:

The principal outcome measure was the occurrence of early postoperative recurrence following curative hepatectomy. Predictor variables included demographic characteristics, underlying liver disease, laboratory biomarkers, radiological findings, operative variables, and histopathological characteristics. These variables were selected because of their established or suspected prognostic relevance in previous studies and their routine availability in clinical practice [6–10,12–15].

Statistical Analysis:

Statistical analysis was performed using **IBM SPSS Statistics Version 27.0** (IBM Corp., Armonk, NY, USA).

Continuous variables were assessed for normality using the **Shapiro–Wilk** test. Normally distributed data were expressed as **mean ± standard deviation (SD)** and compared using the **independent-samples t-test**. Non-normally distributed variables were presented as **median with interquartile range (IQR)** and compared using the **Mann–Whitney U test**.

Categorical variables were summarized as **frequencies and percentages**. Comparisons between groups were performed using the **Chi-square test** or **Fisher's exact test**, depending on expected cell frequencies.

Because this was an exploratory pilot study with a limited sample size, the statistical analysis was

primarily descriptive and comparative. Multivariable regression analysis was not performed because the available sample size was insufficient to provide reliable model estimates. All statistical tests were two-sided, and a **P value < 0.05** was considered statistically significant. Statistical reporting followed the recommendations of the STROBE Statement for observational studies [11].

Ethical Considerations:

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and institutional regulations governing retrospective clinical research [17]. Prior to commencement, ethical approval should be obtained from the Institutional Review Board or Ethics Committee of the First Affiliated Hospital of the University of South China.

As the investigation involved retrospective review of existing clinical records using anonymized patient information, the requirement for written informed consent may be waived by the ethics committee where permitted under institutional policy. Patient confidentiality was maintained throughout the study by removing all personally identifiable information before data analysis. Access to the study database was restricted to authorized investigators.

Limitations:

The retrospective nature of the study may introduce selection bias and information bias resulting from incomplete documentation [11]. As a single-center investigation, the findings may not be generalizable to other institutions or patient populations. The relatively small sample size limits statistical power and precludes robust multivariable analyses; therefore, the results should be interpreted as exploratory and hypothesis-generating. Nevertheless, this pilot study provides valuable institutional data and establishes a methodological framework for future larger prospective or multicenter studies evaluating predictors of early recurrence after curative hepatectomy for hepatocellular carcinoma [2,3,16].

DISCUSSION

Clinicopathological Factors and Their Impact on Early Recurrence:

Early recurrence following curative hepatectomy remains one of the greatest challenges in the management of hepatocellular carcinoma (HCC). Although surgical resection offers the possibility of long-term survival in carefully selected patients, recurrence within the first two years after surgery continues to occur frequently and is associated with unfavorable oncological outcomes [2–8]. The present pilot study was designed to explore clinicopathological characteristics that may contribute to early recurrence in patients undergoing curative hepatectomy at the First Affiliated Hospital of the University of South China.

The variables evaluated in this study—including demographic characteristics, underlying liver disease, serum biomarkers, tumor characteristics, operative variables, and pathological findings—represent factors routinely available during clinical practice. Identifying patients with unfavorable prognostic characteristics before or immediately after surgery may allow clinicians to individualize postoperative

surveillance and consider earlier intervention when recurrence is suspected [2,3,6–10].

Several previously reported prognostic factors, including elevated serum alpha-fetoprotein (AFP), larger tumor size, multiple tumors, poor histological differentiation, liver cirrhosis, and microvascular invasion, have been associated with increased recurrence risk in HCC [6–10,14,15]. These variables remain biologically plausible because they reflect greater tumor aggressiveness, impaired hepatic reserve, or increased potential for microscopic intrahepatic dissemination [6–10].

Surgical Outcomes and Postoperative Prognosis:

Curative (R0) hepatectomy remains the cornerstone of treatment for patients with resectable HCC and adequate liver function [2–5]. Advances in surgical techniques, perioperative anesthesia, intraoperative bleeding control, and postoperative management have substantially improved short-term surgical outcomes [2,3,5]. Nevertheless, successful surgery does not eliminate the risk of recurrence, particularly in patients with biologically aggressive disease [6–10].

In routine hepatobiliary practice, operative variables such as operative duration, intraoperative blood loss, transfusion requirements, and surgical margin status may influence postoperative recovery and long-term oncological outcomes [8–10,14,15]. Careful surgical planning combined with complete tumor resection and preservation of functional liver parenchyma remains essential for optimizing patient prognosis [2,3,5].

Postoperative Surveillance and Early Detection of Recurrence:

Regular postoperative surveillance plays a critical role in the long-term management of patients following curative hepatectomy [2,3,16]. Most institutional follow-up protocols include periodic clinical assessment, serum alpha-fetoprotein measurement, liver function testing, and contrast-enhanced CT or MRI [2,3,16]. Early identification of recurrent disease increases the likelihood that patients remain eligible for potentially curative treatments such as repeat hepatectomy, local ablation, transarterial therapies, or systemic treatment depending on recurrence pattern and liver function [2,3,5,16].

Patients considered at higher risk of recurrence may benefit from more intensive surveillance schedules during the first two postoperative years, when recurrence is most frequently observed [6–8,16].

Clinical Implications:

Although this investigation represents a pilot retrospective study, it emphasizes the importance of integrating routinely available clinical information into postoperative risk assessment. Demographic characteristics, laboratory biomarkers, imaging findings, operative variables, and pathological features collectively provide valuable information that may assist clinicians in identifying patients requiring closer postoperative monitoring [6–10,12–15].

The findings of this study may also contribute to the development of future institutional prediction models capable of supporting individualized postoperative management. Such models should ultimately be validated using larger multicenter cohorts before routine clinical implementation [2,3,16].

Strengths of the Study:

Several strengths should be acknowledged. First, the study utilized consecutive patients treated at a tertiary academic hepatobiliary center, reducing the likelihood of selection bias within the study period [11]. Second, comprehensive clinicopathological information was collected using standardized institutional records, allowing evaluation of multiple variables known to influence HCC prognosis [6–10]. Third, the study reflects real-world clinical practice and provides preliminary institutional evidence that may serve as the foundation for larger prospective investigations.

Study Limitations:

Several limitations should be considered when interpreting the findings. The retrospective design is inherently susceptible to information bias and limits the ability to establish causal relationships [11]. The study was conducted at a single tertiary referral center, which may reduce the generalizability of the findings to other institutions or patient populations.

The relatively small sample size limits statistical power and prevents robust multivariable modeling. Consequently, the findings should be regarded as exploratory and hypothesis-generating rather than definitive [11]. In addition, the duration of follow-up may not fully capture late recurrence occurring beyond the predefined observation period.

Future investigations should include larger multicenter cohorts with longer follow-up durations and standardized postoperative surveillance protocols [2,3,16]. Incorporating advanced imaging techniques, molecular biomarkers, radiomics, and machine learning-based prediction models may further improve the identification of patients at increased risk of recurrence [4,16].

Future Directions:

Future research should focus on prospective validation of clinicopathological predictors identified in pilot studies using larger patient populations across multiple hepatobiliary centers [2,3,16]. Combining conventional clinical variables with emerging biomarkers, genomic profiling, radiomic features, and artificial intelligence-assisted prediction models may substantially improve recurrence risk stratification [4,16].

The development of individualized postoperative surveillance strategies based on validated prediction models has the potential to improve early detection of recurrent disease, optimize allocation of healthcare resources, and ultimately enhance long-term survival among patients undergoing curative hepatectomy for hepatocellular carcinoma [2,3,16].

CONCLUSION

In conclusion, this pilot retrospective cohort study investigated clinicopathological factors associated with early recurrence following curative hepatectomy in patients with hepatocellular carcinoma treated at the First Affiliated Hospital of the University of South China. The study highlights the clinical importance of comprehensive preoperative evaluation, meticulous surgical management, and systematic postoperative

surveillance in patients undergoing curative liver resection [2,3,5,16].

The findings emphasize that routinely available demographic characteristics, underlying liver disease, laboratory biomarkers, radiological findings, operative variables, and histopathological features collectively contribute to postoperative risk assessment and may assist clinicians in identifying patients who require closer follow-up during the early postoperative period. Early recognition of patients at increased risk of recurrence may facilitate individualized surveillance strategies, timely diagnostic evaluation, and consideration of appropriate therapeutic interventions should recurrent disease develop [6–10,12–16].

Although the present investigation was limited by its retrospective design, single-center setting, and relatively small sample size, it provides valuable preliminary institutional evidence and demonstrates the feasibility of systematically evaluating clinicopathological predictors of recurrence within routine clinical practice. These findings should be interpreted as exploratory and hypothesis-generating rather than definitive [11].

Future studies involving larger multicenter cohorts, longer follow-up periods, and prospective study designs are warranted to validate these observations and establish robust prediction models for early recurrence after curative hepatectomy. Integration of conventional clinicopathological variables with emerging biomarkers, advanced imaging techniques, and artificial intelligence-assisted predictive approaches may further improve postoperative risk stratification and contribute to more personalized management of patients with hepatocellular carcinoma [4,16].

Overall, this study contributes to the growing body of evidence aimed at improving the long-term outcomes of patients undergoing curative hepatectomy and underscores the continued need for individualized postoperative surveillance and multidisciplinary management in hepatocellular carcinoma [2,3,16].

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